Supplemental Materials

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A. Research Methods

A1.1. Background

The design and implementation criteria for fair access are taken from the September 28, 2020 white paper, Cornerstones of "Fair" Drug Coverage: Appropriate Cost-Sharing and Utilization Management Policies for Pharmaceuticals. These criteria represent requirements that must be met in order for the prior authorization protocol to be appropriate, or, in other words, to ensure fair access. The criteria are based on analysis of prior policy and ethical research, and have undergone active deliberation and revision following a December 2019 ICER Policy Summit with representatives from patient groups, clinical specialty societies, private payers, and the life science industry.

A1.2. Objectives

The 2022 ICER Barriers to Fair Access Assessment assessed the concordance of drug coverage policies with fair access criteria for ICER-reviewed drugs in 2020. We evaluated coverage policies from the leading formularies of large payers in the United States, including the largest 15 commercial payers, the VHA, and the two largest state health exchange plans. In addition to core analyses of concordance with fair access criteria for cost sharing and the content of prior authorization policies, the 2022 report also evaluated concordance on a select set of drugs and formularies on criteria related to the relative burden of prior authorization and the transparency of cost sharing and clinical eligibility criteria to prospective plan enrollees.

A1.3. Research Questions

The overarching research question this project addressed is whether the prior authorization policies for drugs reviewed by ICER in 2020 meet the criteria for fair access. Within this broad research question, we performed analyses to assess the rate of concordance of prior authorization policies with the fair access criteria. Separate analyses were done to analyze rates of concordance by:

- Individual fair access criterion
- Drug
- Across payers in scope
- Individual payers

A2. Role of the Working Group

To help provide important guidance on this project, the Barriers to Fair Access Assessment benefited from ongoing input from a multi-stakeholder Working Group consisting of representatives from leading patient advocacy groups, clinical societies, private payers/ pharmacy benefit managers, and the life sciences industry. The Working Group advised ICER on the application of the fair access criteria to coverage policies; provided insight into the patient experience with prescription drug coverage and access, including real-world examples; and advised on important nuances in the interpretation of payer coverage policies. The Working Group members were:

- **Cat Davis Ahmed,** MBA, Vice President of Policy and Outreach, Familial Hypercholesterolemia Foundation
- **Alan Balch,** PhD, Chief Executive Officer, Patient Advocate Foundation
- **Patrick Gleason,** PharmD, Assistant Vice President of Health Outcomes, Prime Therapeutics
- **Leah Howard**, JD, Chief Operating Officer, National Psoriasis Foundation
- **Cliff Hudis,** MD, FACP, FASCO, Chief Executive Officer, American Society of Clinical Oncology
- **Anna Hyde,** Vice President of Advocacy and Access, Arthritis Foundation
- **Rebecca Kirch**, JD, Executive Vice President, National Patient Advocate Foundation
- **Sharon Phares, PhD,** Chief Scientific Officer, National Pharmaceutical Council
- **Carl Schmid,** Executive Director, HIV+Hepatitis Policy Institute
- **Saira Sultan,** President, Connect4Strategies (representing The Haystack Project)
- **Bari Talente,** Executive Vice President, Advocacy, National Multiple Sclerosis Society
- **Douglas White,** MD, PhD, Treasurer, American College of Rheumatology (through October 2022)

A3. List of Included Drugs

A3.1. Initial list of drugs

Drugs eligible for consideration were those reviewed by ICER in 2020 and that are currently FDA approved for an indication consistent with the ICER review (Table A3.1). The 2020 ICER review of remdesivir evaluated its use for in-patient treatment of COVID-19. Given that remdesivir for in-patient use is typically reimbursed as part of a bundled payment, and therefore coverage policies and cost sharing specific to remdesivir are unlikely, we have removed it from this review.

For these drugs we updated the ceiling price needed to meet the cost-effectiveness threshold to 2021 prices using the medical care component of the Consumer Price Index.

A3.2. Determining whether drugs are fairly priced

Whether the price for a drug is considered "fair" or "not fair" was determined according to whether the most recent net price of a drug fell at or below ICER's cost-effective price calculated in the relevant 2020 report at the $150,000 per evLYG or QALY threshold (whichever produced a higher price). Net drug prices were obtained from SSR Health, LLC, the health care division of SSR, LLC, an independent investment research firm. To derive a net price, SSR Health combines data on unit sales with publicly disclosed US sales figures. Discounts, rebates, concessions to wholesalers and distributors, and patient assistance programs are subtracted from gross sales to derive a net price.

To estimate the most recent average net price in the US market, we averaged net price data across the four most recently available quarters for which SSR data was available (January 1, 2021-December 31, 2021), to account for seasonal or other sources of annual price fluctuations. To confirm the validity of the SSR net prices, we compared them to the Wholesale Acquisition Cost (WAC) and the Federal Supply Schedule Service (FSS). In cases where we deemed the SSR net prices to be unreliable (such as the net prices being higher than the WAC), or where SSR prices were not available, we used price estimates from FSS. If no data were available in either SSR or FSS, we used list prices reported in Redbook. For physician administered drugs we used the same price data that was used in the report, which consisted of the WAC price plus a markup.

SSR reports net prices on a per unit basis. We converted the unit prices as listed in SSR to annual prices using the dosing assumptions used in the economic evaluation of our reports. For drugs with loading doses or dose-escalation regimens, we used the maintenance dose to calculate annual costs (i.e., second year costs) for consistency. Drugs that required weight-based dosing used the same weight assumptions as described in the economic evaluation section of our reports. The remainder of partially used vials were counted as medical waste. Pricing calculations and assumptions were

independently validated by another member of the research team and discrepancies were resolved via a consensus process.

A3.3. Final list

A final list of drugs was generated using the methodology described above. Information on the cost-effective drugs were abstracted according to the table shell below.

Table A3.1. Drug List

Brand Drug Name	Generic Drug Name	Indication	Route of Administration	ICER Health Benefit Price Benchmark[ɬ]	Annual Net Price Estimated Above or Below ICER HBPB *
Adakveo®	Crizanlizumab	Sickle Cell Disease	IV	$35,046	Above
Endari®	L-glutamine	Sickle Cell Disease	Oral	$19,568	Above
Entyvio®	Vedolizumab	Ulcerative Colitis	IV	$11,844[‡]	Above
Hemlibra®	Emicizumab	Hemophilia A	SC	Cost saving	Cost saving
Humira®	Adalimumab	Ulcerative Colitis	SC	$6,985[‡]	Above
Inflectra®	Infliximab-dyyb	Ulcerative Colitis	IV	$11,034[‡]	Below
Kalydeco®	Ivacaftor	Cystic Fibrosis	Oral	$74,303	Above
Nurtec ®	Rimegepant	Migraine: Acute	Oral	$4,697	Below
Orkambi®	Lumacaftor/Ivacaftor	Cystic Fibrosis	Oral	$61,750	Above
Oxbryta®	Voxelotor	Sickle Cell Disease	Oral	$23,668	Above
Remicade®	Infliximab	Ulcerative Colitis	IV	$11,034[‡]	Below
Renflexis®	Infliximab-abda	Ulcerative Colitis	IV	$11,034[‡]	Below
Reyvow®	Lasmiditan	Migraine: Acute	Oral	$3,189	Above
Simponi®	Golimumab	Ulcerative Colitis	SC	$7,693[‡]	Above
Stelara®	Ustekinumab	Ulcerative Colitis	SC	$16,804[‡]	Above
Symdeko®	Tezacaftor/Ivacaftor	Cystic Fibrosis	Oral	$70,760	Above
Trikafta®	Elexacaftor/Tezacaftor/Ivacaftor	Cystic Fibrosis	Oral	$86,552	Above
Ubrelvy™	Ubrogepant	Migraine: Acute	Oral	$4,687	Below
Xeljanz®	Tofacitinib	Ulcerative Colitis	Oral	$15,488	Above

HBPB: Health Benefit Price Benchmark

*Average prices net of all discounts and rebates, for the year of 2021, obtained from SSR Health. For prices not available or deemed unreliable, prices taken from Federal Supply Schedule (FSS).

ɬ ICER health benefit price benchmarks for the higher of the $150,000 per QALY or $150,000 per evLYG threshold, inflated to 2021 prices.

‡ Reflects HBPB from the biologic-naïve ulcerative colitis population

A4. List of Payers and Identification of Relevant Coverage Policies

We reviewed and abstracted data from the coverage policies of the leading formulary, by number of enrollees, of the 15 largest commercial payers in the US. We also reviewed the formulary of the VHA and the two largest state Health Exchange plan formularies as identified in the MMIT Analytics Market Access Database. The entity (payer or PBM) that controlled the coverage decision was assigned the covered life. We leveraged the MMIT Analytics Market Access Database to identify relevant prior authorization forms, documents, and formulary tiering information. As needed, we also supplemented this database with targeted outreach to payers to obtain additional information to clarify coverage policies. The final list of payer formularies is listed in Table A4.1.

Table A4.1. Payer Formularies In Scope

Payer	Formulary Name	Plan Type	Tiers Available	Individuals Covered*
CVS Health	CVS Caremark Standard Control w/ Advanced Specialty Control	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Generic or Non-Preferred Brand	12,350,549
Express Scripts	Express Scripts National Preferred with Advantage Plus	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Generic or Non-Preferred Brand	8,537,786
UnitedHealthcare	UnitedHealthcare Advantage Three Tier	Commercial	Tier 1: Lowest cost Tier 2: Mid-range cost Tier 3: Highest cost	6,685,150
Department of Veterans Affairs	VHA National Formulary	Federal	Not applicable	5,027,479
Cigna Corporation	Cigna Standard Three Tier	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Generic or Non-Preferred Brand	4,551,743
OptumRx	OptumRx Select Standard	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Generic or Non-Preferred Brand	4,286,829
Kaiser Foundation Health Plans, Inc.	Kaiser Permanente Southern California	Commercial	Tier 1: Generic Tier 2: Brand	2,524,502
Anthem	Anthem Essential Four Tier	Commercial	Tier 1: Preferred Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Generic or Non-Preferred Brand Tier 4: Specialty	2,395,491

Payer	Formulary Name	Plan Type	Tiers Available	Individuals Covered*
Blue Cross Blue Shield (BCBS) of Massachusetts	BCBS Massachusetts Three Tier	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Generic or Non-Preferred Brand	1,197,859
Health Care Service Corporation (HCSC)	BCBS of Illinois Basic 6 Tier	Commercial	Tier 1: Preferred Generic Tier 2: Non-Preferred Generic Tier 3: Preferred Brand Tier 4: Non-Preferred Brand Tier 5: Preferred Specialty Tier 6: Non-Preferred Specialty	1,090,416
Elixir PBM	Elixir Standard Formulary	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Brand	1,055,753
MedImpact Healthcare Systems, Inc	MedImpact Portfolio High Formulary	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Brand	1,022,156
Highmark, Inc.	Highmark Blue Cross Blue Shield 3 Tier	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Generic or Non-Preferred Brand	1,003,888
Blue Shield of California	Blue Shield of California Plus Formulary	Commercial	Tier 1: Preferred Generic or Low-Cost Preferred Brand Tier 2: Non-Preferred Generic or Preferred Brand Tier 3: Non- Preferred Brand Tier 4: Biologics or Specialty	981,773
Florida Blue	Florida Blue Care Choices HIX	State Exchange	Tier 1: Preventive Tier 2: Condition Care Generic Tier 3: Other Generic Tier 4: Condition Care Brand Tier 5: Preferred Brand Tier 6: Non-Preferred Brand Tier 7: Specialty	776,470
Premera Blue Cross	Premera Preferred 3-Tier-B3	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Brand	767,426
Kaiser Foundation Health Plans, Inc.	Kaiser Permanente California HIX	State Exchange	Tier 1: Generic Tier 2: Brand Tier 4: Specialty	598,827
Blue Cross Blue Shield of Michigan	BCBS Michigan Custom 3 Tier	Commercial	Tier 1: Generic Tier 2: Preferred Brand Tier 3: Non-Preferred Brand	508,856

*Covered lives as of 07/14/2022 according to MMIT

A5. Determination of Concordance of Coverage Policies with Fair Access Criteria

As with the 2021 report, the 2022 report evaluated formulary concordance with fair access criteria related to cost sharing, clinical eligibility, step therapy, and restrictions on prescriber qualifications. Additionally, this year's report included evaluation of the transparency and documentation burden related to prior authorizations. All of the criteria in these domains from the original 2020 white paper are shown in the Tables below. The criteria that were in scope for this review were those that we believed we can reliably judge through review of available coverage documents.

Table A5.1. Cost Sharing Fair Design Criteria

	Cost Sharing	
Fair Access Criteria	**2021 Review**	**In scope for this review?**
Patient cost sharing should be based on the net price to the plan sponsor, not the unnegotiated list price.	No	No
All medications identified by the Internal Revenue Service as high-value therapies should receive pre-deductible coverage within high deductible health plans.	No	No
At least one drug in every class should be covered at the *lowest relevant* cost-sharing level unless all drugs are priced higher than an established fair value threshold.	Yes	Yes
If all drugs in a class are priced so that there is not a single drug that represents a fair value as determined through value assessment, it is reasonable for payers to have all drugs on a higher cost-sharing level.	No	Yes
If all drugs in a class are priced so that they represent a fair value, it remains reasonable for payers to use preferential formulary placement with tiered cost sharing to help achieve lower overall costs.	Yes	Yes
As part of economic step therapy, when patients try a lower cost option with a lower cost sharing level but do not achieve an adequate clinical response, cost sharing for further therapies should also be at the lower cost-sharing level as long as those further therapies are priced fairly according to transparent criteria.	No	No

See Figure A5.1 for a visual representation of the cost sharing criteria algorithm.

Table A5.2. Clinical Eligibility Fair Design Criteria

Clinical Eligibility		
Fair Design Criteria	**2021 Review**	**In scope for this review?**
Payers should offer alternatives to prior authorization protocols such as programs that give feedback on prescribing patterns to clinicians or exempt them from prior authorization requirements ("gold carding") if they demonstrate high fidelity to evidence-based prescribing.	No	No
Payers should document at least once annually that clinical eligibility criteria are based on high quality, up-to date evidence, with input from clinicians with experience in the same or similar clinical specialty.	No	No
Clinical eligibility criteria should be developed with explicit mechanisms that require payer staff to document that they have: • Considered limitations of evidence due to systemic under-representation of minority populations; and • Sought input from clinical experts on whether there are distinctive benefits and harms of treatment that may arise for biological, cultural, or social reasons across different communities; and • Confirmed that clinical eligibility criteria have not gone beyond reasonable use of clinical trial inclusion/exclusion criteria to interpret or narrow the FDA label language in a way that disadvantages patients with underlying disabilities unrelated to the condition being treated.	No	No
For all drugs: Clinical eligibility criteria that complement the FDA label language may be used to: • Set standards for diagnosis; and/or • Define indeterminate clinical terms in the FDA label (e.g., "moderate-to-severe") with explicit reference to clinical guidelines or other standards; and/or • Triage patients by clinical acuity when the payer explicitly documents that triage is both reasonable and necessary because: ○ The size of the population included within the FDA label is extremely large, and there is a reasonable likelihood that many patients would seek treatment in the short term; AND ○ The clinical infrastructure is not adequate to treat all patients seeking care and/or broad coverage would create such substantial increases in short-term insurance premiums or other financial strain that patients would be harmed through loss of affordable insurance; AND ○ Acuity can be determined on objective clinical grounds and waiting for treatment will not cause significant irremediable harm.	Yes	Yes
For drugs with prices or price increases that have been deemed reasonable: Except for the three purposes outlined above, clinical eligibility criteria should not deviate from the FDA label language in a manner that would narrow coverage.	Yes	Yes
For drugs with prices or price increases that have been deemed reasonable: Documentation that patients meet clinical eligibility criteria should represent a light administrative burden, including acceptance of clinician attestation in lieu of more formal medical record documentation unless documentation is critical to ensure patient safety.	No	Yes
For drugs with prices or price increases that have been deemed unreasonable: Clinical eligibility criteria may narrow coverage by applying specific eligibility criteria from the pivotal trials used to generate evidence for FDA approval if implemented with reasonable flexibility and supported by robust appeals procedures as described in the implementation criteria.	No	Yes

FDA: U.S. Food and Drug Administration

Table A5.3. Step Therapy and Required Switching Fair Design Criteria

For the 2022 report we introduced a new element in our evaluation of the fair design of step therapy policies. The original 2020 white paper definition of the fair access criteria did not include a threshold for the number of steps, each appropriate in itself, that would cumulatively represent a failure to meet reasonable standards for fair access. After reviewing data from our 2021 evaluation, and examining clinical policy statements from other groups, we used a threshold of 3 steps, meaning that any step therapy policy requiring 4 or more steps will be judged to fail concordance with step therapy fair access criteria. In a recent analysis of step therapy protocols, the vast majority of payers required 1-3 steps and minority (3%) required more than 3.[*]

Step Therapy and Required Switching		
Fair Access Criteria	**2021 Review**	**In scope for this review?**
In order to justify economic step therapy policies extending beyond FDA labeling as appropriate, payers should explicitly affirm or present evidence to document all of the following: • Use of the first-step therapy reduces overall health care spending, not just drug spending	No	No
• The first-step therapy is clinically appropriate for all or nearly all patients and does not pose a greater risk of any significant side effect or harm. • Patients will have a reasonable chance to meet their clinical goals with first-step therapy. • Failure of the first-step drug and the resulting delay in beginning the second-step agent will not lead to long-term harm for patients. • Patients are not required to retry a first-line drug with which they have previously had adverse side effects or an inadequate response at a reasonable dose and duration.	Yes	Yes – new threshold of a maximum of 3 steps even if all include appropriate first-line therapies
In order to justify required switching policies as appropriate, payers should explicitly affirm or present evidence to document all of the following: • Use of the required drug reduces overall health care spending.	No	No
• The required switch therapy is based on the same mechanism of action or presents a comparable risk and side effect profile to the index therapy. • The required switch therapy has the same route of administration or the difference in route of administration will create no significant negative impact on patients due to clinical or socio-economic factors. • Patients are not required to switch to a drug that they have used before at a reasonable dose and duration with inadequate response and/or significant side effects, including earlier use under a different payer.	No	No

FDA: U.S. Food and Drug Administration

[*] Lenahan KL, Nichols DE, Gertler RM, Chambers JD. Variation in Use and Content of Prescription Drug Step Therapy Protocols, Within and Across Health Plans. *Health Affairs.* 2021; 40 (11): 1749-1757.

Table A5.4. Provider Qualifications Fair Design Criteria

Provider Qualifications		
Fair Access Criteria	**2021 Review**	**In scope for this review?**
Restrictions of coverage to specialty prescribers are reasonable with one or more of the following justifications: • Accurate diagnosis and prescription require specialist training, with the risk that non-specialist clinicians would prescribe the medication for patients who may suffer harm or be unlikely to benefit. • Determination of the risks and benefits of treatment for individual patients requires specialist training due to potential for serious side effects of therapy. • Dosing, monitoring for side effects, and overall care coordination require specialist training to ensure safe and effective use of the medication.	Yes	Yes
Requiring that non-specialist clinicians attest they are caring for the patient in consultation with a relevant specialist is a reasonable option when the condition is frequently treated in primary care settings but some elements of dosing, monitoring for side effects, and/or overall coordination of care would benefit from specialist input for many patients.	Yes	Yes

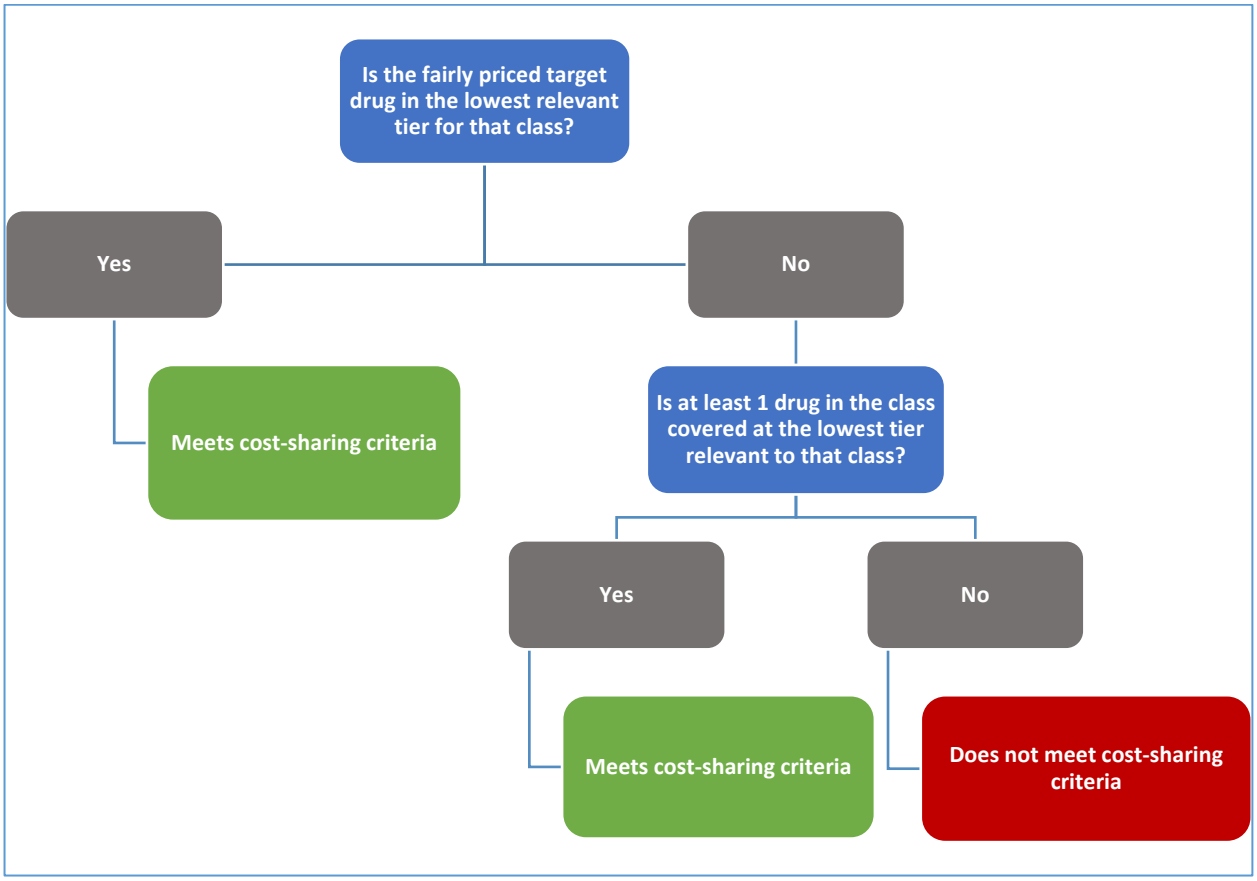
Table A5.5. Transparency Fair Design Criteria

Transparency	
Fair Access Criteria	**In scope for this review?**
Cost-sharing policies should be presented clearly to consumers prior to health plan selection, allowing all individuals to understand what cost sharing they will face for treatments they are currently taking or are considering. Any significant change to formulary or cost sharing structures should not occur mid-cycle unless plan sponsors include this as a qualifying event allowing plan enrollees to switch plans.	Yes
At the point of care, clinicians and patients should be able to rapidly determine the cost-sharing requirements for any treatment along with cost sharing for other alternatives.	No
Individuals considering health plan enrollment should be presented with clear information allowing them to understand whether they meet the insurers' clinical criteria for the treatments they are currently taking. The policies should also set out the rationale behind them and be readily understandable.	Yes
Clinicians and patients should be able to rapidly determine the clinical criteria for any treatment and view the clinical rationale supporting these criteria. The referenced clinical information should be readily available to the prescribing/ordering provider and the public.	No
Individuals considering health plan enrollment should be presented with clear information allowing them to understand whether the treatments they currently take or envision taking will be subject to step therapy or switching policies.	Yes
Clinicians, pharmacists, and patients should be able to rapidly determine the requirements related to step therapy and switching policies and be able to easily view a full justification from the insurer.	No
Individuals considering health plan enrollment should be able to easily find information related to coverage criteria, including prescriber qualifications, for drugs that they or family members are currently taking.	Yes
Clinicians and patients should be able to rapidly determine whether there is a restriction on prescribing for any treatment. Insurers should provide ready assistance to primary care clinicians seeking connection with a relevant specialist for consultation as needed.	No

Table A5.6. Documentation Burden Fair Design Criteria

Documentation Burden	
Fair Access Criteria	**In scope for this review?**
The administrative burden of documenting clinical eligibility should be streamlined and transparent to avoid creating a significant barrier to appropriate care.	Yes

Figure A5.1. Cost-Sharing Fairness Criteria Algorithm



A5.1. Process for Comparing Coverage Policies to Fair Access Criteria

Because the drugs included in our analysis could be covered under pharmacy benefits, medical benefits, or both, we had to decide how to report the findings in a way that conveys fair "apples to apples" comparisons across formularies. For drugs for which both a pharmacy benefit policy and a medical benefit policy were available for an individual payer, we selected the benefit plan type that was used by the greatest number of payers overall (i.e., the "predominant benefit plan type") to represent the prior authorization information for that payer. These results are featured in the main

assessment report. In the individual drug briefs provided below, we provide ratings of coverage through both pharmacy and medical benefits.

MMIT pulls data from a variety of sources known as the MMIT Network, a repository of open-source data including e-prescribing and similar point-of-care solutions, physician educational channels, long-term care and other pharmacies, pharmaceutical manufacturers, and most notably health plans and PBMs. When a policy is not referenced in the MMIT database, it is because MMIT has obtained this information either through a proprietary source, intelligence provided by their network of panelists, and/or other non-publishable digital data assets.

When the MMIT database indicated "No PA," "PA unspecified, "PA appropriate, "PA restrictive," "No Step Therapy" or "Step Therapy unspecified," we sought supporting documents to confirm these policies. If there were no supporting documents available to us, we rated the policy as "not available" for our determination. This approach was taken in order to minimize the risk of mischaracterization – either positive or negative – of payer policies. Payers were encouraged to submit documentation on these policies to inform our final rating.

For each drug, ICER research staff summarized results of the policy abstraction data in Tables A5.1-A5.5 into a policy brief, which included details of the FDA label (including clinical trial eligibility criteria), clinical guidelines, and policy recommendations from ICER reports to provide relevant context. Research staff made preliminary judgments regarding whether the coverage policy does or does not meet each fair design criterion, and then this judgment was reviewed by an internist on the ICER staff (SP). When the ICER clinician felt that clinical expert input was needed to determine whether a coverage policy met the fair design criterion, he discussed the question with an expert involved in the original ICER report on that drug.

