Supplemental Materials

December 19, 2024

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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 a 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 sciences industry.

A1.2. Objectives

The 2024 ICER Barriers to Fair Access Assessment assessed the concordance of drug coverage policies with fair access criteria for ICER-reviewed drugs in 2022. We evaluated coverage policies of the largest formularies by number of covered lives, not associated with a specific employer, of the 10 largest commercial payers/PBMs in the US and the single formulary of the Veterans Health Administration (VHA). In addition to core analyses of concordance with fair access criteria for cost sharing and the content of prior authorization policies, the 2024 report also included exploratory analyses on a select set of drugs and formularies. As in prior years, we sought to understand how transparent drug coverage information such as formulary tiering and clinical eligibility criteria is to prospective plan members for the three gene therapies in scope this year: Zynteglo (beta thalassemia), Hemgenix (hemophilia B), and Roctavian (hemophilia A). In addition, ICER has partnered with IQVIA this year to gain insights into national level cost-sharing and prior authorization metrics from real-world claims data. Based on insights licensed from IQVIA's Market Access Analytic Solutions, we evaluated measures illustrating average *'consumer accessibility'* for a subset of the 11 drugs in scope for the past two years in the commercial line of business.

A1.3. Research Questions

The overarching research question this project addressed is whether the prior authorization policies for drugs reviewed by ICER in 2022 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:

- Fair access criterion
- Drug
- Individual payer

For our exploratory analyses, we assessed the transparency of coverage information for gene therapy is for a prospective plan member and assessed how accessible a set of drugs available at the pharmacy is for consumers, based on prescription fill and cost-sharing data at the point-of-sale.

A2. Role of the Working Group

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

- **Alan Balch,** PhD, Chief Executive Officer, Patient Advocate Foundation
- **Erica Cischke**, MPH, Vice President, Government Affairs, Alliance for Regenerative Medicine
- **Omar Escontrias,** DrPH, MPH, Senior Vice President, Equity, Research & Programs, National Health Council
- **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
- **Rick Kelly,** FSA, SVP & National Pharmacy Practice Leader, Marsh McLennan Agency
- **Rebecca Kirch**, JD, Executive Vice President, National Patient Advocate Foundation
- **M. Kay Scanlan,** JD, Sr. Policy Advisor, Haystack Project
- **Gail Ryan,** PharmD, Director of Pharmaceutical Transformation, Point32Health
- **Carl Schmid,** Executive Director, HIV+Hepatitis Policy Institute
- **Bari Talente,** Executive Vice President, Advocacy, National Multiple Sclerosis Society
- **Diana Thiara,** MD, DABOM, Assistant Clinical Professor of Medicine and Medical Director, UCSF Weight Management Clinic
- **Kimberly Westrich,** MA, Chief Strategy Officer, National Pharmaceutical Council (NPC)

A3. List of Included Drugs

A3.1. Initial List of Drugs

Drugs eligible for consideration were those reviewed by ICER in 2022 and that are currently FDA approved for an indication consistent with the ICER review (Table A3.1). One drug reviewed by ICER in 2022, plinabulin (BeyondSpring Inc.) for prevention of chemotherapy-induced neutropenia, received a complete response letter from the FDA and has yet to gain approval. Another drug, AMX0035 (Relyvrio™, Amylyx Pharmaceuticals) for amyotrophic lateral sclerosis, was granted FDA approval but a subsequent failed readout from the Phase 3 trial prompted the manufacturer to withdraw the product from the market. As such, both drugs will be excluded from the report. In addition, the agents for treating COVID-19 that were reviewed in 2022 will not be included in this analysis as those drugs were part of a "special assessment" and not subject to a traditional ICER review, and because the treatment landscape for COVID-19 has evolved significantly since 2022.