B. Results

ICER's assessment of payer policies was conducted with a data cutoff of July 14, 2022 and, as such, subsequent changes to policies have not been incorporated into the primary results. After reviewing the draft version of this report, multiple payers informed ICER that they had changed their policies; these revisions and our judgment of their impact on concordance ratings are described in Table 18 in the main report.

B1. Policy Brief: Humira® (adalimumab), MAB TNF Blocking Agent (subcutaneous)

B1.1. Condition: Ulcerative colitis (UC), moderate-to-severe

Is Drug Cost-Effective at Current Price?: No

Other Drugs in Class: Simponi, Remicade, Renflexis, Inflectra, Xeljanz, Stelara, Entyvio

B1.2. Clinical Guidelines

2020 AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

2019 ACG Clinical Guideline: Ulcerative Colitis in Adults

B1.3. Background

FDA Label

Indication: Treatment of moderately to severely active ulcerative colitis in adults and pediatric patients 5 years of age and older.

Dosing:

Adults: 160 mg on Day 1 (given in one day or split over two consecutive days), 80 mg on Day 15 and 40 mg every other week starting on Day 29. Discontinue in patients without evidence of clinical remission by eight weeks (Day 57).

Pediatric Patients 5 Years of Age and Older: dosing dependent on weight

Warning: Black box warning for serious infections and malignancy, including TB and lymphoma.

Contraindications: None.

Interactions: Abatacept and anakinra (increased risk of serious infection); avoid use of live vaccines.

Clinical Trial Eligibility: The safety and efficacy of HUMIRA were assessed in adult patients with moderately to severely active ulcerative colitis (Mayo score 6 to 12 on a 12 point scale, with an endoscopy subscore of 2 to 3 on a scale of 0 to 3) despite concurrent or prior treatment with immunosuppressants such as corticosteroids, azathioprine, or 6-MP in two randomized, double-blind, placebo-controlled clinical studies (Studies UC-I and UC-II). Both studies enrolled TNF-blocker naïve patients, but Study UC-II also allowed entry of patients who lost response to or were intolerant to TNF blockers.

The safety and efficacy of HUMIRA were assessed in a multicenter, randomized, double-blind trial (Study PUC-I, NCT02065557) in 93 pediatric patients 5 years to 17 years of age with moderately to severely active ulcerative colitis (Mayo score 6 to 12 with endoscopy subscore of 2 to 3 points, confirmed by centrally read endoscopy) who had an inadequate response or intolerance to therapy with corticosteroids and/or an immunomodulator (i.e., azathioprine, 6 mercaptopurine, or methotrexate).

Link to label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125057s417lbl.pdf

ICER Policy Recommendations from the Ulcerative Colitis 2020 Review

Insurance coverage should be structured to prevent situations in which patients are forced to choose a treatment approach on the basis of cost.
Because there are no clear biomarkers or predictors of the success for any given treatment in UC, it is not unreasonable to consider prior authorization criteria in order to manage the costs of expensive medications and negotiate prices for TIMs priced beyond a fair range. However, prior authorization criteria should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers.
Patients eligible for TIMs include those with moderate-to-severe UC whose disease has had an inadequate response to conventional systemic therapy. Patient eligibility criteria should be flexible given that clinical trials used tools (e.g., Mayo Score for disease severity) that are not routinely used in clinical practice.
Given the lack of biomarkers and other predictors of TIM treatment success in UC, it is not unreasonable to use step therapy in this case to manage the costs of treatment.
TIM therapy should be prescribed and managed by gastroenterologists with specific training and expertise in UC.

Link to report: Targeted Immune Modulators for Ulcerative Colitis: Effectiveness and Value

B1.4. Findings: Coverage Policies

Policies for Humira were available for 12 payers (Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, BCBS MI, BCBS MA, Highmark, Elixir, VHA, Florida Blue HIX) under the pharmacy benefit and six payers (CVS, Kaiser, Anthem, Blue Shield CA, Premera, Kaiser HIX) under both the pharmacy and medical benefits.

Cost Sharing

Because Humira was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B1.1. Humira Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	2 (Preferred Brand)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	2 (Preferred Brand)	N/A	N/A	N/A
Cigna	2 (Preferred Brand)	N/A	N/A	N/A
Kaiser	2 (Brand)	N/A	N/A	N/A
Anthem	4 (Specialty)	N/A	N/A	N/A
HCSC	5 (Preferred Specialty)	N/A	N/A	N/A
MedImpact	2 (Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	4 (Biologics/Specialty)	N/A	N/A	N/A
BCBS MI	2 (Preferred Brand)	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	2 (Preferred Brand)	N/A	N/A	N/A
Highmark	2 (Preferred Brand)	N/A	N/A	N/A
Elixir	2 (Preferred Brand)	N/A	N/A	N/A
VHA	Not applicable	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Three Payers (Kaiser**,** Kaiser HIX**,** VHA) do not require clinical eligibility criteria. This meets our requirement, as it is not a restrictive policy.

The remaining payers require some version of the following: a diagnosis of moderately to severely active ulcerative colitis. This diagnosis is consistent with the FDA label and therefore meets our criteria for clinical eligibility.

Six payers (Express Scripts, Anthem, MedImpact, BCBS MI, Highmark, Florida Blue HIX) specify that patients must be five years of age or older to access Humira. This age requirement is consistent with the FDA label and therefore meets our criteria for clinical eligibility.

One payer (BCBS MA), requires a trial of 2 conventional agents from a list of steroids, 5-ASAs, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended in clinical guidelines.

Provider Qualifications

Eleven payers (Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, Premera, Highmark, Elixir, Florida Blue HIX**,** BCBS MA) require Humira to be prescribed by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

Step Therapy

Most payers require patients to step through one conventional systemic therapy or treatment with a prior biologic before accessing Humira. This meets our criteria for step therapy because the 2019 ACG Clinical Guidelines recommend oral systemic corticosteroids, TNF inhibitors (Humira, Simponi, or Remicade), Entyvio, or Xeljanz for induction of remission in moderately-to-severely active UC.

The following payer has additional step therapy requirements (in addition to the above):

- BCBS MA requires patients to step through two of the following three agents: 5-ASA, corticosteroids, immunosuppressants/immunomodulators, unless the diagnosis is severely active UC. 5-ASAs are not recommended for induction of remission in patients with severely active UC, but this meets our criteria for step therapy because patients with severe UC are exempt from the step therapy requirement.

Table B1.2. Humira Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS		One biologic OR one conventional therapy	
Pharmacy	0-1		Y
Medical	0-1		Y
Express Scripts		One biologic OR one conventional therapy	
Pharmacy	0-1		Y
United		One DMARD OR one conventional therapy	
Pharmacy	0-1		Y
OptumRx		One conventional therapy	
Pharmacy	0		Y
Cigna		One biologic OR one conventional therapy	
Pharmacy	0-1		Y
Kaiser		No step	
Pharmacy	0		Y
Medical	0		Y
Anthem		One conventional therapy	
Pharmacy	0		Y
Medical	0		Y
HCSC		One conventional therapy or one biologic*	
Pharmacy	0-1		Y
MedImpact		One conventional therapy	
Pharmacy	0		Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
Blue Shield CA Pharmacy Medical	 0-1 0	P: One corticosteroid or one immunomodulator M: No step	 Y Y
BCBS MI Pharmacy	 0	One conventional therapy	 Y
BCBS MA Pharmacy	 1	Two conventional therapies*	 Y
Premera Pharmacy Medical	0 0	One conventional therapy	 Y Y
Highmark Pharmacy	 0	No step	 Y
Elixir Pharmacy	 0	One conventional therapy	 Y
VHA Pharmacy	 0	No step	 Y
Florida Blue HIX Pharmacy	 0-1	One conventional therapy OR one biologic immunomodulator	 Y
Kaiser HIX Pharmacy Medical	 0 0	No step	 Y Y

M: medical, P: pharmacy, ST: step therapy, Y: yes

*Unless the patient has severely active UC

B1.5. Summary of Findings

Table B1.3. Humira Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Express Scripts				
Pharmacy	N/A	Y	Y	Y
United				
Pharmacy	N/A	Y	Y	Y
OptumRx				
Pharmacy	N/A	Y	Y	Y
Cigna				
Pharmacy	N/A	Y	Y	Y
Kaiser				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
HCSC				
Pharmacy	N/A	Y	Y	Y
MedImpact				
Pharmacy	N/A	Y	Y	Y
Blue Shield CA				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
BCBS MI				
Pharmacy	N/A	Y	Y	Y
BCBS MA				
Pharmacy	N/A	N	Y	Y
Premera				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Pharmacy	N/A	Y	Y	Y
Elixir				
Pharmacy	N/A	Y	Y	Y
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Pharmacy	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B2. Policy Brief: Adakveo (crizanlizumab), MAB Anti-P-Selectin (intravenous)

B2.1. Condition: sickle cell disease, adults and pediatric patients aged 16 years and older

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: None

B2.2. Clinical Guidelines

Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014

American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain

B2.3. Background

FDA Label

Indication: ADAKVEO is a selectin blocker indicated to reduce the frequency of vasoocclusive crises in adults and pediatric patients aged 16 years and older with sickle cell disease.

Dosing: Administer 5 mg/kg by intravenous infusion over a period of 30 minutes on Week 0, Week 2, and every 4 weeks thereafter.

Warning: Infusion-Related Reactions: Monitor for and advise patients of signs and symptoms. Discontinue ADAKVEO infusion for severe reactions and manage medically. Temporarily interrupt or slow the rate of infusion for mild or moderate infusion-related reactions and initiate symptomatic treatment. Exercise caution with corticosteroids in patients with sickle cell disease unless clinically indicated (e.g., treatment of anaphylaxis).

Interference With Automated Platelet Counts (platelet clumping): Run test as soon as possible or use citrate tubes.

Contraindications: None.

Interactions: None.

Clinical Trial Eligibility:

Key Inclusion Criteria:

- Sickle Cell Disease (HbSS, HbSC, HbSβ^0-thalassemia, or HbSβ^+-thalassemia)
- If receiving hydroxyurea or erythropoietin, treatment must have been prescribed for at least 6 months, with the dose stable for at least 3 months
- Between 2 and 10 sickle cell-related pain crises in the past 12 months

Key Exclusion Criteria:

- On a chronic transfusion program or planning on exchange transfusion during the study
- Hemoglobin <4.0 g/dL
- Planned initiation, termination, or dose alteration of hydroxyurea during the study
- Receiving chronic anticoagulation therapy (e.g. warfarin, heparin) other than aspirin

Link to label: https://www.novartis.us/sites/www.novartis.us/files/adakveo.pdf

***ICER Policy Recommendations from the 2020** Sickle Cell Disease Review*

Due to the COVID-19 pandemic, ICER's March 2020 public meeting on therapies for sickle cell disease was indefinitely postponed and no Key Recommendations were posted. Please refer to the sickle cell disease evidence report for the most updated findings.

Link to report: Adakveo, Oxbryta, and Endari for Sickle Cell Disease: Effectiveness and Value

B2.4. Findings: Coverage Policies

Policies for Adakveo were available for four payers (Express Scripts, OptumRx, VHA, MedImpact) under pharmacy benefits, seven payers (BCBS MI, Blue Shield CA, Cigna, Florida Blue HIX, HCSC, Highmark, United) under medical benefits, and six payers (Anthem, BCBS MA, CVS, Kaiser, Kaiser HIX, Premera) under both the pharmacy and medical benefits.

Adakveo is not covered under any benefit for one payer (Elixir).

One payer (Anthem) has Adakveo listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Cost Sharing

Because Adakveo was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B2.1. Adakveo Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	N/A	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	N/A	N/A	N/A	N/A
Kaiser	2 (Brand)	N/A	N/A	N/A
Anthem	Non-formulary	N/A	N/A	N/A
HCSC	N/A	N/A	N/A	N/A
MedImpact	Not Available	N/A	N/A	N/A
Blue Shield CA	N/A	N/A	N/A	N/A
BCBS MI	N/A	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	4 (Non-Preferred Brand)	N/A	N/A	N/A
Highmark	N/A	N/A	N/A	N/A
Elixir	N/A	N/A	N/A	N/A
VHA	N/A (no tiering)	N/A	N/A	N/A
Florida Blue HIX	N/A	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N/A	N/A	N/A

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Most payers with available clinical eligibility criteria require some version of the following: patients 16 and older with a diagnosis of sickle cell disease and at least two episodes of sickle cell related pain crises in the past 12 months. This meets our criteria for a unfairly priced drug because this requirement was part of the eligibility criteria for the pivotal trials.

One payer (Florida Blue HIX) includes a more specific definition of no concurrent use of Oxbryta. This meets our criteria because Oxbryta is an alternative disease-modifying agent and there is no clinical evidence indicating concurrent use would provide additional clinical benefit.

Three payers (BCBS MA, BCBS MI, Premera) include a more specific definition of not receiving regularly scheduled blood transfusion therapy. This meets our criteria for an unfairly priced drug because chronic transfusion therapy was an exclusion criterion for clinical trials.

Three Payers (Kaiser**,** Kaiser HIX**,** VHA) do not require clinical eligibility criteria. This meets our requirement, as it is not a restrictive policy.

One payer (Anthem) has Adakveo listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Provider Qualifications

Eight payers (BCBS MA, CVS, Kaiser, Kaiser HIX, VHA, Blue Shield CA, HCSC, Highmark) do not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Eight payers (BCBS MI, Cigna, Florida Blue HIX, Premera, United, Express Scripts, OptumRx, MedImpact) require prescribing by or in consultation with a specialist (hematologist). This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Anthem) has Adakveo listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Step Therapy

Ten payers (OptumRx, Express Scripts, United, Cigna, Blue Shield CA, BCBS MI, Premera, HCSC, Highmark, MedImpact) require current use/treatment failure/intolerance of hydroxyurea. This meets our criteria for step therapy because it is a recommended therapy in the National Heart, Lung, and Blood Institute's (NHLBI) 2014 guidelines for evidence-based management of sickle cell disease. The American Society of Hematology 2020 guidelines on management of sickle cell and acute and chronic pain suggest that there is a lack of comparative effectiveness data between hydroxyurea and other disease-modifying therapies and chronic transfusions to make a recommendation on the use of these agents in treatment of acute and chronic pain.

One payer (Anthem) has Adakveo listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Table B2. 2. Adakveo Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS			
Pharmacy	0	No Step	Y
Medical	0	No Step	Y
Express Scripts			
Pharmacy	1	Hydroxyurea	Y
United			
Medical	1	Hydroxyurea	Y
OptumRx			
Pharmacy	1	Hydroxyurea or Endari	Y
Cigna			
Medical	1	Hydroxyurea	Y
Kaiser			
Pharmacy	0	No Step	Y
Medical	0	No Step	Y
Anthem			
Pharmacy	N/A	Non-formulary	N/A
Medical	N/A	Non-formulary	N/A

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
HCSC			
Medical	1	Hydroxyurea	Y
MedImpact	0		
Pharmacy		No Step	Y
Blue Shield CA			
Medical	1	Hydroxyurea	Y
BCBS MI			
Medical	1	Hydroxyurea	Y
BCBS MA			
Pharmacy	0	No Step	Y
Medical	0	No Step	Y
Premera			
Pharmacy	1	Hydroxyurea	Y
Medical	1	Hydroxyurea	Y
Highmark			
Medical	0	No Step	Y
Elixir	N/A	N/A	N/A
VHA			
Pharmacy	0	No Step	Y
Florida Blue HIX			
Medical	0	No Step	Y
Kaiser HIX			
Pharmacy	0	No Step	Y
Medical	0	No Step	Y

M: medical, N/A: not applicable, P: pharmacy, ST: step therapy, Y: yes

B2.5. Summary of Findings

Table B2.3. Adakveo Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Medical	N/A	Y	Y	Y
Pharmacy	N/A	Y	Y	Y
Express Scripts				
Pharmacy	N/A	Y	Y	Y
United				
Medical	N/A	Y	Y	Y
OptumRx				
Pharmacy	N/A	Y	Y	Y
Cigna				
Medical	N/A	Y	Y	Y
Kaiser				
Medical	N/A	Y	Y	Y
Pharmacy	N/A	Y	Y	Y
Anthem				
Medical	N/A	N/A	N/A	N/A
Pharmacy	N/A	N/A	N/A	N/A
HCSC				
Medical	N/A	Y	Y	Y
MedImpact				
Pharmacy	N/A	Y	Y	Y
Blue Shield CA				
Medical	N/A	Y	Y	Y
BCBS MI				
Medical	N/A	Y	Y	Y
BCBS MA				
Medical	N/A	Y	Y	Y
Pharmacy	N/A	Y	Y	Y
Premera				
Medical	N/A	Y	Y	Y
Pharmacy	N/A	Y	Y	Y
Highmark				
Medical	N/A	Y	Y	Y
Elixir	N/A	N/A	N/A	N/A
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Medical	N/A	Y	Y	Y
Kaiser HIX				
Medical	N/A	Y	Y	Y
Pharmacy	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B3. Policy Brief: Trikafta (elexacaftor/tezacaftor/ivacaftor), CFTR Modulator (oral)

B3.1. Condition: Cystic Fibrosis

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: Symdeko, Kalydeco, Orkambi

B3.2. Clinical Guidelines

Cystic fibrosis: Treatment with CFTR modulators, UpToDate 2021

Cystic Fibrosis Foundation Pulmonary Guidelines 2018

B3.3. Background

FDA Label

Indication: for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data.

Dosing:

6 to less than 12 years weighing less than 30 kgs: Morning: Two tablets, each containing elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg. Evening: One tablet of ivacaftor 75 mg

6 to less than 12 years weighing 30 kgs or more: Morning: Two tablets, each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg. Evening: One tablet of ivacaftor 150 mg

12 years and older: Morning: Two tablets, each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg. Evening: One tablet of ivacaftor 150 mg

Warning: Elevated transaminases and hepatic injury: Liver failure leading to transplantation has been reported in a patient with cirrhosis and portal hypertension while receiving TRIKAFTA; Use with CYP3A inducers significantly decrease ivacaftor exposure and are expected to decrease elexacaftor and tezacaftor exposure, which may reduce TRIKAFTA efficacy; Cataracts: Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with ivacaftor-containing regimens.

Contraindications: None

Interactions: Strong CYP3A inducers: Avoid co-administration. Strong or moderate CYP3A inhibitors: Reduce TRIKAFTA dosage when co-administered. Avoid food or drink containing grapefruit.

Clinical Trial Eligibility:

Trial 1 enrolled patients ages 12 and older with at least one F508del mutation and a mutation on the second allele resulting in no CFTR protein or a CFTR protein that is not responsive to ivacaftor and tezacaftor/ivacaftor.

Trial 2 enrolled patients ages 12 and older, who were homozygous for the F508del mutation.

Patients in both trials had a ppFEV1 between 40-90%. Participants were excluded if they had an abnormal liver function test at screening (ALT, AST, ALP, or GGT ≥3 x ULN, or total bilirubin ≥2 x ULN).

Link to label: https://pi.vrtx.com/files/uspi_elexacaftor_tezacaftor_ivacaftor.pdf

ICER Policy Recommendations from the 2020 Cystic Fibrosis Report

The manufacturer should lower the price of Trikafta to align fairly with its demonstrated benefits.
Prior authorization criteria for Trikafta should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups.

https://icer.org/wp-content/uploads/2020/08/ICER_CF_Policy_Recs_092320.pdf

B3.4. Findings: Coverage Policies

Policies or coverage information for Trikafta were available for all 18 payers under the pharmacy benefit.

Cost Sharing

Because Trikafta was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B3.1. Trikafta Cost Sharing by Payer

Payer*	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	3 (Non-Preferred Brand)	N/A	N/A	N/A
Kaiser	2 (Brand)	N/A	N/A	N/A
Anthem	4 (Specialty)	N/A	N/A	N/A
HCSC	5 (Preferred Specialty)	N/A	N/A	N/A
MedImpact	2 (Preferred Brand)	N/A	N/A	N/A

Payer*	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
Blue Shield CA	4 (Specialty)	N/A	N/A	N/A
BCBS MI	2 (Preferred Brand)	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	2 (Preferred Brand)	N/A	N/A	N/A
Highmark	3 (Non-preferred Brand)	N/A	N/A	N/A
Elixir	2 (Preferred Brand)	N/A	N/A	N/A
VHA	N/A (no tiering)	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N/A	N/A	N/A

* All payers covered under pharmacy benefit only

N/A: not applicable

Clinical Eligibility

Three payers (Kaiser, Kaiser HIX**,** VHA) do not have a clinical eligibility requirement. This meets our clinical eligibility criteria.

Fifteen payers (CVS, Express Scripts, United, OptumRx, Cigna, Anthem, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, Elixir, Florida Blue HIX) require some version of the following: A diagnosis of cystic fibrosis in an individual six years of age or older with documentation of at least one *F508del* mutation in the CFTR gene or one mutation of the CFTR gene that is responsive to Trikafta. This meets our clinical eligibility criteria.

The following eight payers (CVS, Anthem, HCSC, Blue Shield CA, BCBS MI, BCBS MA, Elixir, Florida Blue HIX) include a more specific definition requiring that patients not use Trikafta in combination with other ivacaftor-containing medications. One payer (Anthem) does not approve individuals with severe hepatic impairment (Child-Pugh Class C). One payer (Premera) requires patients to have a liver function test below three times the upper limit of normal. These requirements meet our criteria because they are consistent with the label's indication for Trikafta in treating cystic fibrosis.

Two payers (Blue Shield CA, Highmark) limit eligibility to 12 years of age or older. This requirement meets our criteria for an unfairly priced drug because it is consistent with the enrollment age criteria of the clinical trials of Trikafta in treating cystic fibrosis.

Provider Qualifications

Eleven payers (CVS, Kaiser, Anthem, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, VHA, Florida Blue HIX, Kaiser HIX) do not have specialist prescribing or consultation. This meets our criteria for provider qualifications.

Seven payers (Express Scripts, OptumRx, United, Cigna, HCSC**,** MedImpact**,** Elixir) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

Step Therapy

Step therapy is not required by any payer. This meets our criteria for step therapy because it is in line with the FDA label.

Table B3.2. Trikafta Step Therapy by Payer

Payer*	Steps	Details	Meets ST Criteria? Y/N
CVS	0	No step	Y
Express Scripts	0	No step	Y
United	0	No step	Y
OptumRx	0	No step	Y
Cigna	0	No step	Y
Kaiser	0	No step	Y
Anthem	0	No step	Y
HCSC	0	No step	Y
MedImpact	0	No step	Y
Blue Shield CA	0	No step	Y
BCBS MI	0	No step	Y
BCBS MA	0	No step	Y
Premera	0	No step	Y
Highmark	0	No step	Y
Elixir	0	No step	Y
VHA	0	No step	Y
Florida Blue HIX	0	No step	Y
Kaiser HIX	0	No step	Y

N: no, N/A: not applicable, ST: step therapy, Y: yes

* All payers covered under pharmacy benefit only

B3.5. Summary of Findings

Table B3.3. Trikafta Fair Access Criteria by Payer

Payer*	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS	N/A	Y	Y	Y
Express Scripts	N/A	Y	Y	Y
United	N/A	Y	Y	Y
OptumRx	N/A	Y	Y	Y
Cigna	N/A	Y	Y	Y
Kaiser	N/A	Y	Y	Y
Anthem	N/A	Y	Y	Y
HCSC	N/A	Y	Y	Y
MedImpact	N/A	Y	Y	Y
Blue Shield CA	N/A	Y	Y	Y
BCBS MI	N/A	Y	Y	Y
BCBS MA	N/A	Y	Y	Y
Premera	N/A	Y	Y	Y
Highmark	N/A	Y	Y	Y
Elixir	N/A	Y	Y	Y
VHA	N/A	Y	Y	Y
Florida Blue HIX	N/A	Y	Y	Y
Kaiser HIX	N/A	Y	Y	Y

* All payers covered under pharmacy benefit only

N: no, N/A: not applicable, Y: yes

B4. Policy Brief: Hemlibra (emicizumab), factor IXa- and factor X-directed antibody (subcutaneous)

B4.1. Condition: Hemophilia A, adult and pediatric patients newborn and older

Is Drug Cost-Effective at Current Prices?: Yes

Other Drugs in Class: None

B4.2. Clinical Guidelines

MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders

Recommendation on the Use and Management of Emicizumab-kxwh (Hemlibra) for Hemophilia A with and without Inhibitors

World Federation of Hemophilia Guidelines for the Management of Hemophilia

B4.3. Background

FDA Label

Indication: HEMLIBRA is a bispecific factor Ixa- and factor X-directed antibody indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

Dosing: Recommended loading dose is 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by a maintenance dose of: 1.5 mg/kg once every week, or 3 mg/kg once every two weeks, or 6 mg/kg once every four weeks.

Warning: Immunogenicity: Anti-emicizumab antibodies (including neutralizing antibodies) have developed in HEMLIBRA-treated patients. In case of clinical signs of loss of efficacy, promptly assess the etiology and consider a change in treatment if neutralizing antibodies are suspected. Laboratory Coagulation Test Interference: HEMLIBRA interferes with activated clotting time (ACT), activated partial thromboplastin time (aPTT), and coagulation laboratory tests based on aPTT, including onestage aPTT-based single-factor assays, aPTT-based Activated Protein C Resistance (APC-R), and Bethesda assays (clotting-based) for factor VIII (FVIII) inhibitor titers. Intrinsic pathway clotting-based laboratory tests should not be used.

Contraindications: None

Interactions: Anti-inhibitor Coagulant Complex (Human): Emicizumab may enhance the thrombogenic effect of Anti-inhibitor Coagulant Complex (Human). Risk C: Monitor therapy Efgartigimod Alfa: May diminish the therapeutic effect of Fc Receptor-Binding Agents. Risk C: Monitor therapy

Clinical Trial Eligibility: The HAVEN 3 study (NCT02847637) was a randomized, multicenter, open-label, clinical trial in 152 adult and adolescent males (aged ≥ 12 years and ≥ 40 kg) with hemophilia A without FVIII inhibitors who previously received either episodic (on demand) or prophylactic treatment with FVIII. The HAVEN 4 study (NCT03020160) was a single-arm, multicenter, open-label, clinical trial in 41 adult and adolescent males (aged ≥ 12 years and ≥ 40 kg) with hemophilia A with or without FVIII inhibitors who previously received either episodic (on demand) or prophylactic treatment with FVIII or bypassing agents. The HAVEN 1 study (NCT02622321) was a randomized, multicenter, open-label, clinical trial in 109 adult and adolescent males (aged ≥ 12 years and ≥ 40 kg) with hemophilia A with FVIII inhibitors who previously received either episodic (on-demand) or prophylactic treatment with bypassing agents. The HAVEN 2 study (NCT02795767) was a single-arm, multicenter, open-label, clinical trial in pediatric males (age < 12 years, or 12 – 17 years who weigh < 40 kg) with hemophilia A with FVIII inhibitors.

Link to label: https://www.gene.com/download/pdf/hemlibra_prescribing.pdf

***ICER Policy Recommendations from the* 2020 Hemophilia A Review**

Manufacturers and researchers should study the effects of Hemlibra on the development of inhibitors in infancy and early childhood.
Considering the evidence of equivalent to improved comparative effectiveness, relative convenience, and lower overall cost, Hemlibra will be the preferred agent for prophylaxis for many patients. Payers should ensure appropriate access to Hemlibra and may wish to share information with clinicians and patients regarding its potential advantages over factor VIII prophylaxis.
Prior authorization criteria should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers. Options for specific elements of coverage criteria within insurance coverage policy are discussed below.

Link to report: Valoctocogene Roxaparvovec and Emicizumab for Hemophilia A without Inhibitors: Effectiveness and Value

B4.4. Findings: Coverage Policies

Policies for Hemlibra were available for eight payers (Express Scripts, HCSC, MedImpact, BCBS MI, Elixir, VHA, Florida Blue HIX) under pharmacy benefits, two payers (Blue Shield CA, BCBS MA) under medical benefits, and eight payers (CVS, United, Cigna, Kaiser, Anthem, Premera, Highmark, Kaiser HIX) under both the pharmacy and medical benefits.

One payer (OptumRx) has open access for Hemlibra and does not require prior authorization.

Cost Sharing

Nine payers have Hemlibra placed on the lowest relevant tier: Express Scripts, United, Kaiser, BCBS MI, Highmark, Elixir, Kaiser HIX have Hemlibra placed on Brand/Preferred Brand and HCSC has Hemlibra placed on Preferred Specialty. This meets our cost-sharing criteria.

The following six payers do not have Hemlibra placed on the lowest relevant tier when a lower tier is available: CVS, OptumRx, Cigna, MedImpact, Premera, Florida Blue HIX. This does not meet our cost-sharing criteria because a preferred tier is available and Hemlibra is the only drug in its class.

Hemlibra is non-formulary for Anthem. This does not meet our cost-sharing criteria because a preferred tier is available and Hemlibra is the only drug in its class.

Table B4.1. Hemlibra Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N	2 (Preferred Brand), none	N
Express Scripts	2 (Preferred Brand)	Y	N/A	Y
United	2 (Preferred Brand)	Y	N/A	Y
OptumRx	3 (Non-Preferred Brand)	N	2 (Preferred Brand), none	N
Cigna	3 (Non-Preferred Brand)	N	2 (Preferred Brand), none	N
Kaiser	2 (Brand)	Y	N/A	Y
Anthem	Non-Formulary	N	2 (Preferred Brand), none	N
HCSC	5 (Preferred Specialty)	Y	N/A	Y
MedImpact	3 (Non-Preferred Brand)	N	2 (Preferred Brand), none	N
Blue Shield CA	N/A (covered under Medical)	N/A	N/A	N/A
BCBS MI	2 (Preferred Brand)	Y	N/A	Y
BCBS MA	N/A (covered under Medical)	N/A	N/A	N/A
Premera	3 (Non-Preferred Brand)	N	2 (Preferred Brand), none	N
Highmark	2 (Preferred Brand)	Y	N/A	Y
Elixir	2 (Preferred Brand)	Y	N/A	Y
VHA	N/A (no tiering)	Y	N/A	Y
Florida Blue HIX	7 (Specialty)	N	5 (Preferred Brand), none	N
Kaiser HIX	2 (Brand)	Y	N/A	Y

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three payers (Kaiser, Kaiser HIX**,** VHA) do not have a clinical eligibility requirement. This meets our clinical eligibility criteria.

All other payers require some version of the following: patients with hemophilia A using Hemlibra for routine prophylaxis to prevent or reduce the frequency of bleeding episodes. This meets our criteria because it is consistent with the FDA label's criteria, which indicates that Hemlibra is approved for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric

patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

One payer (Cigna) requires patients with mild or moderate hemophilia A to have prior bleeding episodes or evidence of prior joint damage from bleeding. This does not meet our criteria as neither the FDA label nor the clinical guidelines include these restrictions.

One payer (MedImpact) requires those with mild or moderate hemophilia A to have a history of two or more bleeds per year. This does not meet our criteria as neither the FDA label nor the clinical guidelines include these restrictions.

One payer (Elixir) requires documentation of at least two spontaneous bleeding events into the joints. This does not meet our criteria as neither the FDA label nor the clinical guidelines include these restrictions.

One payer (Florida Blue HIX) requires a prior history of bleeding into joints, soft tissue, and/or the central nervous system. This does not meet our criteria as neither the FDA label nor the clinical guidelines include these restrictions.

One payer (Anthem) has Hemlibra listed as non-formulary and was not evaluated on clinical eligibility criteria.

Provider Qualifications

Eleven payers (CVS, Express Scripts, United, OptumRx, Kaiser, Blue Shield CA, BCBS MA, Premera, Highmark, VHA, Kaiser HIX) do not require specialist prescribing or consultation. This meets our criteria.

Six payers (Cigna, HCSC, MedImpact, BCBS MI, Elixir, Florida Blue HIX) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Anthem) has Hemlibra listed as non-formulary and was not evaluated on provider qualifications criteria.

Step Therapy

Fourteen payers (Express Scripts, OptumRx, Cigna, Kaiser, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, Elixir, VHA, Kaiser HIX) do not require step therapy. This meets our criteria for step therapy.

Two payers (United, Florida Blue HIX) require use of at least one prophylactic recombinant Factor VIII replacement product. Florida Blue HIX required this regardless of severity and United required this

only in patients with mild hemophilia. This does not meet our criteria for step therapy because the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF) guidelines do not require Factor VIII prior to initiating Hemlibra.

One payer (CVS) requires prior use and failure of desmopressin in patients with mild hemophilia. This meets our criteria for step therapy.

One payer (Anthem) has Hemlibra listed as non-formulary and was not evaluated on step therapy criteria.

Table B4.2. Hemlibra Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS			
Pharmacy	1	Desmopressin	Y
Medical	1		Y
Express Scripts			
Pharmacy	0	No step	Y
United			
Pharmacy	1	Use of at least one prophylactic recombinant Factor	N
Medical	1	VIII replacement product for mild hemophilia	N
OptumRx			
Pharmacy	0	No step	Y
Cigna			
Pharmacy	0	No step	Y
Medical	0		Y
Kaiser			
Pharmacy	0	No step	Y
Medical	0		Y
Anthem			
Pharmacy	N/A	Non-formulary	N/A
Medical	N/A	Non-formulary	N/A
HCSC			
Pharmacy	0	No step	Y
MedImpact			
Pharmacy	0	No step	Y
Blue Shield CA			
Medical	0	No step	Y
BCBS MI			
Pharmacy	0	No step	Y
BCBS MA			
Medical	0	No step	Y
Premera			
Pharmacy	0	No step	Y
Medical	0		Y
Highmark			
Pharmacy	0	No step	Y
Medical	0		Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
Elixir			
Pharmacy	0	No step	Y
VHA			
Pharmacy	0	No step	Y
Florida Blue HIX		Use of at least one prophylactic recombinant Factor	
Pharmacy	1	VIII replacement product	N
Kaiser HIX			
Pharmacy	0	No step	Y
Medical	0		Y

ST: step therapy, Y: yes, N: no

B4.5. Summary of Findings

Table B4.3. Hemlibra Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Pharmacy	N	Y	Y	Y
Medical	N/A	Y	Y	Y
Express Scripts				
Pharmacy	Y	Y	Y	Y
United				
Pharmacy	Y	Y	N	Y
Medical	N/A	Y	N	Y
OptumRx				
Pharmacy	N	Y	Y	Y
Cigna				
Pharmacy	N	N	Y	Y
Medical	N/A	N	Y	Y
Kaiser				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N	N/A	N/A	N/A
Medical	N/A	N/A	N/A	N/A
HCSC				
Pharmacy	Y	Y	Y	Y
MedImpact				
Pharmacy	N	N	Y	Y
Blue Shield CA				
Medical	N/A	Y	Y	Y
BCBS MI				
Pharmacy	Y	N	Y	Y
BCBS MA				
Medical	N/A	Y	Y	Y
Premera				
Pharmacy	N	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Elixir				
Pharmacy	Y	N	Y	Y
VHA				
Pharmacy	Y	Y	Y	Y
Florida Blue HIX				
Pharmacy	N	N	N	Y
Kaiser HIX				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B5. Policy Brief: Simponi (golimumab), MAB TNF Blocking Agent (subcutaneous)

B5.1. Condition: Ulcerative colitis (UC), moderate-to-severe

Is Drug Cost-Effective at Current Price?: No

Other Drugs in Class: Humira, Remicade, Renflexis, Inflectra, Xeljanz, Stelara, Entyvio

B5.2. Clinical Guidelines

2020 AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

2019 ACG Clinical Guideline: Ulcerative Colitis in Adults

B5.3. Background

FDA Label

Indication: SIMPONI is a tumor necrosis factor (TNF) blocker indicated for the treatment of adult patients with moderate to severe ulcerative colitis (UC) with an inadequate response or intolerant to prior treatment or requiring continuous steroid therapy

Dosing: 200 mg initially administered by subcutaneous injection at Week 0, followed by 100 mg at Week 2 and then 100 mg every 4 weeks

Warning: Black box warning for serious infections and malignancy, including TB and lymphoma.

Contraindications: None.

Interactions: Abatacept and anakinra (increased risk of serious infection); avoid use of live vaccines/therapeutic infectious agents.

Clinical Trial Eligibility: The safety and efficacy of SIMPONI were evaluated in 2 multicenter, randomized, double-blind, placebo-controlled clinical trials in patients ≥ 18 years of age (Trials UC-1 and UC-2). Trial UC-1 was an induction trial conducted in patients with moderately to severely active ulcerative colitis (UC), defined as a Mayo score of 6 to 12. At baseline, subjects also had an endoscopy subscore of 2 or 3 on a 3-point scale. Patients were corticosteroid dependent or had an inadequate response to or had failed to tolerate at least one of the following therapies: oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine.

Link to label: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/SIMPONI-pi.pdf

ICER Policy Recommendations from the 2020 Review of Treatments for Ulcerative Colitis

Insurance coverage should be structured to prevent situations in which patients are forced to choose a treatment approach on the basis of cost.
Because there are no clear biomarkers or predictors of the success for any given treatment in UC, it is not unreasonable to consider prior authorization criteria in order to manage the costs of expensive medications and negotiate prices for TIMs priced beyond a fair range. However, prior authorization criteria should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers.
Patients eligible for TIMs include those with moderate-to-severe UC whose disease has had an inadequate response to conventional systemic therapy. Patient eligibility criteria should be flexible given that clinical trials used tools (e.g., Mayo Score for disease severity) that are not routinely used in clinical practice.
Given the lack of biomarkers and other predictors of TIM treatment success in UC, it is not unreasonable to use step therapy in this case to manage the costs of treatment.
TIM therapy should be prescribed and managed by gastroenterologists with specific training and expertise in UC.

Link to report: Targeted Immune Modulators for Ulcerative Colitis: Effectiveness and Value

B5.4. Findings: Coverage Policies

Policies for Simponi were available for 10 payers (Express Scripts**,** Elixir**,** OptumRx, Cigna, HCSC, MedImpact, BCBS MI, BCBS MA, VHA, Florida Blue HIX) under pharmacy benefits, two payers (CVS and Kaiser HIX) under medical benefits, and six payers (United, Kaiser, Anthem, Blue Shield CA, Premera, and Highmark) under both the pharmacy and medical benefits.

Cost Sharing

Because Simponi was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B5.1. Simponi Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	N/A	N/A	N/A	N/A
Express Scripts	3 (Non-Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	2 (Preferred Brand)	N/A	N/A	N/A
Cigna	3 (Non-Preferred Brand)	N/A	N/A	N/A
Kaiser	N/A (no tiering)	N/A	N/A	N/A
Anthem	4 (Specialty)	N/A	N/A	N/A
HCSC	6 (Non-Preferred Specialty)	N/A	N/A	N/A
MedImpact	3 (Non-Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	4 (Biologics or Specialty)	N/A	N/A	N/A
BCBS MI	3 (Non-Preferred Brand)	N/A	N/A	N/A
BCBS MA	3 (Non-Preferred Brand)	N/A	N/A	N/A
Premera	3 (Non-Preferred Brand)	N/A	N/A	N/A
Highmark	3 (Non-Preferred Brand)	N/A	N/A	N/A
Elixir	2 (Preferred Brand)	N/A	N/A	N/A
VHA	Not applicable	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	N/A (no tiering)	N/A	N/A	N/A

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three Payers (Kaiser**,** Kaiser HIX**,** VHA) do not require clinical eligibility criteria. This meets our requirement, as it is not a restrictive policy.

Eleven payers (CVS, United, OptumRx, Cigna, Anthem, HCSC, Blue Shield CA, BCBS MA, Highmark, Florida Blue HIX**,** MedImpact) require a diagnosis of some version of moderately to severely active ulcerative colitis. Three payers (Elixir**,** BCBS MI, Premera) require a diagnosis of ulcerative colitis. These requirements meet our criteria for clinical eligibility because the FDA label specifies that Simponi is indicated for moderate-to-severe ulcerative colitis.

Five payers (Anthem, BCBS MI, Highmark, Florida Blue HIX**,** MedImpact) also specify that patients must be age 18 years or older to access Simponi. This meets our criteria for clinical eligibility because this age restriction is consistent with the FDA label.

One payer (BCBS MA), requires a trial of 2 conventional agents from a list of steroids, 5-ASAs, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended in clinical guidelines.

Provider Qualifications

Seven payers (Anthem, Blue Shield CA, Kaiser, Kaiser HIX, BCBS MA, Express Scripts, VHA) did not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Ten payers (Elixir, MedImpact, United, OptumRx, Cigna, HCSC, BCBS MA, Premera, Highmark, Florida Blue HIX) require prescribing by or in consultation with a gastroenterologist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

Step Therapy

Seven payers (Premera, Cigna, Elixir, MedImpact, BCBS MI, United, HCSC) require step therapy with one conventional systemic therapy (such as corticosteroids, 5-ASA, azathioprine, or 6-mercaptopurine) and/or preferred biologic(s). This meets our criteria for step therapy because the FDA label states that Simponi is indicated for patients "with an inadequate response or intolerant to prior treatment or requiring continuous steroid therapy." In addition, the 2019 ACG Clinical Guidelines recommend oral systemic corticosteroids, TNF inhibitors (Humira, Simponi, or Remicade), Entyvio, or Xeljanz for induction of remission in moderately-to-severely active UC.

One payer (BCBS MA) requires patients to step through two of the following three agents: 5-ASA, corticosteroids, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended for induction of remission in patients with severely active UC.

One payer (BCBS MI) requires patients to step through two conventional therapies (e.g., 5-ASA, corticosteroids, thiopurines), Humira, Stelara, Xeljanz, and Rinvoq. This does not meet our criteria because it exceeds the max

imum number of steps allowable.

Table B5.2. Simponi Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS Medical	 0-1	One conventional therapy OR one biologic	 Y
Express Scripts Pharmacy	 1	Humira	 Y
United Pharmacy Medical	 0-1 0	P: One conventional therapy OR one DMARD M: No step	 Y Y
OptumRx Pharmacy	 0	One conventional therapy	 Y
Cigna Pharmacy	 1	One conventional therapy AND Humira	 Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
Kaiser		No step	
Pharmacy	0		Y
Medical	0		Y
Anthem		One conventional therapy	
Pharmacy	0		Y
Medical	0		Y
HCSC		One conventional therapy OR one biologic	
Pharmacy	0-1		Y
MedImpact		One conventional therapy AND Humira	
Pharmacy	1		Y
Blue Shield CA		Two preferred biologics (Humira, Remicade, and/or	
Medical	2	Xeljanz)	Y
BCBS MI		One conventional therapy AND Humira AND Stelara	
Pharmacy	4	AND Xeljanz AND Rinvoq	N
BCBS MA		Two conventional therapies AND one preferred	
Pharmacy	2	biologic	N
Premera		One conventional therapy AND Humira	
Pharmacy	1		Y
Medical	1		Y
Highmark		Humira	
Pharmacy	1		Y
Medical	1		Y
Elixir		One conventional therapy AND Humira	
Pharmacy	1		Y
VHA		One preferred biologic	
Pharmacy	1		Y
Florida Blue HIX		One conventional therapy AND Humira	
Pharmacy	1		Y
Kaiser HIX		No step	
Medical	0		Y

M: medical, P: pharmacy, ST: step therapy, Y: yes

B5.5. Summary of Findings

Table B5.3. Simponi Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Medical	N/A	Y	Y	Y
Express Scripts				
Pharmacy	N/A	Y	Y	Y
United				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
OptumRx				
Pharmacy	N/A	Y	Y	Y
Cigna				
Pharmacy	N/A	Y	Y	Y
Kaiser				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
HCSC				
Pharmacy	N/A	Y	Y	Y
MedImpact				
Pharmacy	N/A	Y	Y	Y
Blue Shield CA				
Medical	N/A	Y	Y	Y
BCBS MI				
Pharmacy	N/A	Y	N	Y
BCBS MA				
Pharmacy	N/A	N	N	Y
Premera				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Elixir				
Pharmacy	N/A	Y	Y	Y
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Pharmacy	N/A	Y	Y	Y
Kaiser HIX				
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B6. Policy Brief: Remicade (infliximab), TNF-alpha (intravenous)

B6.1. Condition: Ulcerative Colitis, moderate-to-severe

Is Drug Cost-Effective at Current Prices?: Yes

Other Drugs in Class: Inflectra, Renflexis, Simponi, Xeljanz, Stelara, Entyvio

B6.2. Clinical Guidelines

2020 AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

2019 ACG Clinical Guideline: Ulcerative Colitis in Adults

B6.3. Background

FDA Label

Indication: 1) reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in **adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.** 2) reducing signs and symptoms and inducing and maintaining clinical remission in **pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.**

Dosing: **Adults and Pediatric (≥ 6 years old):** 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.

Warning: Serious infections, invasive fungal infections, malignancies, heart failure, hepatoxicity, cytopenia

Contraindications: Infliximab doses >5 mg/kg in moderate or severe heart failure. Previous severe hypersensitivity reaction to infliximab or any inactive ingredients of Infliximab or to any murine proteins.

Interactions: Vaccines and use of live vaccines

Clinical Trial Eligibility:

Adults: The safety and efficacy of Infliximab were assessed in 2 randomized, double-blind, placebo controlled clinical studies in 728 adult patients with moderately to severely active UC (Mayo score 6 to 12 [of possible range 0 to 12], Endoscopy sub-score ≥2) with an inadequate response to conventional oral therapies (Studies UC I and UC II). Concomitant treatment with stable doses of amino salicylates, corticosteroids and/or immunomodulatory agents was permitted. Corticosteroid

taper was permitted after Week 8. Patients were randomized at week 0 to receive either placebo, 5 mg/kg Infliximab or 10 mg/kg Infliximab at Weeks 0, 2, 6, and every 8 weeks thereafter through Week 46 in Study UC I, and at Weeks 0, 2, 6, and every 8 weeks thereafter through Week 22 in Study UC II. In Study UC II, patients were allowed to continue blinded therapy to Week 46 at the investigator's discretion.

Pediatric: The safety and effectiveness of Infliximab for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients aged 6 years and older with moderately to severely active UC who have had an inadequate response to conventional therapy are supported by evidence from adequate and well-controlled studies of Infliximab in adults. Additional safety and pharmacokinetic data were collected in an open-label pediatric UC trial in 60 pediatric patients aged 6 through 17 years (median age 14.5 years) with moderately to severely active UC (Mayo score of 6 to 12; Endoscopic sub-score ≥2) and an inadequate response to conventional therapies. At baseline, the median Mayo score was 8, 53% of patients were receiving immunomodulator therapy (6-MP/AZA/MTX), and 62% of patients were receiving corticosteroids (median dose 0.5 mg/kg/day in prednisone equivalents). Discontinuation of immunomodulators and corticosteroid taper were permitted after Week 0.

Link to label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103772s5401lbl.pdf

ICER Policy Recommendations from the 2020 Ulcerative Colitis Review

The significantly lower prices seen for Remicade and its biosimilars speaks to the important potential for improved value with broader availability and uptake of biosimilar treatment options. All stakeholders should collaborate to ensure that TIM biosimilars have an increasing and comprehensive role in the UC treatment landscape
Because there are no clear biomarkers or predictors of the success for any given treatment in UC, it is not unreasonable to consider prior authorization criteria in order to manage the costs of expensive medications and negotiate prices for TIMs priced beyond a fair range. However, prior authorization criteria should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers.
Required switching of TIM therapy for patients who are stable on current treatment should be limited to switches to another medication with the same mechanism of action or from an originator to a biosimilar agent.

Link to report: Targeted Immune Modulators for Ulcerative Colitis: Effectiveness and Value

B6.4. Findings: Coverage Policies

Policies for Remicade were available for four payers (Express Scripts**,** OptumRx**,** VHA**,** MedImpact) under pharmacy benefits, six payers (BCBS MI**,** Blue Shield CA**,** Florida Blue HIX**,** HCSC**,** Highmark**,** United) under medical benefits, and seven payers (CVS, Cigna, Kaiser, Anthem, BCBS MA, Premera, Kaiser HIX) under both the pharmacy and medical benefits.

One payer (Elixir) has Remicade listed as non-formulary. Non-formulary drugs are only assessed on cost sharing. This drug/payer combination will not be assessed on any other criteria.

Cost Sharing

Two payers (Kaiser**,** Express Scripts) have Remicade on a Brand tier, the lowest relevant tier.

Five payers (CVS, OptumRx, Cigna, BCBS MA, Premera) place Remicade on a Non-Preferred tier, which is not the lowest relevant tier, but they have other drugs in class on a Preferred tier. This meets our cost-sharing criteria.

Two payers (Anthem, Kaiser HIX) do not have Remicade placed on the lowest relevant tier when a lower tier is available, and they do not have any other drugs in class on the lowest relevant tier. This does not meet our cost-sharing criteria.

One payer (MedImpact) does not include Remicade on its drug list, however infliximab is available on the generic tier, the lowest relevant tier. This does meet our cost-sharing criteria.

One payer (Elixir) has Remicade listed as non-formulary, however other drugs in class are available on the lowest relevant tier. This does meet our cost-sharing criteria. Non-formulary drugs are only assessed on cost sharing.

Table B6.1. Remicade Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N	2 (Preferred Brand), Humira, Stelara, Xeljanz	Y
Express Scripts	2 (Preferred-Brand)	Y	N/A	Y
United	N/A (covered under medical)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N	2 (Preferred Brand), Inflectra	Y
Cigna	3 (Non-Preferred Brand)	N	2 (Preferred Brand), Avsola and Inflectra	Y
Kaiser	2 (Brand)	Y	N/A	Y
Anthem	4 (Specialty)	N	2 (Preferred Brand), none	N
HCSC	N/A	N/A	N/A	N/A
MedImpact	Not available	N/A	1 (Generic), Infliximab	Y
Blue Shield CA	N/A (covered under medical)	N/A	N/A	N/A
BCBS MI	N/A (covered under medical)	N/A	N/A	N/A
BCBS MA	3 (Non-Preferred Brand)	N	2 (Preferred Brand), Avsola and Inflectra	Y
Premera	3 (Non-Preferred Brand)	N	2 (Preferred Brand), Humira, Stelara, Xeljanz	Y
Highmark	N/A (covered under medical)	N/A	N/A	N/A
Elixir	N/A (Non-formulary)	N/A	2 (Preferred Brand), Simponi	Y
VHA	N/A (no-tiering)	N/A	N/A	Y
Florida Blue HIX	N/A	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N	2 (Preferred Brand), none	N

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

All payers require some version of the following: patients with moderate to severe ulcerative colitis. This meets our clinical eligibility criteria.

Six payers (Express Scripts, BCBS MI, Anthem, Cigna, CVS, MedImpact) include an age requirement of 6 years or older. This meets our criteria because it is consistent with the FDA label's criteria, which indicates that Remicade is approved for individuals 6 and older with moderate to severe UC.

One payer (BCBS MA), requires a trial of 2 conventional agents from a list of steroids, 5-ASAs, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended in clinical guidelines.

One payer (Elixir) has Remicade listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Provider Qualifications

Ten payers (Anthem, BCBS MI, Blue Shield CA, Cigna, CVS, HCSC, Highmark, Kaiser, Kaiser HIX, VHA) do not mention requiring specialist prescribing or consultation. This meets our prescriber qualifications criteria.

Seven payers (BCBS MA, Florida Blue HIX, Premera, United, Express Scripts, OptumRx, MedImpact) require prescribing by or in consultation with a specialist. This meets our prescriber criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Premera) requires chart notes. This additional documentation requirement is appropriate for the condition.

One payer (Elixir) has Remicade listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Step Therapy

Three payers (Kaiser, Kaiser HIX, VHA) do not require step therapy. This meets our criteria for step therapy.

One payer (Elixir) has Remicade listed as non-formulary. This drug/payer combination was not assessed on our criteria.

All others required ONE of the following: Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for at least one conventional therapy:

(for example, aminosalicylate, corticosteroids or immunosuppressants). This meets our step therapy criteria because it is in line with the FDA label.

Table B6.2. Remicade Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS Pharmacy Medical	 1 1	P: Previously received a biologic or targeted synthetic drug OR inadequate response, intolerance, or contraindication to at least one conventional therapy option OR hospitalized for acute severe UC M: Previously received a biologic or targeted synthetic drug OR inadequate response, intolerance, or contraindication to at least one conventional therapy option OR hospitalized for acute severe UC	 Y Y
Express Scripts Pharmacy	 1	P:Systemic agent or has pouchitis and tried an antibiotic, probiotic, corticosteroid enema, or Rowasa	 Y
United Medical	 2	M: at least one conventional therapy AND treatment with Remicade, Renflexis, or other non-preferred Remicade biosimilar is medically necessary for the indications specified in this policy	 Y
OptumRx Pharmacy	 2	P: Trial and failure, contraindication, or intolerance to one of the following conventional therapies: 6-mercaptopurine, Aminosalicylate, Azathioprine, Corticosteroids	 Y
Cigna Pharmacy Medical	 2 2	P: at least one conventional therapy OR Individual has pouchitis AND has tried therapy AND BOTH the following: A. trial of ONE of (Avsola, inflectra) OR intolerance to Avsola OR Inflectra AND No documented therapeutic loss of response to infliximab product(s) M: 1 of (avsola or inflectra) and 1 of any of the non-biological DMARDs	 Y Y
Kaiser Pharmacy Medical	 0 0	 P: No step therapy M: No step therapy	 Y Y
Anthem Pharmacy Medical	 0 0	 P: conventional therapy M: conventional therapy	 Y Y
HCSC Medical	 1	M: ONE conventional agent OR hypersensitivity to ONE of the conventional agents OR FDA labeled contraindication to ALL of the conventional agents	 Y
MedImpact Pharmacy	 2	P: Patient is 6 to 17 and has tried or has a contraindication to humira. Patient is 18 and had a trial of or contraindication to TWO of the following preferred immunomodulators: Humira, Stelara, Xeljanz (IR/XR), Rinvoq	 Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
Blue Shield CA Medical	 1	M: Intolerable side effect with infliximab (Avsola and Inflectra)	 Y
BCBS MI Medical	 1	 M: conventional therapy	 Y
BCBS MA Pharmacy Medical	 2 2	P: trial or contraindication to two conventional therapies AND a preferred product M: trial or contraindication to two conventional therapies AND a preferred product	 Y Y
Premera Pharmacy Medical	 1 1	P: one systemic agent OR has pouchitis and has tried therapy M: one systemic agent OR has pouchitis and has tried therapy	 Y Y
Highmark Medical	 1-2	M: an adequate therapeutic trial or intolerance to both of the preferred products	 Y
Elixir Pharmacy	 N/A	 P: Conventional agent or severe disease that requires immediate biologic use	 N/A
VHA Pharmacy	 0	 P: No step	 Y
Florida Blue HIX Medical	 0	M: ONE conventional agent OR has an intolerance or hypersensitivity to ONE of the conventional agents OR has an FDA labeled contraindication to ALL of the conventional agents OR medication history indicates use of another biologic immunomodulator agent	 Y
Kaiser HIX Pharmacy Medical	 0 0	 P: No step therapy M: No step therapy	 Y Y

M: medical, P: pharmacy, ST: step therapy, Y: yes

B6.5. Summary of Findings

Table B6.3. Remicade Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Express Scripts				
Pharmacy	Y	Y	Y	Y
United				
Medical	N/A	N/A	Y	Y
OptumRx				
Pharmacy	Y	Y	Y	Y
Cigna				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Kaiser				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N	Y	Y	Y
Medical	N/A	Y	Y	Y
HCSC				
Medical	N/A	Y	Y	Y
MedImpact				
Pharmacy	Y	Y	Y	Y
Blue Shield CA				
Medical	N/A	Y	Y	Y
BCBS MI				
Medical	N/A	Y	Y	Y
BCBS MA				
Pharmacy	Y	N	Y	Y
Medical	N/A	N	Y	Y
Premera				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Medical	N/A	Y	Y	Y
Elixir				
Pharmacy	Y	N/A	N/A	N/A
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Medical	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N	Y	Y	Y
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B7. Policy Brief: Renflexis (infliximab-abda), TNF-alpha (intravenous)

B7.1. Condition: Ulcerative Colitis, moderate-to-severe

Is Drug Cost-Effective at Current Prices?: Yes

Other Drugs in Class: Remicade, Inflectra, Simponi, Xeljanz, Stelara, Entyvio

B7.2. Clinical Guidelines

2020 AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

2019 ACG Clinical Guideline: Ulcerative Colitis in Adults

B7.3. Background

FDA Label

Indication: 1) reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in **adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.** 2) reducing signs and symptoms and inducing and maintaining clinical remission in **pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.**

Dosing: **Adults and Pediatric (≥ 6 years old):** 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.

Warning: Serious infections, invasive fungal infections, malignancies, heart failure, hepatoxicity, cytopenia

Contraindications: Infliximab doses >5 mg/kg in moderate or severe heart failure. Previous severe hypersensitivity reaction to infliximab or any inactive ingredients of Infliximab or to any murine proteins.

Interactions: Vaccines and use of live vaccines

Clinical Trial Eligibility:

Adults: The safety and efficacy of Infliximab were assessed in 2 randomized, double-blind, placebo controlled clinical studies in 728 adult patients with moderately to severely active UC (Mayo score 6 to 12 [of possible range 0 to 12], Endoscopy sub-score ≥2) with an inadequate response to conventional oral therapies (Studies UC I and UC II). Concomitant treatment with stable doses of amino salicylates, corticosteroids and/or immunomodulatory agents was permitted. Corticosteroid

taper was permitted after Week 8. Patients were randomized at week 0 to receive either placebo, 5 mg/kg Infliximab or 10 mg/kg Infliximab at Weeks 0, 2, 6, and every 8 weeks thereafter through Week 46 in Study UC I, and at Weeks 0, 2, 6, and every 8 weeks thereafter through Week 22 in Study UC II. In Study UC II, patients were allowed to continue blinded therapy to Week 46 at the investigator's discretion.

Pediatric: The safety and effectiveness of Infliximab for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients aged 6 years and older with moderately to severely active UC who have had an inadequate response to conventional therapy are supported by evidence from adequate and well-controlled studies of Infliximab in adults. Additional safety and pharmacokinetic data were collected in an open-label pediatric UC trial in 60 pediatric patients aged 6 through 17 years (median age 14.5 years) with moderately to severely active UC (Mayo score of 6 to 12; Endoscopic sub-score ≥2) and an inadequate response to conventional therapies. At baseline, the median Mayo score was 8, 53% of patients were receiving immunomodulator therapy (6-MP/AZA/MTX), and 62% of patients were receiving corticosteroids (median dose 0.5 mg/kg/day in prednisone equivalents). Discontinuation of immunomodulators and corticosteroid taper were permitted after Week 0.

Link to label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103772s5401lbl.pdf

ICER Policy Recommendations from the 2020 Ulcerative Colitis Review

The significantly lower prices seen for Remicade and its biosimilars speaks to the important potential for improved value with broader availability and uptake of biosimilar treatment options. All stakeholders should collaborate to ensure that TIM biosimilars have an increasing and comprehensive role in the UC treatment landscape
Because there are no clear biomarkers or predictors of the success for any given treatment in UC, it is not unreasonable to consider prior authorization criteria in order to manage the costs of expensive medications and negotiate prices for TIMs priced beyond a fair range. However, prior authorization criteria should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers.
Required switching of TIM therapy for patients who are stable on current treatment should be limited to switches to another medication with the same mechanism of action or from an originator to a biosimilar agent.

Link to report: Targeted Immune Modulators for Ulcerative Colitis: Effectiveness and Value

B7.4. Findings: Coverage Policies

Policies for Renflexis were available for eight payers (BCBS MI**,** Blue Shield CA**,** Cigna**,** CVS**,** Florida Blue HIX**,** HCSC**,** Highmark**,** United) under medical benefits, three payers (OptumRx, VHA**,** MedImpact) under pharmacy benefits, and five payers (Kaiser, Kaiser HIX**,** Anthem, BCBS MA, Premera) under both the pharmacy and medical benefits.

Renflexis was not covered for one payer (Express Scripts).

One payer (Elixir) has Renflexis listed as non-formulary. Non-formulary drugs are only assessed on cost sharing. This drug/payer combination will not be assessed on any other criteria.

Cost Sharing

Three payers (OptumRx, BCBS MA, Premera) place Renflexis on a Non-Preferred tier, which is not the lowest relevant tier, but they have drugs in class on a Preferred tier. This meets our cost-sharing criteria.

Two payers (Anthem**,** Kaiser HIX) do not have Renflexis placed on the lowest relevant tier when a lower tier is available and they do not have any other drugs in class on the lowest relevant tier. This does not meet our cost-sharing criteria.

One payer (MedImpact) does not include Renflexis on its drug list, however infliximab is available on the generic tier, the lowest relevant tier. This does meet our cost-sharing criteria.

One payer (Elixir) has Renflexis listed as non-formulary, however other drugs in class are available on the lowest relevant tier. This does meet our cost-sharing criteria. Non-formulary drugs are only assessed on cost sharing.

Table B7.1. Renflexis Cost Sharing by Payer Within Pharmacy Benefit Coverage

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	N/A (covered under medical)	N/A	N/A	N/A
Express Scripts	N/A (not covered)	N/A	N/A	N/A
United	N/A (covered under medical)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N	2 (Preferred Brand), Inflectra	Y
Cigna	N/A (covered under medical)	N/A	N/A	N/A
Kaiser	2 (brand)	Y	N/A	Y
Anthem	4 (Specialty)	N	2 (Preferred Brand), none	N
HCSC	N/A (covered under medical)	N/A	N/A	N/A
MedImpact	Not available	N/A	1 (Generic), Infliximab	Y
Blue Shield CA	N/A (covered under medical)	N/A	N/A	N/A
BCBS MI	N/A (covered under medical)	N/A	N/A	N/A
BCBS MA	3 (Non-Preferred Brand)	N	2 (Preferred Brand), Inflectra	Y
Premera	3 (Non-Preferred Brand)	N	2 (Preferred Brand), Inflectra	Y

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
Highmark	N/A (covered under medical)	N/A	N/A	N/A
Elixir	N/A (Non-formulary)	N/A	2 (Preferred Brand), Simponi	Y
VHA	N/A (no tiering)	N/A	N/A	Y
Florida Blue HIX	N/A (covered under medical)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N	5 (Preferred-Brand), none	N

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three payers (Kaiser, Kaiser HIX, VHA) do not have a clinical eligibility requirement. This meets our clinical eligibility criteria.

All other payers require some version of the following: patients with moderate to severe ulcerative colitis, who have an inadequate response, or intolerance to conventional therapy. This meets our clinical eligibility criteria.

Eight payers (Cigna, CVS, Anthem, HCSC, BCBS MI, Blue Shield CA, Highmark, MedImpact) included an age requirement of 6 or older. This meets our criteria because it is consistent with the FDA label's criteria, which indicates that Renflexis is approved for individuals 6 and older with moderate to severe UC.

One payer (BCBS MA), requires a trial of 2 conventional agents from a list of steroids, 5-ASAs, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended in clinical guidelines.

One payer (Elixir) has Renflexis listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Provider Qualifications

Nine payers (Anthem, BCBS MI, Blue Shield CA, CVS, HCSC, Highmark, Kaiser, Kaiser HIX, VHA) do not mention requiring specialist prescribing or consultation for their medical benefits plan. This meets our provider qualifications criteria.

Seven payers (BCBS MA, Cigna, Florida Blue HIX, Premera, United, OptumRx, MedImpact) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Premera) requires chart notes. This additional documentation requirement is appropriate for the condition.

One payer (Elixir) has Renflexis listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Step Therapy

Three payers (Kaiser, Kaiser HIX**,** VHA) do not require step therapy. This meets our criteria for step therapy.

Most payers require ONE of the following: an adequate trial and treatment failure with one systemic agent OR a conventional therapy. This meets our criteria step therapy because it is in line with the clinical guidelines.

The following payers have additional step therapy requirements (in addition to the above):

- Seven payers (Cigna, HCSC, Blue Shield CA, Highmark, VHA**,** Premera**,** OptumRx) require documented trial of either the reference agent (Remicade) OR one or both biosimilar products (Avsola or Inflectra). This meets our step therapy criteria because these agents are appropriate for most patients and patients have a reasonable chance to meet their clinical goals with these agents.

One payer (Elixir) has Renflexis listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Table B7.2. Renflexis Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS Medical	1	Biologic or targeted synthetic drug OR least one conventional therapy option OR hospitalized for acute severe UC	Y
Express Scripts	N/A	N/A	N/A
United Medical	1	History of failure, contraindication, or intolerance to at least one conventional therapy	Y
OptumRx Pharmacy	1	Trial and failure, contraindication, or intolerance to one conventional therapy AND trial, failure, or intolerance of avsola or inflectra	Y
Cigna Medical	2	Individual meets BOTH of the following: A. Individual has a documented trial of ONE* of the following: Avsola OR Inflectra or B. Documented intolerance to Avsola OR Inflectra AND 2. No documented therapeutic loss of response to infliximab product(s)	Y
Kaiser Pharmacy Medical	 0 0	 P: No step M: No step	 Y Y
Anthem Pharmacy Medical	 0 0	 P: an inadequate response to, is intolerant of, or has a contraindication to conventional therapy M: an inadequate response to, is intolerant of, or has a contraindication to conventional therapy	 Y Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
HCSC Medical	1	ONE conventional agent OR severely active ulcerative colitis OR intolerance or hypersensitivity to ONE of the conventional agents OR FDA labeled contraindication to ALL of the conventional agents OR The patient's medication history indicates use of another biologic immunomodulator agent	Y
MedImpact Pharmacy	1	Aged 6-17: trial or contraindication to humira, aged 18 and older trial or contraindication to two of the preferred immunomodulators	Y
Blue Shield CA Medical	1	Intolerable side effect with infliximab (Avsola and Inflectra) that is not expected with the requested drug, or contraindication to both Avsola and Inflectra	Y
BCBS MI Medical	0	trial or contraindication to conventional therapy	Y
BCBS MA Pharmacy Medical	2 2	P: trial or contraindication to two conventional therapies AND a preferred product M: trial or contraindication to two conventional therapies AND a preferred product	Y Y
Premera Pharmacy Medical	2 2	P: one systemic agent OR Patient has pouchitis and has tried therapy AND Patient has had an inadequate response or intolerance to Remicade® AND Inflectra®, Renflexis® or Avsola™ M: one systemic agent OR Patient has pouchitis and has tried therapy AND Patient has had an inadequate response or intolerance to Remicade® AND Inflectra®, Renflexis® or Avsola™	Y Y
Highmark Medical	2	an adequate therapeutic trial and experienced a documented drug therapy failure or intolerance to both of the preferred products	Y
Elixir Pharmacy	N/A	Trial and failure of conventional therapy or severe UC	N/A
VHA Pharmacy	0	No step	Y
Florida Blue HIX Medical	1	ONE of the following: 1. tried and had an inadequate response to ONE conventional agent OR 2. The member has an intolerance or hypersensitivity to ONE of the conventional agents FDA labeled contraindication to ALL of the conventional agents used in the treatment of UC OR 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled	Y
Kaiser HIX Pharmacy Medical	0 0	No step No step	Y Y

M: medical, P: pharmacy, ST: step therapy, Y: yes

B7.5. Summary of Findings

Table B7.3. Renflexis Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Medical	N/A	Y	Y	Y
Express Scripts				
N/A	N/A	N/A	N/A	N/A
United				
Medical	N/A	Y	Y	Y
OptumRx				
Pharmacy	Y	Y	Y	Y
Cigna				
Medical	N/A	Y	Y	Y
Kaiser				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N	Y	Y	Y
Medical	N/A	Y	Y	Y
HCSC				
Medical	N/A	Y	Y	Y
MedImpact				
Pharmacy	Y	Y	Y	Y
Blue Shield CA				
Medical	N/A	Y	Y	Y
BCBS MI				
Medical	N/A	Y	Y	Y
BCBS MA				
Pharmacy	Y	N	Y	Y
Medical	N/A	N	Y	Y
Premera				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Medical	N/A	Y	Y	Y
Elixir				
Pharmacy	Y	N/A	N/A	N/A
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Medical	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N	Y	Y	Y
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B8. Policy Brief: Inflectra (infliximab-dyyb), TNF-Alpha (intravenous)

B8.1. Condition: Ulcerative Colitis (UC), moderate to severe

Is Drug Cost-Effective at Current Prices?: Yes

Other Drugs in Class: Inflectra, Renflexis, Simponi, Xeljanz, Stelara, Entyvio

B8.2. Clinical Guidelines

2020 AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

2019 ACG Clinical Guideline: Ulcerative Colitis in Adults

B8.3. Background

FDA Label

Indication: 1) reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in **adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.** 2) reducing signs and symptoms and inducing and maintaining clinical remission in **pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.**

Dosing: **Adults and Pediatric (≥ 6 years old):** 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.

Warning: Serious infections, invasive fungal infections, malignancies, heart failure, hepatoxicity, cytopenia

Contraindications: INFLECTRA doses >5 mg/kg in moderate or severe heart failure. Previous severe hypersensitivity reaction to infliximab products or any inactive ingredients of INFLECTRA or to any murine proteins.

Interactions: Vaccines and use of live vaccines

Clinical Trial Eligibility:

Adults: The safety and efficacy of infliximab were assessed in 2 randomized, double-blind, placebo-controlled clinical studies in 728 adult patients with moderately to severely active UC (Mayo score 6 to 12 [of possible range 0 to 12], Endoscopy sub score ≥2) with an inadequate response to conventional oral therapies (Studies UC I and UC II). Concomitant treatment with stable doses of amino-salicylates, corticosteroids and/or immunomodulatory agents was permitted. Corticosteroid

taper was permitted after Week 8. Patients were randomized at Week 0 to receive either placebo, 5 mg/kg infliximab or 10 mg/kg infliximab at Weeks 0, 2, 6, and every 8 weeks thereafter through Week 46 in Study UC I, and at Weeks 0, 2, 6, and every 8 weeks thereafter through Week 22 in Study UC II. In Study UC II, patients were allowed to continue blinded therapy to Week 46 at the investigator's discretion.

Pediatric: The safety and effectiveness of infliximab products for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients aged 6 years and older with moderately to severely active UC who have had an inadequate response to conventional therapy are supported by evidence from adequate and well-controlled studies of infliximab in adults. Additional safety and pharmacokinetic data were collected in an open-label pediatric UC trial in 60 pediatric patients aged 6 through 17 years (median age 14.5 years) with moderately to severely active UC (Mayo score of 6 to 12; Endoscopic sub score ≥2) and an inadequate response to conventional therapies. At baseline, the median Mayo score was 8, 53% of patients were receiving immunomodulator therapy (6- MP/AZA/MTX), and 62% of patients were receiving corticosteroids (median dose 0.5 mg/kg/day in prednisone equivalents). Discontinuation of immunomodulators and corticosteroid taper were permitted after Week 0.

Link to label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125544s018lbl.pdf

ICER Policy Recommendations from the Ulcerative Colitis 2020 Review

The significantly lower prices seen for Remicade and its biosimilars speaks to the important potential for improved value with broader availability and uptake of biosimilar treatment options. All stakeholders should collaborate to ensure that TIM biosimilars have an increasing and comprehensive role in the UC treatment landscape
Because there are no clear biomarkers or predictors of the success for any given treatment in UC, it is not unreasonable to consider prior authorization criteria in order to manage the costs of expensive medications and negotiate prices for TIMs priced beyond a fair range. However, prior authorization criteria should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers.
Required switching of TIM therapy for patients who are stable on current treatment should be limited to switches to another medication with the same mechanism of action or from an originator to a biosimilar agent.

Link to report: Targeted Immune Modulators for Ulcerative Colitis: Effectiveness and Value

B8.4. Findings: Coverage Policies

Policies for Inflectra were available for seven payers (BCBS MI, Blue Shield CA, CVS, Florida Blue HIX, HCSC, Highmark, United) under medical benefits, four payers (Express Scripts, MedImpact, OptumRx, VHA) under pharmacy benefits, and six payers (Anthem, BCBS MA, Cigna, Kaiser, Kaiser HIX, Premera) under both the pharmacy and medical benefits.

One payer (Elixir) has Inflectra listed as non-formulary. Non-formulary drugs are only assessed on cost sharing. This drug/payer combination will not be assessed on any other criteria.

Cost Sharing

Six payers (BCBS MA**,** Cigna**,** Express Scripts**,** Kaiser**,** OptumRx**,** Premera) have Inflectra placed on a preferred brand tier, the lowest relevant tier. This meets our cost-sharing criteria.

Two payers (Anthem, Kaiser HIX) do not have Inflectra placed on the lowest relevant tier when a lower tier is available. This does not meet our cost-sharing criteria because a preferred tier is available and all drugs in the class were placed on the highest tier.

One payer (MedImpact) does not include Remicade on its drug list, however infliximab is available on the generic tier, the lowest relevant tier. This does meet our cost-sharing criteria.

One payer (Elixir) has Inflectra listed as non-formulary, however other drugs in class are available on the lowest relevant tier. This does meet our cost-sharing criteria. Non-formulary drugs are only assessed on cost sharing.

Table B8.1. Inflectra Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	N/A (covered under medical)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	Y	N/A	Y
United	N/A	N/A	N/A	N/A
OptumRx	2 (Preferred Brand)	Y	N/A	Y
Cigna	2 (Preferred Brand)	Y	N/A	Y
Kaiser	2 (Brand)	Y	N/A	Y
Anthem	4 (Specialty)	N	2 (Preferred Brand), none	N
HCSC	N/A	N/A	N/A	N/A
MedImpact	Not available	N/A	1 (Generic), Infliximab	Y
Blue Shield CA	N/A	N/A	N/A	N/A
BCBS MI	N/A	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	Y	N/A	Y
Premera	2 (Preferred Brand)	Y	N/A	Y
Highmark	N/A	N/A	N/A	N/A
Elixir	N/A (non-formulary)	N/A	2 (Preferred Brand), Simponi	Y
VHA	N/A (no tiering)	N/A	N/A	Y
Florida Blue HIX	N/A (covered under medical)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N	2 (Preferred Brand), none	N

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three payers (Kaiser, Kaiser HIX, VHA) do not have a clinical eligibility requirement. This meets our clinical eligibility requirement.

All other payers require some version of the following: patients with moderate to severe ulcerative colitis. This meets our clinical eligibility requirement.

Nine payers (Anthem, BCBS MI, Blue Shield CA, Cigna, CVS, HCSC, Highmark, Express Scripts, MedImpact) included an age requirement of 6 years and older. This meets our criteria because it is consistent with the FDA label's criteria, which indicates that Inflectra is approved for individuals 6 and older with moderate to severe UC.

One payer (BCBS MA), requires a trial of 2 conventional agents from a list of steroids, 5-ASAs, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended in clinical guidelines.

One payer (Elixir) has Inflectra listed as non-formulary, so the drug was not evaluated on our criteria.

Provider Qualifications

Nine payers (Anthem, BCBS MI, Blue Shield CA, CVS, HCSC, Highmark, Kaiser, Kaiser HIX, VHA) do not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Eight payers (BCBS MA, Cigna, Florida Blue HIX, Premera, United, Express Scripts, MedImpact, OptumRx) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Premera) requires chart notes. This additional documentation requirement is appropriate for the condition.

One payer (Elixir) has Inflectra listed as non-formulary, so the drug was not evaluated on our criteria.

Step Therapy

Four payers (Kaiser, VHA, Kaiser HIX, Anthem) do not require step therapy. This meets our step therapy criteria.

Most payers require a variation of the following: a documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for at least one conventional therapy: (for example, aminosalicylate, corticosteroids or immunosuppressants). This meets our criteria for step therapy because it is in line with the clinical guidelines.

- Two payers (Express Scripts, Premera) require a variation of the following: patient has had an adequate trial and treatment failure with one systemic agent. This meets our criteria for step therapy because it is in line with the clinical guidelines.

- One payer (MedImpact) requires patients to either try or have a contraindication to Humira (patients aged 6-17) or two of Humira, Stelara, Xeljanz or Rinvoq (ages 18 and older). This meets our criteria for step therapy because it is reasonable to have a patient try two treatments of a similar class on a lower tier, before trying Inflectra.

One payer (Elixir) has Inflectra listed as non-formulary, so the drug was not evaluated on our criteria.

Table B8.2. Inflectra Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS Pharmacy Medical	 1 1	P: a biologic or targeted synthetic drug OR contraindication to at least one conventional therapy OR hospitalized for acute severe UC M: P: a biologic or targeted synthetic drug OR contraindication to at least one conventional therapy OR hospitalized for acute severe UC	 Y Y
Express Scripts Pharmacy	 2	Trial and failure of one systemic therapy OR pouchitis	 Y
United Medical	 1	M: trial or contraindication least one conventional therapy	 Y
OptumRx Pharmacy	 1	Trial and failure, contraindication, or intolerance to one conventional therapies	 Y
Cigna Pharmacy Medical	 1 1	P: A. one conventional therapy OR B. Individual has pouchitis AND has tried therapy M: A. one conventional therapy OR B. Individual has pouchitis AND has tried therapy	 Y Y
Kaiser Pharmacy Medical	 0 0	 P: No step M: No step	 Y Y
Anthem Pharmacy Medical	 1 1	 P: trial or contraindication to conventional therapy M: trial or contraindication to conventional therapy	 Y Y
HCSC Medical	 1	Trial or contraindication to a conventional therapy or severe UC	 Y
MedImpact Pharmacy	2	Humira (ages 6-17) or two of humira, Stelara or xeljanz (18 and older)	Y
Blue Shield CA Medical	 0	No steps	 Y
BCBS MI Medical	 1	trial or contraindication to conventional therapy	 Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
BCBS MA			
Pharmacy	2	P: trial or contraindication to two conventional	Y
Medical	2	therapies AND a preferred product M: trial or contraindication to two conventional therapies AND a preferred product	Y
Premera			
Pharmacy	2	P: one systemic agent or pouchitis	Y
Medical	2	M: one systemic agent or pouchitis	Y
Highmark			
Medical	0	No steps	Y
Elixir		Trial and failure with one conventional treatment or	
Pharmacy	N/A	severe UC	N/A
VHA			
Pharmacy	0	No step	Y
Florida Blue HIX			
Medical	1	M: ONE conventional agent OR hypersensitivity to ONE of the conventional agents OR FDA labeled contraindication to ALL of the conventional agents	Y
Kaiser HIX			
Pharmacy	0	P: No steps	Y
Medical	0	M: No steps	Y

M: medical, N/A: not applicable, P: pharmacy, ST: step therapy, Y: yes

B8.5. Summary of Findings

Table B8.3. Inflectra Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Medical	N/A	Y	Y	Y
Express Scripts				
Pharmacy	Y	Y	Y	Y
United				
Medical	N/A	Y	Y	Y
OptumRx				
Pharmacy	Y	Y	Y	Y
Cigna				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Kaiser				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N	Y	Y	Y
Medical	N/A	Y	Y	Y
HCSC				
Medical	N/A	Y	Y	Y
MedImpact				
Pharmacy	Y	Y	Y	Y
Blue Shield CA				
Medical	N/A	Y	Y	Y
BCBS MI				
Medical	N/A	Y	Y	Y
BCBS MA				
Pharmacy	Y	N	Y	Y
Medical	N/A	N	Y	Y
Premera				
Pharmacy	Y	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Medical	N/A	Y	Y	Y
Elixir				
Pharmacy	Y	N/A	N/A	N/A
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Medical	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N	Y	Y	Y
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B9. Policy Brief: Kalydeco (ivacaftor), CFTR Modulator (oral)

B9.1. Condition: Cystic Fibrosis

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: Symdeko, Trikafta, Orkambi

B9.2. Clinical Guidelines

Cystic fibrosis: Treatment with CFTR modulators, UpToDate 2021

Cystic Fibrosis Foundation Pulmonary Guidelines 2018

B9.3. Background

FDA Label

Indication: For the treatment of cystic fibrosis (CF) in patients age 4 months and older who have one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data.

Dosing:

Adults and pediatric patients age 6 years and older: one 150 mg tablet

Pediatric patients 4 months to less than 6 months of age and 5 kg or greater: one 25 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid

Pediatric patients 6 months to less than 6 years of age and weighing 5 kg to less than 7 kg: one 25 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid

Pediatric patients 6 months to less than 6 years of age and weighing 7 kg to less than 14 kg: one 50 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid

Pediatric patients 6 months to less than 6 years of age and 14 kg or greater: one 75 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid

For all patients doses administered orally every 12 hours with fat-containing foods.

Warning: Elevated transaminases (ALT or AST); Use with CYP3A inducers substantially decreases exposure of ivacaftor, which may diminish effectiveness; Cataracts: Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with KALYDECO

Contraindications: None

Interactions: CYP3A inhibitors: Reduce KALYDECO dose when co-administered with strong CYP3A inhibitors (e.g., ketoconazole) or moderate CYP3A inhibitors (e.g., fluconazole). Avoid food containing grapefruit

Clinical Trial Eligibility: Trial 1 enrolled patients with CF who were 12 years of age or older with FEV1 at screening between 40-90% predicted. Trial 2 enrolled patients who were 6 to 11 years of age with FEV1 at screening between 40-105% predicted. Patients with abnormal liver function defined as 3 or more liver function tests (ALT, AST, AP, GGT, total bilirubin) ≥3 times the upper limit of normal were excluded.

Link to label: https://pi.vrtx.com/files/uspi_ivacaftor.pdf

ICER Policy Recommendations from the 2020 Cystic Fibrosis Report

No recommendations specific to Kalydeco

Link to report: Modulator Treatments for Cystic Fibrosis: Effectiveness and Value

B9.4. Findings: Coverage Policies

Policies or coverage information for Kalydeco were available for all 18 payers under pharmacy benefits.

Cost Sharing

Because Kalydeco was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B9.1. Kalydeco Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	3 (Non-Preferred Brand)	N/A	N/A	N/A
Kaiser	2 (Brand)	N/A	N/A	N/A
Anthem	Non-formulary	N/A	N/A	N/A
HCSC	5 (Preferred Specialty)	N/A	N/A	N/A
MedImpact	2 (Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	4 (Specialty)	N/A	N/A	N/A
BCBS MI	2 (Preferred Brand)	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	2 (Preferred Brand)	N/A	N/A	N/A
Highmark	2 (Preferred Brand)	N/A	N/A	N/A
Elixir	2 (Preferred Brand)	N/A	N/A	N/A
VHA	N/A (no tiering)	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Three payers (Kaiser, Kaiser HIX**,** VHA) do not have a clinical eligibility requirement. This meets our clinical eligibility requirement.

Fourteen payers (CVS, Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, Elixir, Florida Blue HIX) require some version of the following: A diagnosis of cystic fibrosis in an individual four months of age or older with documentation of at least one listed mutation of the CFTR gene. This meets our clinical eligibility criteria.

Three payers (HCSC, Elixir, Florida Blue HIX) include a more specific definition requiring that patients not use Kalydeco in combination with other ivacaftor-containing medications. One payer (Premera) requires patients to have a liver function test below three times the upper limit of normal. One payer (MedImpact) requires patients between 4 months and less than 6 years of age to document their weight. These requirements meet our criteria because they are consistent with the label's indication for Kalydeco in treating cystic fibrosis.

One payer (Anthem) has Kalydeco listed as non-formulary and was not evaluated on clinical eligibility criteria.

Provider Qualifications

Ten payers (CVS, Kaiser, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, VHA, Florida Blue HIX, Kaiser HIX) do not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Seven payers (Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, Elixir) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Anthem) has Kalydeco listed as non-formulary and was not evaluated on provider qualifications criteria.

Step Therapy

One payer (Anthem) has Kalydeco listed as non-formulary and was not evaluated on step therapy criteria.

Step therapy is not required by any other payer. This meets our criteria for step therapy because it is in line with the FDA label.

Table B9.2. Kalydeco Step Therapy by Payer

Payer*	Steps	Details	Meets ST Criteria? Y/N
CVS	0	No step	Y
Express Scripts	0	No step	Y
United	0	No step	Y
OptumRx	0	No step	Y
Cigna	0	No step	Y
Kaiser	0	No step	Y
Anthem	N/A	Non-formulary	N/A
HCSC	0	No step	Y
MedImpact	0	No step	Y
Blue Shield CA	0	No step	Y
BCBS MI	0	No step	Y
BCBS MA	0	No step	Y
Premera	0	No step	Y
Highmark	0	No step	Y
Elixir	0	No step	Y
VHA	0	No step	Y
Florida Blue HIX	0	No step	Y
Kaiser HIX	0	No step	Y

N: no, N/A: not applicable, ST: step therapy, Y: yes

* All payers covered under pharmacy benefit only

B9.5. Summary of Findings

Table B9.3. Kalydeco Fair Access Criteria by Payer

Payer*	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS	N/A	Y	Y	Y
Express Scripts	N/A	Y	Y	Y
United	N/A	Y	Y	Y
OptumRx	N/A	Y	Y	Y
Cigna	N/A	Y	Y	Y
Kaiser	N/A	Y	Y	Y
Anthem	N/A	N/A	N/A	N/A
HCSC	N/A	Y	Y	Y
MedImpact	N/A	Y	Y	Y
Blue Shield CA	N/A	Y	Y	Y
BCBS MI	N/A	Y	Y	Y
BCBS MA	N/A	Y	Y	Y
Premera	N/A	Y	Y	Y
Highmark	N/A	Y	Y	Y
Elixir	N/A	Y	Y	Y
VHA	N/A	Y	Y	Y
Florida Blue HIX	N/A	Y	Y	Y
Kaiser HIX	N/A	Y	Y	Y

N/A: not applicable, Y: yes

* All payers covered under pharmacy benefit only

B10. Policy Brief: Reyvow (lasmiditan), serotonin receptor agonist (oral)

B10.1. Condition: Acute migraine, adults

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: Nurtec, Ubrelvy

B10.2. Clinical Guidelines

The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice (2018)

B10.3. Background

FDA Label

Indication: acute treatment of migraine with or without aura in adults

Dosing: 50 mg, 100 mg, or 200 mg taken orally, as needed. No more than one dose should be taken in 24 hours.

Warning: driving impairment; central nervous system (CNS) depression; serotonin syndrome; overuse headache

Contraindications: None

Interactions: Lasmiditan may further lower heart rate when administered with heart rate lowering drugs; avoid use with P-gp and Breast Cancer Resistant Protein (BCRP) substrates.

Clinical Trial Eligibility: The efficacy of REYVOW in the acute treatment of migraine was demonstrated in two randomized, double-blind, placebo-controlled trials [Study 1 (NCT02439320) and Study 2 (NCT02605174)]. These studies enrolled patients with a history of migraine with and without aura according to the International Classification of Headache Disorders (ICHD-II) diagnostic criteria. Patients were predominantly female (84%), and White (78%), with a mean age of 42 years (range 18-81). Twenty two percent of patients were taking preventive medication for migraine at baseline. Study 1 randomized patients to REYVOW 100 mg (n=744), or 200 mg (n=745) or placebo (n=742) and Study 2 randomized patients to REYVOW 50 mg (n=750), 100 mg (n=754), or 200 mg (n=750) or placebo (n=751). Patients were allowed to take a rescue medication 2 hours after taking study drug; however, opioids, barbiturates, triptans, and ergots were not allowed within 24 hours of study drug administration.

Link to label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211280s000lbl.pdf

ICER Policy Recommendations from the 2020 Acute Treatments for Migraine Report

The Food and Drug Administration (FDA) indication for Reyvow includes acute treatment of all adults with migraine, with or without aura. Clinical trials for Reyvow included a narrower spectrum of adult: patients generally had a long history of migraine with a high frequency and intensity of symptoms. On average, over 80% were female, with an average age of approximately 40 years, having had migraines for 15-20 years, with 3-5 migraine attacks per month of a moderate (approximately 70%) or severe (approximately 30%) intensity, and about 20-25% were receiving medications to prevent migraine attacks. Clinical experts and patient advocates suggest that although the clinical trial populations were more severely affected, on average, than all patients with migraine, there is no evidence-based reason to try to limit coverage based on some metric of severity such as number of migraines per month.
Given that the evidence of response to Reyvow does not suggest it is superior to triptans, clinical experts, patient advocates, and manufacturers agreed that requiring patients to try triptans first before receiving coverage is reasonable if patients are clinically eligible. Clinical experts highlighted that triptans are under-prescribed, and some patients have not tried triptans due to concerns about side effects or concerns about vasoconstriction in those who not at high risk for cardiovascular disease. Attestation of clinical ineligibility was still favored over formal medical record documentation given the long-term nature of migraine and the difficulty of finding past medical records to document CV events that would make a patient ineligible.
For patients who are eligible to try triptans, there is no evidence-based basis for a threshold number of different triptans that should be tried to determine whether adequate treatment is achieved. Clinical experts and patient advocates acknowledge that many patients find adequate relief with one triptan even after finding other triptans inadequate. The likelihood of finding a triptan that works does diminish after each trial, however, so a requirement of trying 1-2 triptans was viewed as reasonable whereas requiring more was viewed as less reasonable. Trying to devise a metric for "inadequate" response by looking at rescue medication use or other factors was not viewed as clinically reasonable.

Link to report: Acute Treatments for Migraine: Final Evidence Report

B10.4. Findings: Coverage Policies

Policies for Reyvow were available for 16 payers (Anthem**,** CVS, Express Scripts, United, OptumRx, Kaiser, HCSC, MedImpact, Blue Shield CA, BCBS MI, Premera, Highmark, Elixir, VHA, Florida Blue HIX, Kaiser HIX) under pharmacy benefits.

Reyvow was not covered by two payers (Cigna, BCBS MA).

One payer (Anthem) has Reyvow listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Cost Sharing

Because Reyvow was deemed not fairly priced at current prices, we did not issue ratings for cost sharing.

Table B10.1. Reyvow Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts	3 (Non-Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	N/A (not covered)	N/A	N/A	N/A
Kaiser	N/A (no tiering)	N/A	N/A	N/A
Anthem	Non-Formulary	N/A	N/A	N/A
HCSC	3 (Preferred Brand)	N/A	N/A	N/A
MedImpact	2 (Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	3 (Non-Preferred Brand)	N/A	N/A	N/A
BCBS MI	3 (Non-Preferred Brand)	N/A	N/A	N/A
BCBS MA	N/A (not covered)	N/A	N/A	N/A
Premera	3 (Non-Preferred Brand)	N/A	N/A	N/A
Highmark	3 (Non-Preferred Brand)	N/A	N/A	N/A
Elixir	2 (Preferred Brand)	N/A	N/A	N/A
VHA	Not applicable	N/A	N/A	N/A
Florida Blue HIX	5 (Preferred Brand)	N/A	N/A	N/A
Kaiser HIX	N/A (no tiering)	N/A	N/A	N/A

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three Payers (Kaiser, Kaiser HIX, VHA) do not require clinical eligibility criteria. This meets our requirement, as it is not a restrictive policy.

Clinical eligibility information is available for 12 payers (BCBS MI, Blue Shield CA, CVS, Elixir, Express Scripts, Florida Blue HIX, HCSC, Highmark, MedImpact, Premera, OptumRx, United) under the pharmacy benefit. All payers require some version of the following: adults with acute migraine. This meets our criteria for clinical eligibility.

Two payers (OptumRx, United) include a requirement of current use of prophylactic therapy OR <4 migraine days/month OR ≥4 migraine days per month and has contraindication or intolerance to prophylactic therapies. This meets our criteria because it is consistent with the definition of acute migraine and suggested use of prophylactic therapies according to the American Headache Society Consensus Statement.

One payer (Anthem) has Reyvow listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Provider Qualifications

Thirteen payers (CVS, Express Scripts, Kaiser**,** Kaiser HIX**,** Anthem, HCSC, MedImpact, Blue Shield CA, BCBS MI, Premera, Highmark, Elixir, Florida Blue HIX) do not require specialist prescribing or consultation. This meets our provider qualifications criteria.

Two payers (OptumRx**,** United) require prescribing by or in consultation with a neurologist, pain specialist, or headache specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Anthem) listed Reyvow as non-formulary and therefore did not have policies outlining prescriber requirements. We listed non-formulary drugs as not applicable for this criteria.

Step Therapy

Three payers (Kaiser, VHA, Kaiser HIX) do not require step therapy. This meets our step therapy criteria.

Eight payers (Elixir**,** Express Scripts, HCSC, MedImpact, Blue Shield CA, Premera, Highmark, Florida Blue HIX) require inadequate response or intolerance to one or two generic triptans. This meets our step therapy criteria because triptans are appropriate for most patients and patients have a reasonable chance to meet their clinical goals with triptans.

Three payers (United, OptumRx, BCBS MI) require a step through two triptans plus Ubrelvy and Nurtec. This does not meet our criteria because it exceeds our maximum of three steps to access Reyvow.

One payer (Anthem) has Reyvow listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Table B10.2. Reyvow Step Therapy by Payer

Payer	Steps	Details	Meets Step Therapy Criteria? Y/N
CVS	0	No Step	Y
Express Scripts	1	1 Triptan	Y
United	4	2 Triptans and Ubrelvy and Nurtec	N
OptumRx	4	2 Triptans and Ubrelvy and Nurtec	N
Cigna	N/A	Not Covered	N/A
Kaiser	0	No Step	Y
Anthem	N/A	Non-formulary	N/A
HCSC	1	1 Triptan	Y

Payer	Steps	Details	Meets Step Therapy Criteria? Y/N
MedImpact	1	1 Triptan	Y
Blue Shield CA	2	2 Triptans	Y
BCBS MI	4	2 Triptans and Ubrelvy and Nurtec	N
BCBS MA	N/A	Not covered	N/A
Premera	2	2 Triptans	Y
Highmark	2	2 Triptans	Y
Elixir	2	2 Triptans	Y
VHA	0	No Step	Y
Florida Blue HIX	1	1 Triptan	Y
Kaiser HIX	0	No Step	Y

N: no, N/A: not applicable, Y: yes

B10.5. Summary of Findings

Table B10.3. Reyvow Fair Access Criteria by Payer

Payer	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS	N/A	Y	Y	Y
Express Scripts	N/A	Y	Y	Y
United	N/A	Y	N	Y
OptumRx	N/A	Y	N	Y
Cigna	N/A	N/A	N/A	N/A
Kaiser	N/A	Y	Y	Y
Anthem	N/A	N/A	N/A	N/A
HCSC	N/A	Y	Y	Y
MedImpact	N/A	Y	Y	Y
Blue Shield CA	N/A	Y	Y	Y
BCBS MI	N/A	Y	N	N
BCBS MA	N/A	N/A	N/A	N/A
Premera	N/A	Y	Y	Y
Highmark	N/A	Y	Y	Y
Elixir	N/A	Y	Y	Y
VHA	N/A	Y	Y	Y
Florida Blue HIX	N/A	Y	Y	Y
Kaiser HIX	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B11. Policy Brief: Endari (L-glutamine), amino acid (oral)

B11.1. Condition: sickle cell disease, adults and pediatric patients aged 5 years and older

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: None

B11.2. Clinical Guidelines

Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014

American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain

B11.3. Background

FDA Label

Indication: ENDARI is an amino acid indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.

Dosing: 5 grams to 15 grams orally, twice daily based on body weight
Each dose of Endari should be mixed in 8 oz. (240 mL) of cold or room temperature beverage or 4 oz. to 6 oz. of food before ingestion

Warning: None.

Contraindications: None.

Interactions: None.

Clinical Trial Eligibility:

Key Inclusion Criteria:

- Patient is at least five years of age.
- Patient has been diagnosed with sickle cell anemia or sickle ß°-thalassemia (documented by hemoglobin electrophoresis).
- Patient has had at least two documented episodes of sickle cell crises within 12 months of the screening visit

Key Exclusion Criteria:

- Patient has prothrombin time INR > 2.0.
- Patient has serum albumin < 3.0 g/dl.
- Patient has received any blood products within three weeks of the Screening Visit.
- Patient has uncontrolled liver disease or renal insufficiency.

Link to label: https://www.endarirx.com/pi

ICER Policy Recommendations from the 2020 Sickle Cell Disease Review

Due to the COVID-19 pandemic, ICER's March 2020 public meeting on therapies for sickle cell disease was indefinitely postponed and no Key Recommendations were posted. Please refer to the sickle cell disease evidence report for the most updated findings.

Link to report: Adakveo, Oxbryta, and Endari for Sickle Cell Disease: Effectiveness and Value

B11.4. Findings: Coverage Policies

Policies or coverage information for Endari were available for 15 payers (CVS, Express Scripts, United, OptumRx, Kaiser, Anthem, HCSC, Blue Shield CA, BCBS MI, Highmark, Elixir, VHA, Florida Blue HIX, Kaiser HIX**,** MedImpact) under pharmacy benefits.

Endari was covered under pharmacy and medical benefit for two payers (Premera**,** BCBS MA).

Endari was not covered under any benefit for one payer (Cigna).

One payer (Anthem) has Endari listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Cost Sharing

Because Endari was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B11.1. Endari Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts	3 (Non-Preferred Brand)	N/A	N/A	N/A
United	3 (Non-Preferred Brand)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	N/A (Not Covered)	N/A	N/A	N/A
Kaiser	N/A (no tiering)	N/A	N/A	N/A
Anthem	Non-Formulary	N/A	N/A	N/A
HCSC	6 (Non-Preferred Specialty)	N/A	N/A	N/A
MedImpact	Not Available	N/A	N/A	N/A
Blue Shield CA	4 (Specialty)	N/A	N/A	N/A
BCBS MI	3 (Non-Preferred Brand)	N/A	N/A	N/A
BCBS MA	3 (Non-Preferred Brand)	N/A	N/A	N/A
Premera	3 (Non-Preferred Specialty)	N/A	N/A	N/A
Highmark	3 (Non-Preferred Brand)	N/A	N/A	N/A
Elixir	3 (Non-Preferred Brand)	N/A	N/A	N/A
VHA	N/A (No tiering)	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	N/A	N/A	N/A	N/A

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Five payers (CVS, Express Scripts, BCBS MA, Florida Blue HIX**,** VHA) do not have clinical eligibility requirements. This meets our clinical eligibility criteria.

Ten payers (Anthem**,** BCBS MI**,** Blue Shield CA**,** Elixir**,** HCSC**,** Highmark**,** MedImpact**,** OptumRx**,** Premera**,** United) clinical eligibility have some version of the following: patients 5 and older with a diagnosis of sickle cell disease and at least two episodes of sickle cell-related pain crises in the past 12 months. This meets our clinical eligibility criteria.

One payer (HCSC) included a more specific definition of not using in combination with Adakveo or Oxbryta. This meets our criteria because Adakveo and Oxbryta are both alternative disease-modifying agents and there is no clinical evidence indicating concurrent use would provide additional clinical benefit.

One payer (Anthem) has Endari listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Provider Qualifications

Three payers (OptumRx**,** Premera**,** Elixir) required specialist prescribing or consultation. This meets our provider qualifications criteria.

One payer (Anthem) has Endari listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Step Therapy

Six payers (Blue Shield CA, Elixir, HCSC, Premera, United, MedImpact) require concurrent use/treatment failure/intolerance of hydroxyurea. This meets our criteria step therapy because it is a recommended therapy in the National Heart, Lung, and Blood Institute's (NHLBI) 2014 guidelines for evidence-based management of sickle cell disease. The American Society of Hematology 2020 guidelines on management of sickle cell and acute and chronic pain suggest that there is a lack of comparative effectiveness data between hydroxyurea and other disease-modifying therapies and chronic transfusions to make a recommendation on the use of these agents in treatment of acute and chronic pain.

Three payers (United, BCBS MI, Highmark) have additional step therapy requiring therapeutic failure/intolerance to one over-the-counter Endari product. This meets our criteria for step therapy for an unfairly priced drug because there is no clinical evidence establishing clinical effectiveness or superiority over standard Endari dietary supplements.

One payer (Anthem) has Endari listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Table B11.2. Endari Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS Pharmacy	0	No Step	Y
Express Scripts Pharmacy	0	No Step	Y
United Pharmacy	2	Hydroxyurea and OTC L-glutamine	Y
OptumRx Pharmacy	0	No step	Y
Cigna	N/A	N/A	N/A
Kaiser Pharmacy	0	No Step	Y
Anthem Pharmacy	N/A	Non-formulary	N/A
HCSC Pharmacy	1	Hydroxyurea	Y
MedImpact Pharmacy	0	No Step	Y
Blue Shield CA Pharmacy	1	Hydroxyurea	Y
BCBS MI Pharmacy	2	Hydroxyurea and OTC L-glutamine	Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
BCBS MA			
Pharmacy	0	No Step	Y
Medical	0	No Step	Y
Premera			
Pharmacy	1	Hydroxyurea	Y
Medical	1	Hydroxyurea	Y
Highmark			
Pharmacy	2	Hydroxyurea and OTC L-glutamine	Y
Elixir			
Pharmacy	Y	Hydroxyurea	Y
VHA			
Pharmacy	0	No Step	Y
Florida Blue HIX			
Pharmacy	0	No Step	Y
Medical	0	No Step	Y
Kaiser HIX			
Pharmacy	0	No Step	Y

N: no, N/A: not applicable, ,ST: step therapy, Y: yes

B11.5. Summary of Findings

Table B11.3. Endari Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Pharmacy	N/A	Y	Y	Y
Express Scripts				
Pharmacy	N/A	Y	Y	Y
United				
Pharmacy	N/A	Y	Y	Y
OptumRx				
Pharmacy	N/A	Y	Y	Y
Cigna	N/A	N/A	N/A	N/A
Kaiser				
Pharmacy	N/A	Y	Y	Y
Anthem				
Pharmacy	N/A	N/A	N/A	N/A
HCSC				
Pharmacy	N/A	Y	Y	Y
MedImpact				
Pharmacy	N/A	Y	Y	Y
Blue Shield CA				
Pharmacy	N/A	Y	Y	Y
BCBS MI				
Pharmacy	N/A	Y	Y	Y
BCBS MA				
Pharmacy	N/A	Y	Y	Y
Medical				
Premera				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Pharmacy	N/A	Y	Y	Y
Elixir				
Pharmacy	N/A	Y	Y	Y
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B12. Policy Brief: Orkambi (Lumacaftor/ivacaftor), CFTR Modulator (oral)

B12.1. Condition: Cystic Fibrosis, homozygous for F508del mutation in *CFTR* gene

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: Symdeko, Kalydeco, Trikafta

B12.2. Clinical Guidelines

Cystic fibrosis: Treatment with CFTR modulators, UpToDate 2021

Cystic Fibrosis Foundation Pulmonary Guidelines 2018

B12.3. Background

FDA Label

Indication: For the treatment of cystic fibrosis (CF) in patients age 2 years and older who are homozygous for the F508del mutation in the CFTR gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene.

Dosing:

Pediatric patients age 2-5 years weighing <14 kg: one packet of granules (each containing lumacaftor 100 mg/ivacaftor 125 mg) mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours with fat-containing food.

Pediatric patients age 2-5 years and weighing ≥14 kg: one packet of granules (each containing lumacaftor 150 mg/ivacaftor 188 mg) mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours with fat-containing food.

Pediatric patients age 6-11 years: two tablets (each containing lumacaftor 100 mg/ivacaftor 125 mg) taken orally every 12 hours with fat-containing food.

Adults and pediatric patients age 12 years and older: two tablets (each containing lumacaftor 200 mg/ivacaftor 125 mg) taken orally every 12 hours with fat-containing food.

Reduce dose in patients with moderate or severe hepatic impairment. In patients taking strong CYP3A inhibitors, reduce ORKAMBI dose for the first week of treatment.

Warning:

Liver-related events: Elevated transaminases; Respiratory events: Chest discomfort, dyspnea, and respiration abnormal; Blood pressure: Increased blood pressure; Cataracts: Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with ORKAMBI and ivacaftor, a component of ORKAMBI. Patients with advanced liver disease: use with caution in these patients and only if the benefits are expected to outweigh the risks. Liver function decompensation, including liver failure leading to death, has been reported in CF patients with pre-existing cirrhosis with portal hypertension.

Contraindications: None.

Interactions: Use with sensitive CYP3A substrates or CYP3A substrates with a narrow therapeutic index may decrease systemic exposure of the medicinal products and co-administration is not recommended. Hormonal contraceptives should not be relied upon as an effective method of contraception and their use is associated with increased menstruation-related adverse reactions. Use with strong CYP3A inducers may diminish exposure of ivacaftor, which may diminish its effectiveness; therefore, co-administration is not recommended.

Clinical Trial Eligibility:

Trials 1 & 2: Patients with CF ages 12 and older homozygous for the *F508del* mutation, $ppFEV_1$ at screening between 40-90.

Link to label: https://pi.vrtx.com/files/uspi_lumacaftor_ivacaftor.pdf

ICER Policy Recommendations from the 2020 Cystic Fibrosis Report

No recommendations specific to Orkambi

Link to report: Modulator Treatments for Cystic Fibrosis: Effectiveness and Value

B12.4. Findings: Coverage Policies

Policies or coverage information for Orkambi were available for all 18 payers under pharmacy benefits.

Cost Sharing

Because Orkambi was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B12.1. Orkambi Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	3 (Non-Preferred Brand)	N/A	N/A	N/A
Kaiser	2 (Brand)	N/A	N/A	N/A
Anthem	Non-formulary	N/A	N/A	N/A
HCSC	6 (Non-Preferred Specialty)	N/A	N/A	N/A
MedImpact	2 (Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	4 (Specialty)	N/A	N/A	N/A
BCBS MI	2 (Preferred Brand)	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	3 (Non-Preferred Brand)	N/A	N/A	N/A
Highmark	3 (Non-Preferred Brand)	N/A	N/A	N/A
Elixir	3 (Non-Preferred Brand)	N/A	N/A	N/A
VHA	N/A (no tiering)	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Three payers (Kaiser, Kaiser HIX**,** VHA) do not have a clinical eligibility requirement. This meets our clinical eligibility criteria.

Fourteen payers (CVS, Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, Elixir, Florida Blue HIX) require some version of the following: A diagnosis of cystic fibrosis in an individual two years of age or older with documentation of two copies of the *F508del* mutation of the *CFTR* gene. This meets our clinical eligibility criteria.

Five payers (CVS, HCSC, BCBS MA, Elixir, Florida Blue HIX) include a more specific definition requiring that patients not use other ivacaftor-containing medications and one payer (Premera) additionally requires patients to have a liver function test below three times the upper limit of normal. This meets our criteria because it is consistent with the label's indication for Orkambi in treating cystic fibrosis.

One payer (Anthem) has Orkambi listed as non-formulary and was not evaluated on clinical eligibility criteria.

Provider Qualifications

Ten payers (CVS, Express Scripts, Kaiser, Anthem, Blue Shield CA, BCBS MA, Premera, Highmark, Florida Blue HIX, Kaiser HIX) do not require specialist prescribing or consultation. This meets our provider qualifications criteria.

Eight payers (Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, BCBS MI**,** Elixir) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Anthem) has Orkambi listed as non-formulary and was not evaluated on provider qualifications criteria.

Step Therapy

One payer (Anthem) has Orkambi listed as non-formulary and was not evaluated on step therapy criteria.

Step therapy is not required by any other payer. This meets our criteria for step therapy because it is in line with the FDA label.

Table B12.2. Orkambi Step Therapy by Payer

Payer*	Steps	Details	Meets ST Criteria? Y/N
CVS	0	No step	Y
Express Scripts	0	No step	Y
United	0	No step	Y
OptumRx	0	No step	Y
Cigna	0	No step	Y
Kaiser	0	No step	Y
Anthem	N/A	Non-formulary	N/A
HCSC	0	No step	Y
MedImpact	0	No step	Y
Blue Shield CA	0	No step	Y
BCBS MI	0	No step	Y
BCBS MA	0	No step	Y
Premera	0	No step	Y
Highmark	0	No step	Y
Elixir	0	No step	Y
VHA	0	No step	Y
Florida Blue HIX	0	No step	Y
Kaiser HIX	0	No step	Y

N: no, N/A: not applicable, ST: step therapy, Y: yes

* All payers covered under pharmacy benefit only

B12.5. Summary of Findings

Table B12.3. Orkambi Fair Access Criteria by Payer

Payer*	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS	N/A	Y	Y	Y
Express Scripts	N/A	Y	Y	Y
United	N/A	Y	Y	Y
OptumRx	N/A	Y	Y	Y
Cigna	N/A	Y	Y	Y
Kaiser	N/A	Y	Y	Y
Anthem	N/A	N/A	N/A	N/A
HCSC	N/A	Y	Y	Y
MedImpact	N/A	Y	Y	Y
Blue Shield CA	N/A	Y	Y	Y
BCBS MI	N/A	Y	Y	Y
BCBS MA	N/A	Y	Y	Y
Premera	N/A	Y	Y	Y
Highmark	N/A	Y	Y	Y
Elixir	N/A	Y	Y	Y
VHA	N/A	Y	Y	Y
Florida Blue HIX	N/A	Y	Y	Y
Kaiser HIX	N/A	Y	Y	Y

N/A: not applicable, Y: yes

* All payers covered under pharmacy benefit only

B13. Policy Brief: Nurtec (rimegepant), CGRP Inhibitor (oral)

B13.1. Condition: Acute migraine, adults

Is Drug Cost-Effective at Current Prices?: Yes

Other Drugs in Class: Ubrelvy and Reyvow

B13.2. Clinical Guidelines

The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice (2018)

B13.3. Background

FDA Label

Indication: acute treatment of migraine with or without aura in adults

Dosing: 75 mg taken orally, as needed, not to exceed 75mg in a 24-hour period

Warning: Hypersensitivity Reactions: If a serious hypersensitivity reaction occurs, discontinue NURTEC ODT and initiate appropriate therapy. Severe hypersensitivity reactions have included dyspnea and rash, and can occur days after administration.

Contraindications: Patients with a history of hypersensitivity reaction to rimegepant, NURTEC ODT, or to any of its components.

Interactions: Strong CYP3A4 Inhibitors: avoid concomitant administration; moderate CYP3A4 Inhibitors: avoid another dose within 48 hours when administered with a moderate CYP3A4 inhibitor; strong and moderate CYP3A Inducers: avoid concomitant administration; Inhibitors of P-gp or BCRP: avoid concomitant administration.

Clinical Trial Eligibility: The efficacy of NURTEC ODT for the acute treatment of migraine with and without aura in adults was demonstrated in a randomized, double-blind, placebo-controlled trial: Study 1 (NCT03461757). The study randomized patients to 75 mg of NURTEC ODT (N=732) or placebo (N=734). Patients were instructed to treat a migraine of moderate to severe headache pain intensity. Rescue medication (i.e., NSAIDs, acetaminophen, and/or an antiemetic) was allowed 2 hours after the initial treatment. Other forms of rescue medication such as triptans were not allowed within 48 hours of initial treatment. Approximately 14% of patients were taking preventive medications for migraine at baseline. The average age of participants was 40 and the majority were female. None of the patients in Study 1 were on concomitant preventive medication that act on the CGRP pathway.

Link to label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212728s000lbl.pdf

ICER Policy Recommendations from the 2020 Acute Treatments for Migraine Report

Given that the evidence of response to these newer agents does not suggest they are superior to triptans, clinical experts, patient advocates, and manufacturers agreed that requiring patients to try triptans first before receiving coverage for the newer agents is reasonable if patients are clinically eligible. For patients who are eligible to try triptans, there is no evidence-based basis for a threshold number of different triptans that should be tried to determine whether adequate treatment is achieved. Clinical experts and patient advocates acknowledge that many patients find adequate relief with one triptan even after finding other triptans inadequate. The likelihood of finding a triptan that works does diminish after each trial, however, so a requirement of trying 1-2 triptans was viewed as reasonable whereas requiring more was viewed as less reasonable. Trying to devise a metric for "inadequate" response by looking at rescue medication use or other factors was not viewed as clinically reasonable.
For Ubrelvy and Nurtec, given their similar mechanisms of action and available evidence suggesting no major differences in safety or effectiveness, it is not unreasonable for payers to negotiate lower prices by offering preferential formulary status to one or the other drug, including the possibility of exclusion of one of the drugs. If only one drug is covered, however, clinicians and patients should have the ability to appeal for coverage for the other gepant drug should a trial of the favored drug not produce adequate success.
The Food and Drug Administration (FDA) indication for Ubrelvy includes acute treatment of all adults with migraine, with or without aura. We anticipate the same broad language will be used should Nurtec be approved. Clinical trials for both agents included a narrower spectrum of adults: patients generally had a long history of migraine with a high frequency and intensity of symptoms. On average, over 80% were female, with an average age of 40 years, having had migraines for approximately 20 years, with 3-5 migraine attacks per month of a moderate (70%) or severe (30%) intensity. About 20-25% of trial participants were receiving medications to prevent migraine attacks. Clinical experts and patient advocates suggest that although the clinical trial populations were more severely affected, on average, than all patients with migraine, there is no evidence-based reason to try to limit coverage based on some metric of severity such as number of migraines per month.

Link to report: Acute Treatments for Migraine: Final Evidence Report

B13.4. Findings: Coverage Policies

Policies or coverage information Nurtec were available for all 18 payers under pharmacy benefits.

Cost Sharing

Eleven payers (CVS, United, OptumRx**,** MedImpact**,** Cigna, Anthem, HCSC, BCBS MI, BCBS MA, Elixir, Florida Blue HIX) place Nurtec on a Preferred Brand tier, the lowest relevant tier. This meets our cost-sharing criteria.

Six payers (Kaiser**,** Kaiser HIX**,** Express Scripts, Blue Shield CA, Premera, Highmark) do not have Nurtec placed on the lowest relevant tier nor do they nor do they have an alternative in the class (Ubrelvy) or

reasonable alternative treatment (Reyvow) on the lowest relevant tier. This does not meet our cost-sharing criteria because at least one alternative in class needs to be on the lowest relevant tier.

Table B13.1. Nurtec Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	2 (Preferred Brand)	Y	N/A	Y
Express Scripts	3 (Non-Preferred Brand)	N	2 (Preferred Brand), none	N
United	2 (Preferred Brand)	Y	N/A	Y
OptumRx	2 (Preferred Brand)	Y	N/A	Y
Cigna	2 (Preferred Brand)	Y	N/A	Y
Kaiser	Non-Formulary	N	2 (Preferred Brand), none	N
Anthem	2 (Preferred Brand)	Y	N/A	Y
HCSC	3 (Preferred Brand)	Y	N/A	Y
MedImpact	2 (Preferred Brand)	Y	N/A	Y
Blue Shield CA	4 (Specialty)	N	2 (Preferred Brand), none	N
BCBS MI	2 (Preferred Brand)	Y	N/A	Y
BCBS MA	2 (Preferred Brand)	Y	N/A	Y
Premera	3 (Non-Preferred Brand)	N	2 (Preferred Brand), none	N
Highmark	3 (Non-Preferred Brand)	N	2 (Preferred Brand), none	N
Elixir	2 (Preferred Brand)	Y	N/A	Y
VHA	Not applicable	N/A	N/A	Y
Florida Blue HIX	5 (Preferred Brand)	Y	N/A	Y
Kaiser HIX	Non-Formulary	N	2 (Preferred Brand), none	N

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three Payers (Kaiser, Kaiser HIX, VHA) do not require clinical eligibility criteria. This meets our requirement, as it is not a restrictive policy.

Clinical eligibility information is available for 16 payers (CVS, Blue Shield CA, Express Scripts, Highmark, Premera, BCBS MA, Anthem, BCBS MI, Cigna, Elixir, Florida Blue HIX, HCSC, MedImpact, VHA, OptumRx, United) under the pharmacy benefit. All payers require some version of the following: adults with acute migraine. This meets our clinical eligibility criteria.

Four payers (Elixir, OptumRx, United, HCSC) include a requirement of current use of prophylactic therapy OR <4 migraine days/month OR ≥4 migraine days per month and has contraindication or intolerance to prophylactic therapies. This meets our criteria because it is consistent with the definition of acute migraine and suggested use of prophylactic therapies according to the American Headache Society Consensus Statement.

Provider Qualifications

Fifteen payers (CVS, Express Scripts, Cigna, Kaiser, Anthem, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, Elixir, Florida Blue HIX, Kaiser HIX) do not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Three payers (United, OptumRx, VHA) require prescribing by or in consultation with a specialist (headache specialist, neurologist, or pain specialist). This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

Step Therapy

Three payers (Kaiser, CVS, Kaiser HIX) do not require step therapy. This meets our step therapy criteria.

Fifteen payers (Elixir, Express Scripts, United, OptumRx, Cigna, Anthem, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, VHA, Florida Blue HIX) require inadequate response or intolerance to one or two generic triptans. This meets our step therapy criteria because triptans are appropriate for most patients and patients have a reasonable chance to meet their clinical goals with triptans.

Table B13.2. Nurtec Step Therapy by Payer

Payer*	Steps	Details	Meets ST Criteria? Y/N
CVS	0	No Step	Y
Express Scripts	1	1 Triptan	Y
United	2	2 Triptans	Y
OptumRx	2	2 Triptans	Y
Cigna	1	1 Triptan	Y
Kaiser	0	No Step	Y
Anthem	2	2 Triptans	Y
HCSC	1	1 Triptan	Y
MedImpact	1	1 Triptan	Y
Blue Shield CA	2	2 Triptans	Y
BCBS MI	2	2 Triptans	Y
BCBS MA	2	2 Triptans	Y
Premera	2	2 Triptans	Y
Highmark	2	2 Triptans	Y
Elixir	2	2 Triptans	Y
VHA	2	2 Triptans	Y
Florida Blue HIX	1	1 Triptan	Y
Kaiser HIX	0	No Step	Y

M: medical, P: pharmacy, ST: step therapy, Y: yes

* All payers covered under pharmacy benefit only

B13.5. Summary of Findings

Table B13.3. Nurtec Fair Access Criteria by Payer

Payer*	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS	Y	Y	Y	Y
Express Scripts	N	Y	Y	Y
United	Y	Y	Y	Y
OptumRx	Y	Y	Y	Y
Cigna	Y	Y	Y	Y
Kaiser	N	Y	Y	Y
Anthem	Y	Y	Y	Y
HCSC	Y	Y	Y	Y
MedImpact	Y	Y	Y	Y
Blue Shield CA	N	Y	Y	Y
BCBS MI	Y	Y	Y	Y
BCBS MA	Y	Y	Y	Y
Premera	N	Y	Y	Y
Highmark	N	Y	Y	Y
Elixir	Y	Y	Y	Y
VHA	Y	Y	Y	Y
Florida Blue HIX	Y	Y	Y	Y
Kaiser HIX	N	Y	Y	Y

N: no, Y: yes

* All payers covered under pharmacy benefit only

B14. Policy Brief: Symdeko (Tezacaftor/Ivacaftor), CFTR Modulator (oral)

B14.1. Condition: Cystic Fibrosis

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: Orkambi, Kalydeco, Trikafta

B14.2. Clinical Guidelines

Cystic fibrosis: Treatment with CFTR modulators, UpToDate 2021

Cystic Fibrosis Foundation Pulmonary Guidelines 2018

B14.3. Background

FDA Label

Indication: For the treatment of cystic fibrosis (CF) in patients age 6 years and older who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.

Dosing:

Pediatric patients age 6 to less than 12 years weighing < 30 kg: one tablet (containing tezacaftor 50 mg/ivacaftor 75 mg) in the morning and one tablet (containing ivacaftor 75 mg) in the evening, approximately 12 hours apart. SYMDEKO should be taken with fat-containing food.

Adults and pediatric patients age ≥12 years or **pediatric patients age 6 to less than 12 years weighing ≥30 kg**: one tablet (containing tezacaftor 100 mg/ivacaftor 150 mg) in the morning and one tablet (containing ivacaftor 150 mg) in the evening, approximately 12 hours apart. SYMDEKO should be taken with fat-containing food.

Reduce dose in patients with moderate and severe hepatic impairment.

Warning: Elevated transaminases (ALT or AST); Use with CYP3A inducers: Concomitant use with strong CYP3A inducers (e.g., rifampin, St. John's wort) substantially decrease exposure of ivacaftor and may decrease the exposure of tezacaftor, which may reduce therapeutic effectiveness; Cataracts: Non-congenital lens opacities/cataracts have been reported in pediatric patients.

Elevated transaminases: Dosing should be interrupted in patients with significant elevations of transaminases, e.g., patients with ALT or AST >5 x upper limit of normal (ULN), or ALT or AST >3 x ULN with bilirubin >2 x ULN.

Contraindications: None.

Interactions: CYP3A inhibitors: Reduce SYMDEKO dose when co-administered with strong (e.g., ketoconazole) or moderate (e.g., fluconazole) CYP3A inhibitors. Avoid food containing grapefruit.

Clinical Trial Eligibility:

Trial 1: Patient with CF who were homozygous for F508del mutation; ages 12 years and older

Trial 2: Patient with CF who were heterozygous for F508del mutation and a second CFTR mutation predicted to be responsive to tezacaftor/ivacaftor; ages 12 years and older

Trial 3: Patient with CF who were heterozygous for F508del mutation and a second CFTR mutation predicted to be responsive to tezacaftor/ivacaftor; ages 12 years and older

Patients had a ppFEV[1] at screening between **40-90%** of normal.

Patients that "had 2 or more abnormal liver function tests at screening (ALT, AST, AP, GGT =3 x ULN or total bilirubin =2 x ULN) or AST or ALT =5 x ULN, were excluded from the trials."

Link to label: https://pi.vrtx.com/files/uspi_tezacaftor_ivacaftor.pdf

ICER Policy Recommendations from the 2020 Cystic Fibrosis Report

No recommendations specific to Symdeko

Link to report: Modulator Treatments for Cystic Fibrosis: Effectiveness and Value

B14.4. Findings: Coverage Policies

Policies or coverage information for Symdeko were available for all 18 payers under pharmacy benefits.

Cost Sharing

Because Symdeko was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B14.1. Symdeko Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	3 (Non-Preferred Brand)	N/A	N/A	N/A
Kaiser	2 (Brand)	N/A	N/A	N/A
Anthem	Non-formulary	N/A	N/A	N/A
HCSC	5 (Preferred Specialty)	N/A	N/A	N/A
MedImpact	2 (Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	4 (Specialty)	N/A	N/A	N/A
BCBS MI	2 (Preferred Brand)	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	2 (Preferred Brand)	N/A	N/A	N/A
Highmark	3 (Non-Preferred Brand)	N/A	N/A	N/A
Elixir	2 (Preferred Brand)	N/A	N/A	N/A
VHA	N/A (no tiering)	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Three payers (Kaiser, Kaiser HIX**,** VHA) do not have a clinical eligibility requirement. This meets our clinical eligibility criteria.

Fourteen payers (CVS, Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, Elixir, Florida Blue HIX) require some version of the following: A diagnosis of cystic fibrosis in an individual six years of age or older with documentation of two copies of the *F508del* mutation or at least one other mutation in the *CFTR* gene. This meets our clinical eligibility criteria.

Five payers (CVS, Blue Shield CA, BCBS MA, Elixir, Florida Blue HIX) include a more specific definition requiring patients to not use other ivacaftor-containing medications and one payer (Premera) additionally requires patients to have a liver function test below three times the upper limit of normal. These requirements meet our criteria because they are consistent with the label's indication for Symdeko in treating cystic fibrosis.

One payer (Anthem) has Symdeko listed as non-formulary and was not evaluated on clinical eligibility criteria.

Provider Qualifications

Eleven payers (CVS, Kaiser, Anthem, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, Florida Blue HIX, Kaiser HIX) do not require specialist prescribing or consultation. This meets our provider qualifications criteria.

Seven payers (Express Scripts, United, OptumRx, Cigna, HCSC**,** MedImpact**,** Elixir) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Anthem) has Symdeko listed as non-formulary and was not evaluated on provider requirement criteria.

Step Therapy

One payer (Anthem) has Symdeko listed as non-formulary and was not evaluated on step therapy criteria.

Step therapy is not required by any other payer. This meets our criteria for step therapy because it is in line with the FDA label.

Table B14.2. Symdeko Step Therapy by Payer

Payer*	Steps	Details	Meets ST Criteria? Y/N
CVS	0	No step	Y
Express Scripts	0	No step	Y
United	0	No step	Y
OptumRx	0	No step	Y
Cigna	0	No step	Y
Kaiser	0	No step	Y
Anthem	N/A	Non-formulary	N/A
HCSC	0	No step	Y
MedImpact	0	No step	Y
Blue Shield CA	0	No step	Y
BCBS MI	0	No step	Y
BCBS MA	0	No step	Y
Premera	0	No step	Y
Highmark	0	No step	Y
Elixir	0	No step	Y
VHA	0	No step	Y
Florida Blue HIX	0	No step	Y
Kaiser HIX	0	No step	Y

N: no, N/A: not applicable, ST: step therapy, Y: yes

* All payers covered under pharmacy benefit only

B14.5. Summary of Findings

Table B14.3. Symdeko Fair Access Criteria by Payer

Payer*	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS	N/A	Y	Y	Y
Express Scripts	N/A	Y	Y	Y
United	N/A	Y	Y	Y
OptumRx	N/A	Y	Y	Y
Cigna	N/A	Y	Y	Y
Kaiser	N/A	Y	Y	Y
Anthem	N/A	N/A	N/A	N/A
HCSC	N/A	Y	Y	Y
MedImpact	N/A	Y	Y	Y
Blue Shield CA	N/A	Y	Y	Y
BCBS MI	N/A	Y	Y	Y
BCBS MA	N/A	Y	Y	Y
Premera	N/A	Y	Y	Y
Highmark	N/A	Y	Y	Y
Elixir	N/A	Y	Y	Y
VHA	N/A	Y	Y	Y
Florida Blue HIX	N/A	Y	Y	Y
Kaiser HIX	N/A	Y	Y	Y

N/A: not applicable, Y: yes

* All payers covered under pharmacy benefit only

B15. Policy Brief: Xeljanz (tofacitinib), JAK Inhibitor (oral)

B15.1. Condition: Ulcerative colitis, moderate-to-severe

Is Drug Cost-Effective at Current Price?: No

Other Drugs in Class: Humira, Simponi, Remicade, Renflexis, Inflectra, Stelara, Entyvio

B15.2. Clinical Guidelines

2020 AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

2019 ACG Clinical Guideline: Ulcerative Colitis in Adults

B15.3. Background

FDA Label

Indication: treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response or intolerance to one or more TNF blockers.

Dosing: Induction: XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily for 8 weeks; Maintenance: XELJANZ 5 mg twice daily or XELJANZ XR 11 mg once daily.

Warning: Black box warning for increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including tuberculosis (TB); higher rate of all-cause mortality, including sudden cardiovascular death; higher rate of lymphomas and lung cancers; higher rate of MACE; and thrombosis.

Contraindications: None.

Interactions: Strong CP3A4 inhibitors, moderate CYP3A4 inhibitors coadministered with strong CYP2C19 inhibitors, strong CYP3A4 inducers, and immunosuppressive drugs

Clinical Trial Eligibility: In two identical induction trials (UC-I and UC-II), 1139 patients were randomized (598 and 541 patients, respectively) to XELJANZ 10 mg twice daily or placebo with a 4:1 treatment allocation ratio. These trials included adult patients with moderately to severely active UC (total Mayo score of 6 to 12, with an endoscopy subscore of at least 2, and rectal bleeding subscore of at least 1) and who had failed or were intolerant to at least 1 of the following treatments: oral or intravenous corticosteroids, azathioprine, 6-MP or TNF blocker.

Link to label: https://labeling.pfizer.com/ShowLabeling.aspx?id=959#section-13.4

Insurance coverage should be structured to prevent situations in which patients are forced to choose a treatment approach on the basis of cost.
Because there are no clear biomarkers or predictors of the success for any given treatment in UC, it is not unreasonable to consider prior authorization criteria in order to manage the costs of expensive medications and negotiate prices for TIMs priced beyond a fair range. However, prior authorization criteria should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers.
Patients eligible for TIMs include those with moderate-to-severe UC whose disease has had an inadequate response to conventional systemic therapy. Patient eligibility criteria should be flexible given that clinical trials used tools (e.g., Mayo Score for disease severity) that are not routinely used in clinical practice.
Given the lack of biomarkers and other predictors of TIM treatment success in UC, it is not unreasonable to use step therapy in this case to manage the costs of treatment.
TIM therapy should be prescribed and managed by gastroenterologists with specific training and expertise in UC.

Link to report: Targeted Immune Modulators for Ulcerative Colitis: Effectiveness and Value

B15.4. Findings: Coverage Policies

Policies for Xeljanz were available for 13 (Express Scripts, United, OptumRx, Cigna, Anthem, HCSC, MedImpact, BCBS MI, Premera, Highmark, Elixir, VHA, Florida Blue HIX) under the pharmacy benefit and five payers (CVS, Kaiser, Blue Shield CA, BCBS MA, Kaiser HIX) under both the pharmacy and medical benefits.

Cost Sharing

Because Xeljanz was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B15.1. Xeljanz Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	2 (Preferred Brand)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	2 (Preferred Brand)	N/A	N/A	N/A
Cigna	2 (Preferred Brand)	N/A	N/A	N/A
Kaiser	2 (Brand)	N/A	N/A	N/A
Anthem	4 (Specialty)	N/A	N/A	N/A
HCSC	5 (Preferred Specialty)	N/A	N/A	N/A
MedImpact	2 (Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	4 (Specialty)	N/A	N/A	N/A
BCBS MI	2 (Preferred Brand)	N/A	N/A	N/A
BCBS MA	3 (Non-Preferred Brand)	N/A	N/A	N/A
Premera	2 (Preferred Brand)	N/A	N/A	N/A
Highmark	2 (Preferred Brand)	N/A	N/A	N/A
Elixir	2 (Preferred Brand)	N/A	N/A	N/A
VHA	Not applicable	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N/A	N/A	N/A

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three Payers (Kaiser**,** Kaiser HIX**,** VHA) do not require clinical eligibility criteria. This meets our requirement, as it is not a restrictive policy.

Eleven payers (CVS, Express Scripts, United, OptumRx, Anthem, HCSC, MedImpact, BCBS MA, Highmark, VHA, Florida Blue HIX) require a diagnosis of some version of the following: moderately to severely active ulcerative colitis. Four payers (Blue Shield CA, BCBS MI**,** Elixir**,** Premera) require a diagnosis of just ulcerative colitis. These requirements meet our criteria for clinical eligibility because the FDA label specifies that Xeljanz is indicated for moderate-to-severe ulcerative colitis.

Twelve payers (CVS, Express Scripts, United, Cigna, Anthem, HCSC, MedImpact, BCBS MI, Premera, Highmark, Elixir, Florida Blue HIX) also specify that patients be aged 18 or over to access Xeljanz. This meets our criteria because it is consistent with the age restriction in the FDA label.

One payer (BCBS MA), requires a trial of 2 conventional agents from a list of steroids, 5-ASAs, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended in clinical guidelines.

Provider Qualifications

Six payers (CVS, Kaiser, Anthem, Blue Shield CA, BCBS MI, Kaiser HIX) do not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Twelve payers (Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, BCBS MA, Premera, Highmark, Elixir, VHA, Florida Blue HIX) require prescribing by or in consultation with a gastroenterologist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

Step Therapy

Two payers (Kaiser, Kaiser HIX) do not require step therapy. This meets our criteria for step therapy.

Eight payers (Anthem, BCBS MI, Elixir, Florida Blue HIX, HCSC, OptumRx, MedImpact, United) require step therapy through some combination of conventional therapy, preferred biologic therapies, and TNF inhibitors. This meets our criteria for step therapy because the FDA label states that Xeljanz is indicated for patients with "moderately to severely active ulcerative colitis (UC), who have had an inadequate response or intolerance to one or more TNF blockers." In addition, the 2019 ACG Clinical Guidelines recommend oral systemic corticosteroids, TNF inhibitors (Humira, Simponi, or Remicade), Entyvio, or Xeljanz for induction of remission in moderately-to-severely active UC.

Table B15.2. Xeljanz Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS			
Pharmacy	0	P: One biologic OR one TNF inhibitor*	Y
Medical	1	M: Humira AND one biologic or one TNF inhibitor*	Y
Express Scripts			
Pharmacy	0	One TNF inhibitor	Y
United		One conventional therapy or one biologic, AND two	
Pharmacy	2	of: Humira, Simponi, and/or Stelara	Y
OptumRx			
Pharmacy	1	One conventional therapy AND one TNF inhibitor	Y
Cigna			
Pharmacy	1	One TNF inhibitor AND Humira	Y
Kaiser		No steps	
Pharmacy	0		Y
Medical	0		Y
Anthem		One conventional therapy AND one TNF inhibitor	
Pharmacy	2	AND two preferred biologics (Humira, Simponi, Stelara)	Y
HCSC		One conventional therapy OR one biologic AND	
Pharmacy	1	Humira or Stelara	Y
MedImpact			
Pharmacy	0	One conventional therapy AND Humira	Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
Blue Shield CA		One TNF inhibitor	
Pharmacy	0		Y
Medical	0		Y
BCBS MI			
Pharmacy	0-1	One conventional therapy AND Humira or Stelara	Y
BCBS MA		Two conventional therapies AND Humira	
Pharmacy	2		Y
Medical	2		Y
Premera			
Pharmacy	0	Humira	Y
Highmark			
Pharmacy	0	Humira	Y
Elixir			
Pharmacy	1	One conventional therapy AND Humira	Y
VHA			
Pharmacy	1	One TNF inhibitor OR Entyvio	Y
Florida Blue HIX		One conventional therapy OR one biologic AND	
Pharmacy	1	Humira or Stelara	Y
Kaiser HIX		No steps	
Pharmacy	0		Y
Medical	0		Y

M: medical, P: pharmacy, ST: step therapy, Y: yes

*Unless patient has been hospitalized for acute, severe UC

Note: Because moderate-to-severe UC is defined as being dependent on corticosteroids, step therapy with one conventional therapy is not counted as a step. Xeljanz is indicated for patients who have had an inadequate response or intolerance to at least one TNF blocker, so step therapy through one TNF blocker is also not counted as a step.

B15.5. Summary of Findings

Table B15.3. Xeljanz Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Express Scripts				
Pharmacy	N/A	Y	Y	Y
United	N/A	Y	Y	Y
Pharmacy				
OptumRx				
Pharmacy	N/A	Y	Y	Y
Cigna				
Pharmacy	N/A	Y	Y	Y
Kaiser				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N/A	Y	Y	Y
HCSC				
Pharmacy	N/A	Y	Y	Y
MedImpact				
Pharmacy	N/A	Y	Y	Y
Blue Shield CA				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
BCBS MI				
Pharmacy	N/A	Y	Y	Y
BCBS MA				
Pharmacy	N/A	N	Y	Y
Medical	N/A	N	Y	Y
Premera				
Pharmacy	N/A	Y	Y	Y
Highmark				
Pharmacy	N/A	Y	Y	Y
Elixir				
Pharmacy	N/A	Y	Y	Y
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Pharmacy	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B16. Policy Brief: Ubrelvy (Ubrogepant), CGRP Inhibitor (oral)

B16.1. Condition: Acute migraine, adults

Is Drug Cost-Effective at Current Prices?: Yes

Other Drugs in Class: Nurtec, Reyvow

B16.2. Clinical Guidelines

The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice (2018)

B16.3. Background

FDA Label

Indication: acute treatment of migraine with or without aura in adults

Dosing: The recommended dose is 50 mg or 100 mg taken orally, as needed. If needed, a second dose may be administered at least 2 hours after the initial dose. The maximum dose in a 24-hour period is 200 mg.

Warning: none

Contraindications: Concomitant use with strong CYP3A4 inhibitors.

Interactions: Strong CYP3A4 Inducers: Should be avoided as concomitant use will result in reduction of ubrogepant exposure

Clinical Trial Eligibility: The efficacy of UBRELVY for the acute treatment of migraine was demonstrated in two randomized, double blind, placebo-controlled trials [Study 1 (NCT02828020) and Study 2 (NCT02867709)]. Study 1 randomized patients to placebo (n=559) or UBRELVY 50 mg (n=556) or 100 mg (n=557) and Study 2 randomized patients to placebo (n=563) or UBRELVY 50 mg (n=562). In all studies, patients were instructed to treat a migraine with moderate to severe headache pain intensity. A second dose of study medication (UBRELVY or placebo), or the patient's usual acute treatment for migraine, was allowed between 2 to 48 hours after the initial treatment for a non-responding or recurrent migraine headache. Up to 23% of patients were taking preventive medications for migraine at baseline. None of these patients were on concomitant preventive medication that act on the CGRP pathway.

Link to label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211765s000lbl.pdf

ICER Policy Recommendations from the 2020 Acute Treatments for Migraine Report

Given that the evidence of response to these newer agents does not suggest they are superior to triptans, clinical experts, patient advocates, and manufacturers agreed that requiring patients to try triptans first before receiving coverage for the newer agents is reasonable if patients are clinically eligible. For patients who are eligible to try triptans, there is no evidence-based basis for a threshold number of different triptans that should be tried to determine whether adequate treatment is achieved. Clinical experts and patient advocates acknowledge that many patients find adequate relief with one triptan even after finding other triptans inadequate. The likelihood of finding a triptan that works does diminish after each trial, however, so a requirement of trying 1-2 triptans was viewed as reasonable whereas requiring more was viewed as less reasonable. Trying to devise a metric for "inadequate" response by looking at rescue medication use or other factors was not viewed as clinically reasonable.
For Ubrelvy and Nurtec, given their similar mechanisms of action and available evidence suggesting no major differences in safety or effectiveness, it is not unreasonable for payers to negotiate lower prices by offering preferential formulary status to one or the other drug, including the possibility of exclusion of one of the drugs. If only one drug is covered, however, clinicians and patients should have the ability to appeal for coverage for the other gepant drug should a trial of the favored drug not produce adequate success.
The Food and Drug Administration (FDA) indication for Ubrelvy includes acute treatment of all adults with migraine, with or without aura. We anticipate the same broad language will be used should Nurtec be approved. Clinical trials for both agents included a narrower spectrum of adults: patients generally had a long history of migraine with a high frequency and intensity of symptoms. On average, over 80% were female, with an average age of 40 years, having had migraines for approximately 20 years, with 3-5 migraine attacks per month of a moderate (70%) or severe (30%) intensity. About 20-25% of trial participants were receiving medications to prevent migraine attacks. Clinical experts and patient advocates suggest that although the clinical trial populations were more severely affected, on average, than all patients with migraine, there is no evidence-based reason to try to limit coverage based on some metric of severity such as number of migraines per month.

Link to report: Acute Treatments for Migraine: Final Evidence Report

B16.4. Findings: Coverage Policies

Policies for Ubrelvy were available for all 18 payers under pharmacy benefits.

Cost Sharing

Ten payers (CVS, United, OptumRx, Cigna, MedImpact, HCSC, BCBS MI, BCBS MA, Elixir, Florida Blue HIX) place Ubrelvy on a Preferred Brand tier, the lowest relevant tier. Ubrelvy is non-formulary for Anthem, however, Nurtec is covered on a Preferred Brand tier, the lowest relevant tier. This meets our cost-sharing criteria.

Four payers (Express Scripts, Blue Shield CA, Premera, Highmark) do not have Ubrelvy placed on the lowest relevant tier nor do they have an alternative in class (Nurtec) or reasonable alternative (Reyvow) on the lowest relevant tier. Ubrelvy is non-formulary for Kaiser and Kaiser HIX, and no

reasonable alternative is covered on the lowest relevant tier. This does not meet our cost-sharing criteria because at least one alternative in class needs to be on the lowest relevant tier.

Table B16.1. Ubrelvy Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	2 (Preferred Brand)	Y	N/A	Y
Express Scripts	3 (Non-Preferred Brand)	N	2, Preferred Brand, None	N
United	2 (Preferred Brand)	Y	N/A	Y
OptumRx	2 (Preferred Brand)	Y	N/A	Y
Cigna	2 (Preferred Brand)	Y	N/A	Y
Kaiser	N/A (no tiering)	N	2, Preferred Brand, None	N
Anthem	Non-Formulary	N	2, Preferred Brand, Nurtec	Y
HCSC	3 (Preferred Brand)	Y	N/A	Y
MedImpact	2 (Preferred Brand)	Y	N/A	Y
Blue Shield CA	4 (Specialty)	N	2, Preferred Brand, None	N
BCBS MI	2 (Preferred Brand)	Y	N/A	Y
BCBS MA	2 (Preferred Brand)	Y	N/A	Y
Premera	3 (Non-Preferred Brand)	N	2, Preferred Brand, None	N
Highmark	3 (Non-Preferred Brand)	N	2, Preferred Brand, None	N
Elixir	2 (Preferred Brand)	Y	N/A	Y
VHA	Not applicable	N/A	N/A	Y
Florida Blue HIX	5 (Preferred Brand)	Y	N/A	Y
Kaiser HIX	N/A (no tiering)	N	2, Preferred Brand, None	N

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three Payers (Kaiser, Kaiser HIX, VHA) do not require clinical eligibility criteria. This meets our requirement, as it is not a restrictive policy.

Clinical eligibility information is available for 15 payers (Express Scripts, Highmark, Premera, Blue Shield CA, VHA, BCBS MA, BCBS MI, Cigna, CVS, Elixir, Florida Blue HIX, HCSC, MedImpact, OptumRx, United) under the pharmacy benefit. All payers require some version of the following: adults with acute migraine. This meets our clinical eligibility criteria.

Three payers (United, OptumRx, HCSC) include a requirement of current use of prophylactic therapy OR <4 migraine days/month OR ≥4 migraine days per month and has contraindication or intolerance to prophylactic therapies. This meets our criteria because it is consistent with the definition of acute migraine and suggested use of prophylactic therapies according to the American Headache Society Consensus Statement.

One payer (Anthem) has Ubrelvy listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Provider Qualifications

Fourteen payers (CVS, Express Scripts, Cigna, Kaiser, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, Elixir, Florida Blue HIX, Kaiser HIX) do not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Three payers (United, OptumRx, VHA) require prescribing by or in consultation with a specialist (headache specialist, neurologist, or pain specialist). This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Anthem) has Ubrelvy listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Step Therapy

Two payers (Kaiser, Kaiser HIX) do not require step therapy. This meets our step therapy criteria.

Fourteen payers (CVS, Express Scripts, United, OptumRx, Cigna, HCSC, MedImpact, Blue Shield CA, BCBS MI, BCBS MA, Premera, Highmark, VHA, Florida Blue HIX) require inadequate response or intolerance to one or two generic triptans. This meets our step therapy criteria because triptans are appropriate for most patients and patients have a reasonable chance to meet their clinical goals with triptans.

One payer (Anthem) has Ubrelvy listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Table B16.2. Ubrelvy Step Therapy by Payer

Payer*	Steps	Details	Meets ST Criteria? Y/N
CVS	2	2 Triptans	Y
Express Scripts	1	1 Triptan	Y
United	2	2 Triptans	Y
OptumRx	2	2 Triptans	Y
Cigna	1	1 Triptan	Y
Kaiser	0	No Step	Y
Anthem	N/A	Non-formulary	N/A
HCSC	1	1 Triptan	Y
MedImpact	1	1 Triptan	Y
Blue Shield CA	2	2 Triptans	Y
BCBS MI	2	2 Triptans	Y
BCBS MA	2	2 Triptans	Y
Premera	2	2 Triptans	Y
Highmark	2	2 Triptans	Y
Elixir	2	2 Triptans	Y
VHA	2	2 Triptans	Y
Florida Blue HIX	1	1 Triptan	Y
Kaiser HIX	0	No Step	Y

M: medical, P: pharmacy, ST: step therapy, Y: yes

* All payers covered under pharmacy benefit only

B16.5. Summary of Findings

Table B16.3. Ubrelvy Fair Access Criteria by Payer

Payer*	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS	Y	Y	Y	Y
Express Scripts	N	Y	Y	Y
United	Y	Y	Y	Y
OptumRx	Y	Y	Y	Y
Cigna	Y	Y	Y	Y
Kaiser	N	Y	Y	Y
Anthem	Y	N/A	N/A	N/A
HCSC	Y	Y	Y	Y
MedImpact	Y	Y	Y	Y
Blue Shield CA	N	Y	Y	Y
BCBS MI	Y	Y	Y	Y
BCBS MA	Y	Y	Y	Y
Premera	N	Y	Y	Y
Highmark	N	Y	Y	Y
Elixir	Y	Y	Y	Y
VHA	Y	Y	Y	Y
Florida Blue HIX	Y	Y	Y	Y
Kaiser HIX	N	Y	Y	Y

N: no, N/A: not applicable, Y: yes

* All payers covered under pharmacy benefit only

B17. Policy Brief: Stelara (ustekinumab), Interleukin 12/23 Monoclonal Antibody (subcutaneous)

B17.1. Condition: Ulcerative colitis, moderate-to-severe

Is Drug Cost-Effective at Current Price?: No

Other Drugs in Class: Humira, Simponi, Remicade, Renflexis, Inflectra, Xeljanz, Entyvio

B17.2. Clinical Guidelines

2020 AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

2019 ACG Clinical Guideline: Ulcerative Colitis in Adults

B17.3. Background

FDA Label

Indication: Adult patients with moderately to severely active ulcerative colitis.

Dosing:

Initial intravenous dosage: A single intravenous infusion using weight-based dosing.

Maintenance subcutaneous dosage: A subcutaneous 90 mg dose 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.

Warning: Serious infections have occurred. Evaluate patients for TB prior to initiating treatment. Stelara may increase the risk of malignancy.

Contraindications: Clinically significant hypersensitivity to ustekinumab or to any of the excipients.

Interactions: None.

Clinical Trial Eligibility: STELARA® was evaluated in two randomized, double-blind, placebo-controlled clinical studies [UC-1 and UC-2 (NCT02407236)] in adult patients with moderately to severely active ulcerative colitis who had an inadequate response to or failed to tolerate a biologic (i.e., TNF blocker and/or Entyvio), corticosteroids, and/or 6-MP or AZA therapy. The 8-week intravenous induction stuy (UC-1) was followed by the 44-week subcutaneous randomized withdrawal maintenance study (UC-2) for a total of 52 weeks of therapy.

Disease assessment was based on the Mayo score, which ranged from 0 to 12 and has four subscores that were each scored from 0 (normal) to 3 (most severe): stool frequency, rectal bleeding, findings on centrally-reviewed endoscopy, and physician global assessment. Moderately to severely active ulcerative colitis was defined at baseline (Week 0) as Mayo score of 6 to 12, including a Mayo endoscopy subscore ≥2. An endoscopy score of 2 was defined by marked erythema, absent vascular pattern, friability, erosions; and a score of 3 was defined by spontaneous bleeding, ulceration. At baseline, patients had a median Mayo score of 9, with 84% of patients having moderate disease (Mayo score 6-10) and 15% having severe disease (Mayo score 11-12).

Patients in these studies may have received other concomitant therapies including aminosalicylates, immunomodulatory agents (AZA, 6-MP, or MTX), and oral corticosteroids (prednisone).

Link to label: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/STELARA-pi.pdf

ICER Policy Recommendations from the 2020 Review of Treatments for Ulcerative Colitis

Insurance coverage should be structured to prevent situations in which patients are forced to choose a treatment approach on the basis of cost.
Because there are no clear biomarkers or predictors of the success for any given treatment in UC, it is not unreasonable to consider prior authorization criteria in order to manage the costs of expensive medications and negotiate prices for TIMs priced beyond a fair range. However, prior authorization criteria should be based on clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers.
Patients eligible for TIMs include those with moderate-to-severe UC whose disease has had an inadequate response to conventional systemic therapy. Patient eligibility criteria should be flexible given that clinical trials used tools (e.g., Mayo Score for disease severity) that are not routinely used in clinical practice.
Given the lack of biomarkers and other predictors of TIM treatment success in UC, it is not unreasonable to use step therapy in this case to manage the costs of treatment.
TIM therapy should be prescribed and managed by gastroenterologists with specific training and expertise in UC.

Link to report: Targeted Immune Modulators for Ulcerative Colitis: Effectiveness and Value

B17.4. Findings: Coverage Policies

Policies for Stelara were available for six payers (Express Scripts, OptumRx, HCSC, MedImpact, Elixir, VHA) under pharmacy benefits, one payer (Premera) under medical benefits, and eleven payers (CVS, United, Cigna, Kaiser, Anthem, Blue Shield CA, BCBS MI, BCBS MA, Highmark, Florida Blue HIX, Kaiser HIX) under both the pharmacy and medical benefits.

Cost Sharing

Because Stelara was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B17.1. Stelara Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	2 (Preferred Brand)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	2 (Preferred Brand)	N/A	N/A	N/A
OptumRx	2 (Preferred Brand)	N/A	N/A	N/A
Cigna	2 (Preferred Brand)	N/A	N/A	N/A
Kaiser	2 (Preferred Brand)	N/A	N/A	N/A
Anthem	4 (Specialty)	N/A	N/A	N/A
HCSC	5 (Preferred Specialty)	N/A	N/A	N/A
MedImpact	2 (Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	4 (Specialty)	N/A	N/A	N/A
BCBS MI	2 (Preferred Brand)	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	N/A	N/A	N/A	N/A
Highmark	2 (Preferred Brand)	N/A	N/A	N/A
Elixir	2 (Preferred Brand)	N/A	N/A	N/A
VHA	Not applicable	N/A	N/A	N/A
Florida Blue HIX	7 (Specialty)	N/A	N/A	N/A
Kaiser HIX	4 (Specialty)	N/A	N/A	N/A

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three Payers (Kaiser**,** Kaiser HIX**,** VHA) do not require clinical eligibility criteria. This meets our requirement, as it is not a restrictive policy.

The remaining payers require some version of the following: a diagnosis of moderately to severely active ulcerative colitis. This is consistent with the FDA label and therefore meets our criteria for clinical eligibility.

Seven payers (Express Scripts, Cigna, Anthem, MedImpact, Blue Shield CA, BCBS MI, Highmark) specify that patients must be 18 years of age or older to access Stelara. This is consistent with the FDA label and therefore meets our criteria for clinical eligibility.

Two payers (Express Scripts, Highmark) specify that Stelara must be used for maintenance therapy following IV induction. This is consistent with the FDA label and therefore meets our criteria for clinical eligibility.

One payer (BCBS MA), requires a trial of 2 conventional agents from a list of steroids, 5-ASAs, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended in clinical guidelines.

Provider Qualifications

Six payers (CVS, Kaiser, Anthem, Blue Shield CA, BCBS MI, Kaiser HIX) do not require specialist prescribing or consultation. This meets our provider qualifications criteria.

Twelve payers (Express Scripts, United, OptumRx, Cigna, HCSC**,** Elixir**,** MedImpact, BCBS MA, Premera, Highmark, VHA, Florida Blue HIX) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

Step Therapy

Thirteen payers (CVS, Express Scripts, United, OptumRx, Cigna, Anthem, HCSC, MedImpact, BCBS MI, Premera, Elixir, VHA, Florida Blue HIX) require patients to step through one conventional systemic therapy or treatment with a prior biologic before accessing Stelara. This meets our criteria for step therapy because the 2019 ACG Clinical Guidelines recommend oral systemic corticosteroids, TNF inhibitors (Humira, Simponi, or Remicade), Entyvio, or Xeljanz for induction of remission in moderately-to-severely active UC.

Table B17.2. Stelara Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS		One biologic OR one conventional therapy	
Pharmacy	1		Y
Medical	1		Y
Express Scripts		One conventional therapy OR one biologic	
Pharmacy	1		Y
United		One oral steroid and/or immunosuppressants OR one biologic	
Pharmacy	1		Y
Medical	1		Y
OptumRx		One conventional therapy	
Pharmacy	0		Y
Cigna		One non-biological DMARD	
Pharmacy	1		Y
Medical	1		Y
Kaiser		No step	
Pharmacy	0		Y
Medical	0		Y
Anthem		One conventional therapy (e.g., 5-ASA, systemic corticosteroids, or immunosuppressants)	
Pharmacy	0		Y
Medical	0		Y
HCSC		One conventional therapy OR one biologic or immunosuppressant*	
Pharmacy	1		Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
MedImpact		One conventional therapy	
Pharmacy	1		Y
Blue Shield CA		No step	
Pharmacy	0		Y
Medical	0		Y
BCBS MI		One conventional therapy	
Pharmacy	0		Y
Medical	0		Y
BCBS MA		2+ conventional therapies (e.g., corticosteroids, 5-	
Pharmacy	1	ASA, or immunosuppressants) OR a preferred drug	Y
Medical	1		Y
Premera		One conventional therapy (e.g., 5-ASA, systemic	
Medical	1	corticosteroids, or immunosuppressants)	Y
Highmark		No step	
Pharmacy	0		Y
Medical	0		Y
Elixir		One conventional therapy	
Pharmacy	1		Y
VHA		One TNF inhibitor	
Pharmacy	1		Y
Florida Blue HIX		One conventional therapy	
Pharmacy	1		Y
Medical	1		Y
Kaiser HIX		No step	
Pharmacy	0		Y
Medical	0		Y

DMARD: disease modifying anti-rheumatic drug, M: medical, N: no,P: pharmacy, ST: step therapy, TNFi: tumor necrosis factor inhibitor, Y: yes

B17.5. Summary of Findings

Table B17.3. Stelara Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Express Scripts				
Pharmacy	N/A	Y	Y	Y
United				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
OptumRx				
Pharmacy	N/A	Y	Y	Y
Cigna				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Kaiser				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
HCSC				
Pharmacy	N/A	Y	Y	Y
MedImpact				
Pharmacy	N/A	Y	Y	Y
Blue Shield CA				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
BCBS MI				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
BCBS MA				
Pharmacy	N/A	N	Y	Y
Medical	N/A	N	Y	Y
Premera				
Medical	N/A	Y	Y	Y
Highmark				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Elixir				
Pharmacy	N/A	Y	Y	Y
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B18. Policy Brief: Entyvio (vedolizumab), α-4 Integrin Inhibitor (intravenous)

B18.1. Condition: Ulcerative colitis (UC), moderate-to-severe

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: Remicade, Inflectra, Renflexis, Simponi, Xeljanz, Stelara

B18.2. Clinical Guidelines

2020 AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis

2019 ACG Clinical Guideline: Ulcerative Colitis in Adults

B18.3. Background

FDA Label

Indication: ENTYVIO is an integrin receptor antagonist indicated in adults for the treatment of moderately to severely active ulcerative colitis.

Dosing: 300 mg vedolizumab administered intravenously

Warning: Infusion-related reactions and hypersensitivity reactions, active, severe infections, progressive multifocal leukoencephalopathy (PML).

Contraindications: Patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.

Interactions: Because of the potential for increased risk of PML and other infections, avoid the concomitant use of ENTYVIO with natalizumab. TNF Blockers Because of the potential for increased risk of infections, avoid the concomitant use of ENTYVIO with TNF blockers. Live vaccines may be administered concurrently with ENTYVIO only if the benefits outweigh the risks.

Clinical Trial Eligibility:

The safety and efficacy of ENTYVIO were evaluated in two randomized, double-blind, placebo-controlled trials (UC Trials I and II) in adult patients with moderately to severely active ulcerative colitis (UC) defined as Mayo score of six to 12 with endoscopy subscore of two or three. The Mayo score ranges from zero to 12 and has four subscales that are each scored from zero (normal) to three (most severe): stool frequency, rectal bleeding, findings on endoscopy, and physician global

assessment. An endoscopy subscore of two is defined by marked erythema, lack of vascular pattern, friability, and erosions; an endoscopy subscore of three is defined by spontaneous bleeding and ulceration.

Link to label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125476s038s039lbl.pdf

ICER Policy Recommendations from the 2020 Ulcerative Colitis Review

Given the lack of biomarkers and other predictors of TIM treatment success in UC, it is not unreasonable to use step therapy in this case to manage the costs of treatment. Step therapy among agents for UC appears to meet criteria for reasonable step therapy: • Use of the first-step therapy reduces overall health care spending, not just drug spending. • The first-step therapy is clinically appropriate for all or nearly all patients and does not pose a greater risk of any significant side effect or harm. • Patients will have a reasonable chance to meet their clinical goals with first-step therapy. • Failure of the first-step drug and the resulting delay in beginning the second-step agent will not lead to long-term harm for patients.
Required switching of TIM therapy for patients who are stable on current treatment should be limited to switches to another medication with the same mechanism of action or from an originator to a biosimilar agent.
TIM therapy should be prescribed and managed by gastroenterologists with specific training and expertise in UC.

Link to report: Targeted Immune Modulators for Ulcerative Colitis: Effectiveness and Value

B18.4. Findings: Coverage Policies

Policies for Entyvio were available for seven payers (BCBS MI, Blue Shield CA, CVS, Florida Blue HIX, HCSC, Highmark, United) under medical benefits, four payers (Express Scripts, MedImpact, OptumRx, VHA) under pharmacy benefits, and six payers (Anthem, BCBS MA, Cigna, Kaiser, Kaiser HIX, Premera) under both the pharmacy and medical benefits.

One payer (Elixir) has Entyvio listed as non-formulary. Non-formulary drugs are only assessed on cost sharing. This drug/payer combination will not be assessed on any other criteria.

Cost Sharing

Because Entyvio was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B18.1. Entyvio Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	N/A (covered under medical)	N/A	N/A	N/A
Express Scripts	2 (Preferred Brand)	N/A	N/A	N/A
United	N/A (covered under medical)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	2 (Preferred Brand)	N/A	N/A	N/A
Kaiser	2 (brand)	N/A	N/A	N/A
Anthem	4 (Specialty)	N/A	N/A	N/A
HCSC	N/A (covered under medical)	N/A	N/A	N/A
MedImpact	Not available	N/A	N/A	N/A
Blue Shield CA	N/A (covered under medical)	N/A	N/A	N/A
BCBS MI	N/A (covered under medical)	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	2 (Preferred Brand)	N/A	N/A	N/A
Highmark	N/A (covered under medical)	N/A	N/A	N/A
Elixir	N/A (non-formulary)	N/A	N/A	N/A
VHA	N/A (no tiering)	N/A	N/A	N/A
Florida Blue HIX	2 (Preferred-brand)	N/A	N/A	N/A
Kaiser HIX	2 (brand)	N/A	N/A	N/A

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

Three payers (Kaiser, Premera, Kaiser HIX) do not have a clinical eligibility requirement. This meets our clinical eligibility criteria.

Most payers require some version of the following: patients 18 and older with moderate to severe ulcerative colitis. This meets our clinical eligibility requirement because it is consistent with the FDA labeled indication.

One payer (BCBS MA), requires a trial of 2 conventional agents from a list of steroids, 5-ASAs, and thiopurines. This does not meet our criteria because 5-ASAs and thiopurines are not recommended in clinical guidelines.

One payer (Elixir) has Entyvio listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Provider Qualifications

Ten payers (Anthem, BCBS MI, Blue Shield CA, CVS, HCSC, Highmark, Kaiser, Kaiser HIX, United, VHA) do not require a specialist prescribing or consultation. This meets our provider qualifications criteria.

Seven payers (BCBS MA, Cigna, Florida Blue HIX, Premera, Express Scripts, MedImpact, OptumRx) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Premera) requires chart notes. This additional documentation requirement is appropriate for the condition.

One payer (Elixir) has Entyvio listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Step Therapy

Three payers (Kaiser, HCSC, Kaiser HIX) do not require step therapy. This meets our criteria for step therapy.

All other payers required some form of the following: treatment, inadequate response, or failure to at least one conventional therapy. This meets our criteria for step therapy because it is in line with the clinical guidelines.

The following payers have additional step therapy requirements (in addition to the above):

- Premera requires an adequate trial and treatment failure with one systemic agent. This meets our criteria for step therapy because it is in line with the clinical guidelines.
- Blue Shield CA requires patients to have an inadequate response to or intolerable side effects with BCS-preferred agents. This meets our step criteria because the preferred agents (PLUS: Remicade or Inflectra) are on a lower tier.

One payer (Elixir) has Entyvio listed as non-formulary. This drug/payer combination was not assessed on our criteria.

Table B18.2. Entyvio Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS			
Medical	1	Trial or contraindication to conventional therapy	Y
Express Scripts			
Pharmacy	1	Trial or contraindication of one systemic agent	Y
United			
Medical	1	Trial or contraindication to at least one conventional therapy	Y
OptumRx			
Pharmacy	3	Trial and failure, contraindication, or intolerance to one conventional therapy AND trial, failure, contraindication or attestation that trial may be inappropriate to two of the following (humira, Simponi, Stelara, rinvoq, xeljanz OR continuing therapy	Y
Cigna			
Pharmacy	1	P: trial or contraindication to conventional therapy	Y
Medical	1	M: trial or contraindication to conventional therapy	Y
Kaiser			
Pharmacy	0	P: No step	Y
Medical	0	M: No step	Y
Anthem			
Pharmacy	1	P: trial or contraindication to conventional therapy	Y
Medical	1	M: trial or contraindication to conventional therapy	Y
HCSC			
Medical	0	No step	Y
MedImpact			
Pharmacy	1	Trial or contraindication to conventional therapy	Y
Blue Shield CA		Trial or contraindication to all preferred products (infliximab:	
Medical	1	Remicade or Inflectra)	Y
BCBS MI		Trial or contraindication to conventional therapy or all	
Medical	1	preferred products in drug list (none)	Y
BCBS MA		P: Trial or contraindication to two or more of: corticosteroids,	
Pharmacy	2	4-ASAs, or immunosuppressants	Y
Medical	2	M: Trial or contraindication to two or more of: corticosteroids, 4-ASAs, or immunosuppressants	Y
Premera			
Pharmacy	1	P: trial or contraindication to one systemic agent OR has pouchitis	Y
Medical	1	M: trial or contraindication to one systemic agent OR has pouchitis	Y
Highmark		Trial and contraindication to conventional therapy OR	
Medical	1	dependent on corticosteroids	Y
Elixir			
Pharmacy	N/A	Trial or contraindication to one conventional therapy OR corticosteroids OR switching from a biologic OR severe disease	N/A
VHA			
Pharmacy	1	No step	Y
Florida Blue HIX			
Medical	1	Trial or contraindication to conventional therapy	Y
Kaiser HIX			
Pharmacy	0	No step	Y
Medical	0	No step	Y

M: medical, N: no P: pharmacy, ST: step therapy, Y: yes, 5-ASA: 5-aminosalacylites

B18.5. Summary of Findings

Table B18.3. Entyvio Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Medical	N/A	Y	Y	Y
Express Scripts				
Pharmacy	N/A	Y	Y	Y
United				
Medical	N/A	Y	Y	Y
OptumRx				
Pharmacy	N/A	Y	Y	Y
Cigna				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Kaiser				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Anthem				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
HCSC				
Medical	N/A	Y	Y	Y
MedImpact				
Pharmacy	N/A	Y	Y	Y
Blue Shield CA				
Medical	N/A	Y	Y	Y
BCBS MI				
Medical	N/A	Y	Y	Y
BCBS MA				
Pharmacy	N/A	N	Y	Y
Medical	N/A	N	Y	Y
Premera				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Medical	N/A	Y	Y	Y
Elixir				
Pharmacy	N/A	N/A	N/A	N/A
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Medical	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

B19. Policy Brief: Oxbryta (voxelotor), hemoglobin S polymerization inhibitor (oral)

B19.1. Condition: sickle cell disease, adults and pediatric patients aged 4 years and older

Is Drug Cost-Effective at Current Prices?: No

Other Drugs in Class: None

B19.2. Clinical Guidelines

Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014

American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain

B19.3. Background

FDA Label

Indication: OXBRYTA is a hemoglobin S polymerization inhibitor indicated for the treatment of sickle cell disease in adults and pediatric patients 4 years of age and older. This indication is approved under accelerated approval based on increase in hemoglobin (Hb). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Dosing:
Adults and pediatric patients 12 years and older: 1,500 mg orally once daily.
Pediatric patients 4 to less than 12 years: Dosing with OXBRYTA is based on body weight. (>40 kg: 1500mg/daily; 20-40 kg: 900mg/daily; 10 to <20 kg: 600mg/daily)

Warning:
Hypersensitivity Reactions: Observe for signs and symptoms and manage promptly.
Laboratory Test Interference: Perform quantification of hemoglobin species when patient is not receiving OXBRYTA.

Contraindications: Prior drug hypersensitivity to voxelotor or excipients.

Interactions:
Sensitive CYP3A4 Substrates: Avoid coadministration of sensitive CYP3A4 substrates with a narrow therapeutic index.

Strong or moderate CYP3A4 Inducers: Avoid coadministration with strong or moderate CYP3A4 inducers. If unavoidable, increase the dose of OXBRYTA.

Clinical Trial Eligibility:
Patients were included if they had from 1 to 10 vasoocclusive crisis (VOC) events within 12 months prior to enrollment and baseline 15 hemoglobin (Hb) ≥5.5 to ≤10.5 g/dL. Eligible patients on stable doses of hydroxyurea for at least 90 days were allowed to continue hydroxyurea therapy throughout the study.

Link to label: https://www.oxbryta.com/pdf/prescribing-information.pdf

ICER Policy Recommendations from the 2020 Sickle Cell Disease Review

Due to the COVID-19 pandemic, ICER's March 2020 public meeting on therapies for sickle cell disease was indefinitely postponed and no Key Recommendations were posted. Please refer to the sickle cell disease evidence report for the most updated findings.

Link to report: Adakveo, Oxbryta, and Endari for Sickle Cell Disease: Effectiveness and Value

B19.4. Findings: Coverage Policies

Policies for Oxbryta were available for 13 payers (BCBS MA**,** BCBS MI**,** Blue Shield CA**,** CVS**,** Elixir**,** HCSC**,** Highmark**,** Kaiser**,** Kaiser HIX**,** MedImpact**,** OptumRx**,** United**,** VHA) under pharmacy benefits, one payer (Premera) covered under both pharmacy and medical benefits, and medical benefit for one payer (Florida Blue HIX).

Oxbryta is not covered under pharmacy or medical benefits for two payers (Express Scripts **and** Cigna)

One payer (Anthem) has Oxbryta listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Cost Sharing

Because Oxbryta was deemed unfairly priced at current prices, we did not issue ratings for the cost-sharing criterion.

Table B19.1. Oxbryta Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Meets Cost-Sharing Criteria?
CVS	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts	N/A (Not Covered)	N/A	N/A	N/A
United	3 (Non-Preferred Brand)	N/A	N/A	N/A
OptumRx	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna	N/A (Not covered)	N/A	N/A	N/A
Kaiser	N/A (no tiering)	N/A	N/A	N/A
Anthem	Non-formulary	N/A	N/A	N/A
HCSC	6 (Non-Preferred Specialty)	N/A	N/A	N/A
MedImpact	3 (Non-Preferred Brand)	N/A	N/A	N/A
Blue Shield CA	4 (Specialty)	N/A	N/A	N/A
BCBS MI	3 (Non-Preferred Brand)	N/A	N/A	N/A
BCBS MA	2 (Preferred Brand)	N/A	N/A	N/A
Premera	4 (Non-Preferred Brand)	N/A	N/A	N/A
Highmark	3 (Non-Preferred Brand)	N/A	N/A	N/A
Elixir	3 (Non-Preferred Brand)	N/A	N/A	N/A
VHA	N/A (no tiering)	N/A	N/A	N/A
Florida Blue HIX	N/A (Covered under medical)	N/A	N/A	N/A
Kaiser HIX	N/A (no tiering)	N/A	N/A	N/A

N: no, N/A: not applicable, Y: yes

Clinical Eligibility

All payers with available clinical eligibility criteria require some version of the following: A diagnosis of sickle cell disease, the occurrence of sickle cell-related vasoocclusive crises within the previous 12 months, current use of hydroxyurea or treatment failure of hydroxyurea, and baseline hemoglobin ≤10.5 g/dL. This meets our criteria because they are consistent with the FDA approval and current guidelines and standard practice.

One payer (Anthem) has Oxbryta listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Provider Qualifications

Eight payers (BCBS MA, Blue Shield CA, CVS, HCSC, Highmark, Kaiser, Kaiser HIX, VHA) do not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Seven payers (BCBS MI, Elixir, MedImpact, OptumRx, Premera, United, Florida Blue HIX) require prescribing by or in consultation with a specialist. This meets our criteria because specialist clinician diagnosis/monitoring is appropriate for this condition.

One payer (Anthem) has Oxbryta listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Step Therapy

Seven payers (BCBS MA, CVS, Kaiser, Kaiser HIX, Florida Blue HIX, Premera, VHA) do not require step therapy. This meets our step therapy criteria.

Eight payers (BCBS MI, Blue Shield CA, Elixir, HCSC, Highmark, MedImpact, OptumRx, United) require patients to have had, after a 6-month trial, an inadequate response to or have a hypersensitivity to hydroxyurea. This meets our step therapy criteria because it is a recommended therapy in the National Heart, Lung, and Blood Institute's (NHLBI) 2014 guidelines for evidence-based management of sickle cell disease. The American Society of Hematology 2020 guidelines on management of sickle cell and acute and chronic pain suggest that there is a lack of comparative effectiveness data between hydroxyurea and other disease-modifying therapies and chronic transfusions to make a recommendation on the use of these agents in treatment of acute and chronic pain.

One payer (Anthem) has Oxbryta listed as non-formulary. This drug/payer combination was not evaluated on our criteria.

Table B19.2. Oxbryta Step Therapy by Payer

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
CVS			
Pharmacy	0	No steps	Y
Express Scripts	N/A	N/A	N/A
United			
Pharmacy	1	Hydroxyurea trial	Y
OptumRx			
Pharmacy	1	Hydroxyurea trial	Y
Cigna	N/A	N/A	N/A
Kaiser			
Pharmacy	0	No steps	Y
Anthem			
Pharmacy	N/A	Non-formulary	N/A
HCSC			
Pharmacy	1	Hydroxyurea trial	Y
MedImpact			
Pharmacy	1	Hydroxyurea trial	Y
Blue Shield CA			
Pharmacy	1	Hydroxyurea trial	Y
BCBS MI			
Pharmacy	1	Hydroxyurea trial	Y
BCBS MA			
Pharmacy	0	No steps	Y
Premera			
Pharmacy	0	No steps	Y
Medical	0	No steps	Y
Highmark			
Pharmacy	1	Hydroxyurea trial	Y

Payer and Benefit Plan Type	Steps	Details	Meets ST Criteria? Y/N
Elixir Pharmacy	2	Hydroxyurea trial and L-Glutamine	Y
VHA Pharmacy	0	No steps	Y
Florida Blue HIX Medical	0	No steps	Y
Kaiser HIX Pharmacy	0	No steps	Y

M: medical, P: pharmacy, ST: step therapy, Y: yes

B19.5. Summary of Findings

Table B19.3. Oxbryta Fair Access Criteria by Payer

Payer and Benefit Plan Type	Meets Cost-Sharing Criteria?	Meets Clinical Eligibility Criteria?	Meets Step Therapy Criteria?	Meets Provider Qualifications Criteria?
CVS				
Pharmacy	N/A	Y	Y	Y
Express Scripts	N/A	N/A	N/A	N/A
United				
Pharmacy	N/A	Y	Y	Y
OptumRx				
Pharmacy	N/A	Y	Y	Y
Cigna	N/A	N/A	N/A	N/A
Kaiser				
Pharmacy	N/A	Y	Y	Y
Anthem				
Pharmacy	N/A	N/A	N/A	N/A
HCSC				
Pharmacy	N/A	Y	Y	Y
MedImpact				
Pharmacy	N/A	Y	Y	Y
Blue Shield CA				
Pharmacy	N/A	Y	Y	Y
BCBS MI				
Pharmacy	N/A	Y	Y	Y
BCBS MA				
Pharmacy	N/A	Y	Y	Y
Premera				
Pharmacy	N/A	Y	Y	Y
Medical	N/A	Y	Y	Y
Highmark				
Pharmacy	N/A	Y	Y	Y
Elixir				
Pharmacy	N/A	Y	Y	Y
VHA				
Pharmacy	N/A	Y	Y	Y
Florida Blue HIX				
Medical	N/A	Y	Y	Y
Kaiser HIX				
Pharmacy	N/A	Y	Y	Y

N: no, N/A: not applicable, Y: yes

Table B20. Fair Access Criteria Concordance by Drug and Payer

Payer	Benefit Plan Type*	Meets Cost Sharing?	Meets Clinical Eligibility?	Meets Step Therapy?	Meets Prescriber Requirements?
Humira					
Anthem	Pharmacy	N/A	Y	Y	Y
BCBS MA	Pharmacy	N/A	N	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	Pharmacy	N/A	Y	Y	Y
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Adakveo					
Anthem	Medical	N/A	N/A	N/A	N/A
BCBS MA	Medical	N/A	Y	Y	Y
BCBS MI	Medical	N/A	Y	Y	Y
Blue Shield CA	Medical	N/A	Y	Y	Y
Cigna	Medical	N/A	Y	Y	Y
CVS	Medical	N/A	Y	Y	Y
Elixir	N/A (Not covered)	N/A	N/A	N/A	N/A
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Medical	N/A	Y	Y	Y
HCSC	Medical	N/A	Y	Y	Y
Highmark	Medical	N/A	Y	Y	Y
Kaiser	Medical	N/A	Y	Y	Y
Kaiser HIX	Medical	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Medical	N/A	Y	Y	Y
United	Medical	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Trikafta					
Anthem	Pharmacy	N/A	Y	Y	Y
BCBS MA	Pharmacy	N/A	Y	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	Pharmacy	N/A	Y	Y	Y
CVS	Pharmacy	N/A	Y	Y	Y

Payer	Benefit Plan Type*	Meets Cost Sharing?	Meets Clinical Eligibility?	Meets Step Therapy?	Meets Prescriber Requirements?
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Hemlibra					
Anthem	Pharmacy	N	N/A	N/A	N/A
BCBS MA	Medical	N/A	Y	Y	Y
BCBS MI	Pharmacy	Y	Y	Y	Y
Blue Shield CA	Medical	N/A	Y	Y	Y
Cigna	Pharmacy	N	N	Y	Y
CVS	Pharmacy	N	Y	Y	Y
Elixir	Pharmacy	Y	N	Y	Y
Express Scripts	Pharmacy	Y	Y	Y	Y
Florida Blue HIX	Pharmacy	N	N	N	Y
HCSC	Pharmacy	Y	Y	Y	Y
Highmark	Pharmacy	Y	Y	Y	Y
Kaiser	Pharmacy	Y	Y	Y	Y
Kaiser HIX	Pharmacy	Y	Y	Y	Y
MedImpact	Pharmacy	N	N	Y	Y
OptumRx	Pharmacy	N	Y	Y	Y
Premera	Pharmacy	N	Y	Y	Y
United	Pharmacy	Y	Y	N	Y
VHA	Pharmacy	Y	Y	Y	Y
Simponi					
Anthem	Pharmacy	N/A	Y	Y	Y
BCBS MA	Pharmacy	N/A	N	Y	Y
BCBS MI	Pharmacy	N/A	Y	N	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	Pharmacy	N/A	Y	Y	Y
CVS	Medical	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Medical	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y

Payer	Benefit Plan Type*	Meets Cost Sharing?	Meets Clinical Eligibility?	Meets Step Therapy?	Meets Prescriber Requirements?
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Remicade					
Anthem	Medical	N†	Y	Y	Y
BCBS MA	Medical	Y†	N	Y	Y
BCBS MI	Medical	N/A	Y	Y	Y
Blue Shield CA	Medical	N/A	Y	Y	Y
Cigna	Medical	Y†	Y	Y	Y
CVS	Medical	Y†	Y	Y	Y
Elixir	Pharmacy	Y	N/A	N/A	N/A
Express Scripts	Pharmacy	Y	Y	Y	Y
Florida Blue HIX	Medical	N/A	Y	Y	Y
HCSC	Medical	N/A	Y	Y	Y
Highmark	Medical	N/A	Y	Y	Y
Kaiser	Medical	Y†	Y	Y	Y
Kaiser HIX	Medical	N†	Y	Y	Y
MedImpact	Pharmacy	Y	Y	Y	Y
OptumRx	Pharmacy	Y	Y	Y	Y
Premera	Medical	Y†	Y	Y	Y
United	Medical	N/A	Y	Y	Y
VHA	Pharmacy	Y	Y	Y	Y
Renflexis					
Anthem	Medical	N†	Y	Y	Y
BCBS MA	Medical	Y†	N	Y	Y
BCBS MI	Medical	N/A	Y	Y	Y
Blue Shield CA	Medical	N/A	Y	Y	Y
Cigna	Medical	N/A	Y	Y	Y
CVS	Medical	N/A	Y	Y	Y
Elixir	Pharmacy	Y	N/A	N/A	N/A
Express Scripts	N/A (Not Covered)	N/A	N/A	N/A	N/A
Florida Blue HIX	Medical	N/A	Y	Y	Y
HCSC	Medical	N/A	Y	Y	Y
Highmark	Medical	N/A	Y	Y	Y
Kaiser	Medical	Y†	Y	Y	Y
Kaiser HIX	Medical	N†	Y	Y	Y
MedImpact	Pharmacy	Y	Y	Y	Y
OptumRx	Pharmacy	Y	Y	Y	Y
Premera	Medical	Y†	Y	Y	Y
United	Medical	N/A	Y	Y	Y
VHA	Pharmacy	Y	Y	Y	Y
Inflectra					
Anthem	Medical	N†	Y	Y	Y
BCBS MA	Medical	Y†	N	Y	Y
BCBS MI	Medical	N/A	Y	Y	Y
Blue Shield CA	Medical	N/A	Y	Y	Y
Cigna	Medical	Y†	Y	Y	Y
CVS	Medical	N/A	Y	Y	Y
Elixir	Pharmacy	Y	N/A	N/A	N/A

Payer	Benefit Plan Type*	Meets Cost Sharing?	Meets Clinical Eligibility?	Meets Step Therapy?	Meets Prescriber Requirements?
Express Scripts	Pharmacy	Y	Y	Y	Y
Florida Blue HIX	Medical	N/A	Y	Y	Y
HCSC	Medical	N/A	Y	Y	Y
Highmark	Medical	N/A	Y	Y	Y
Kaiser	Medical	Y†	Y	Y	Y
Kaiser HIX	Medical	N†	Y	Y	Y
MedImpact	Pharmacy	Y	Y	Y	Y
OptumRx	Pharmacy	Y	Y	Y	Y
Premera	Medical	Y†	Y	Y	Y
United	Medical	N/A	Y	Y	Y
VHA	Pharmacy	Y	Y	Y	Y
Kalydeco					
Anthem	Pharmacy	N/A	N/A	N/A	N/A
BCBS MA	Pharmacy	N/A	Y	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	Pharmacy	N/A	Y	Y	Y
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Reyvow					
Anthem	Pharmacy	N/A	N/A	N/A	N/A
BCBS MA	N/A (Not Covered)	N/A	N/A	N/A	N/A
BCBS MI	Pharmacy	N/A	Y	N	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	N/A (Not Covered)	N/A	N/A	N/A	N/A
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	N	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	N	Y

Payer	Benefit Plan Type*	Meets Cost Sharing?	Meets Clinical Eligibility?	Meets Step Therapy?	Meets Prescriber Requirements?
VHA	Pharmacy	N/A	Y	Y	Y
Endari					
Anthem	Pharmacy	N/A	N/A	N/A	N/A
BCBS MA	Pharmacy	N/A	Y	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	N/A (Not covered)	N/A	N/A	N/A	N/A
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Orkambi					
Anthem	Pharmacy	N/A	N/A	N/A	N/A
BCBS MA	Pharmacy	N/A	Y	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	Pharmacy	N/A	Y	Y	Y
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Nurtec					
Anthem	Pharmacy	Y	Y	Y	Y
BCBS MA	Pharmacy	Y	Y	Y	Y
BCBS MI	Pharmacy	Y	Y	Y	Y
Blue Shield CA	Pharmacy	N	Y	Y	Y
Cigna	Pharmacy	Y	Y	Y	Y
CVS	Pharmacy	Y	Y	Y	Y
Elixir	Pharmacy	Y	Y	Y	Y
Express Scripts	Pharmacy	N	Y	Y	Y

Payer	Benefit Plan Type*	Meets Cost Sharing?	Meets Clinical Eligibility?	Meets Step Therapy?	Meets Prescriber Requirements?
Florida Blue HIX	Pharmacy	Y	Y	Y	Y
HCSC	Pharmacy	Y	Y	Y	Y
Highmark	Pharmacy	N	Y	Y	Y
Kaiser	Pharmacy	N	Y	Y	Y
Kaiser HIX	Pharmacy	N	Y	Y	Y
MedImpact	Pharmacy	Y	Y	Y	Y
OptumRx	Pharmacy	Y	Y	Y	Y
Premera	Pharmacy	N	Y	Y	Y
United	Pharmacy	Y	Y	Y	Y
VHA	Pharmacy	Y	Y	Y	Y
Symdeko					
Anthem	Pharmacy	N/A	N/A	N/A	N/A
BCBS MA	Pharmacy	N/A	Y	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	Pharmacy	N/A	Y	Y	Y
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Xeljanz					
Anthem	Pharmacy	N/A	Y	Y	Y
BCBS MA	Pharmacy	N/A	N	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	Pharmacy	N/A	Y	Y	Y
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y

Payer	Benefit Plan Type*	Meets Cost Sharing?	Meets Clinical Eligibility?	Meets Step Therapy?	Meets Prescriber Requirements?
Ubrelvy					
Anthem	Pharmacy	Y	N/A	N/A	N/A
BCBS MA	Pharmacy	Y	Y	Y	Y
BCBS MI	Pharmacy	Y	Y	Y	Y
Blue Shield CA	Pharmacy	N	Y	Y	Y
Cigna	Pharmacy	Y	Y	Y	Y
CVS	Pharmacy	Y	Y	Y	Y
Elixir	Pharmacy	Y	Y	Y	Y
Express Scripts	Pharmacy	N	Y	Y	Y
Florida Blue HIX	Pharmacy	Y	Y	Y	Y
HCSC	Pharmacy	Y	Y	Y	Y
Highmark	Pharmacy	N	Y	Y	Y
Kaiser	Pharmacy	N	Y	Y	Y
Kaiser HIX	Pharmacy	N	Y	Y	Y
MedImpact	Pharmacy	Y	Y	Y	Y
OptumRx	Pharmacy	Y	Y	Y	Y
Premera	Pharmacy	N	Y	Y	Y
United	Pharmacy	Y	Y	Y	Y
VHA	Pharmacy	Y	Y	Y	Y
Stelara					
Anthem	Pharmacy	N/A	Y	Y	Y
BCBS MA	Pharmacy	N/A	N	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	Pharmacy	N/A	Y	Y	Y
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Pharmacy	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Medical	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Entyvio					
Anthem	Medical	N/A	Y	Y	Y
BCBS MA	Medical	N/A	N	Y	Y
BCBS MI	Medical	N/A	Y	Y	Y
Blue Shield CA	Medical	N/A	Y	Y	Y
Cigna	Medical	N/A	Y	Y	Y
CVS	Medical	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	N/A	N/A	N/A
Express Scripts	Pharmacy	N/A	Y	Y	Y
Florida Blue HIX	Medical	N/A	Y	Y	Y

Payer	Benefit Plan Type*	Meets Cost Sharing?	Meets Clinical Eligibility?	Meets Step Therapy?	Meets Prescriber Requirements?
HCSC	Medical	N/A	Y	Y	Y
Highmark	Medical	N/A	Y	Y	Y
Kaiser	Medical	N/A	Y	Y	Y
Kaiser HIX	Medical	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Medical	N/A	Y	Y	Y
United	Medical	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y
Oxbryta					
Anthem	Pharmacy	N/A	N/A	N/A	N/A
BCBS MA	Pharmacy	N/A	Y	Y	Y
BCBS MI	Pharmacy	N/A	Y	Y	Y
Blue Shield CA	Pharmacy	N/A	Y	Y	Y
Cigna	N/A (Not covered)	N/A	N/A	N/A	N/A
CVS	Pharmacy	N/A	Y	Y	Y
Elixir	Pharmacy	N/A	Y	Y	Y
Express Scripts	N/A (Not covered)	N/A	N/A	N/A	N/A
Florida Blue HIX	Medical	N/A	Y	Y	Y
HCSC	Pharmacy	N/A	Y	Y	Y
Highmark	Pharmacy	N/A	Y	Y	Y
Kaiser	Pharmacy	N/A	Y	Y	Y
Kaiser HIX	Pharmacy	N/A	Y	Y	Y
MedImpact	Pharmacy	N/A	Y	Y	Y
OptumRx	Pharmacy	N/A	Y	Y	Y
Premera	Pharmacy	N/A	Y	Y	Y
United	Pharmacy	N/A	Y	Y	Y
VHA	Pharmacy	N/A	Y	Y	Y

N: no, N/A: Not applicable, PBM: Pharmacy Benefit Manager, Y: yes

*Describes the benefit plan type that is used for the analyses in the report.

†For drugs covered under medical and pharmacy plan types and where the predominant plan type for the drug is medical, the pharmacy benefit plan is used to evaluate cost sharing criteria if applicable.