For these drugs we updated the ceiling price needed to meet the cost-effectiveness threshold to 2023 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 2022 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, 2023 - December 31, 2023), 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 ǂ	Annual Net Price Estimated Above or Below ICER HBPB *
Mounjaro™	Tirzepatide	Diabetes: Type 2	SC	$5,833	Below
Wegovy®	Semaglutide	Obesity Management	SC	$10,029	Below
Qsymia®	Phentermine/ Topiramate	Obesity Management	Oral	$4,912	Below
Saxenda®	Liraglutide	Obesity Management	SC	$4,912	Above
Contrave®	Naltrexone/Bupropion	Obesity Management	Oral	$2,456	Above
Cosela™	Trilaciclib	Chemotherapy-Induced Neutropenia	IV	$512 per vial	Above
Veozah™	Fezolinetant	Menopause: Vasomotor Symptoms	Oral	$2,661	Above
Radicava ORS®	Oral Edaravone	Amyotrophic Lateral Sclerosis	Oral	$3,275	Above
Zynteglo™	Betibeglogene autotemcel	Beta Thalassemia	IV	$2,497,082 per administration	Above
Hemgenix®	Etranacogene dezaparvovec	Hemophilia B	IV	$3,027,200 per administration	Above
Roctavian™	Valoctocogene roxaparvovec	Hemophilia A	IV	$2,006,876 per administration	Above

HBPB: Health Benefit Price Benchmark, IV: Intravenous, SC: Subcutaneous

*Average prices net of all discounts and rebates, for the year of 2023, obtained from SSR Health. For prices not available or deemed unreliable, prices are taken from the Federal Supply Schedule (FSS). For physician administered drugs we will use the ASP price plus 6%, if available.

ǂ ICER health benefit price benchmarks for the higher of the $150,000 per QALY or $150,000 per evLYG threshold, inflated to 2023 prices.

A4. List of Payers and Identification of Relevant Coverage Policies

We assessed coverage policies for the selected drugs across 11 formularies, including the largest formulary by number of covered lives offered by the 10 largest commercial payers in the US and the single formulary of the Veterans Health Administration (VHA). At the time we conducted our research, these formularies represented coverage policies governing pharmaceutical access for approximately 57 million Americans. All payers and formularies except for VHA were identified using the MMIT Analytics Market Access Database. The entity (payer or PBM) that controlled the coverage decision was assigned the covered life. We obtained the necessary coverage policies such as relevant prior authorization forms, documents, and formulary tiering information through targeted outreach to payers, and as needed, supplemented any additional information needed by leveraging the MMIT Analytics Market Access Database. 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	Covered Lives*
CVS Health (Aetna)	CVS Caremark Performance Standard Control w/Advanced Specialty Control	Commercial	1 - Generic 2 - Preferred Brand 3 - Non-Preferred Generic or Non-Preferred Brand	13,399,307
Express Scripts PBM	Express Scripts National Preferred	Commercial	1 - Formulary Generics 2 – Formulary brands 3 – Non-formulary brands	16,227,321
UnitedHealth Group, Inc.	UnitedHealthcare Advantage Three Tier	Commercial	1 – Lower-cost 2 – Mid-range cost 3 – Higher-cost	7,286,487
Cigna Corporation	Cigna Standard Three Tier	Commercial	1 - Generic 2 - Preferred Brand 3 - Non-Preferred Brand	3,570,884
OptumRx	OptumRx Premium Formulary	Commercial	1 – Lower-cost (generics and some brand name) 2 – Mid-range cost (preferred brand name) 3 – Highest-cost (brand name and some generics) E – Excluded	2,730,523
Kaiser Foundation Health Plans, Inc.	Kaiser Permanente Southern California 3 Tier HMO	Commercial	1 – Most Generic drugs 2 – Most Brand-name drugs 3 – High-cost Brand-name or Generic drugs	2,962,497
Elevance Health, Inc.	Anthem Essential 4 Tier	Commercial	1 – Lower-cost (Preferred Generics) 2 – Mid-cost (Preferred Brand) 3 – High-cost (Non-Preferred Brand and Generics) 4 – Highest-cost (Specialty)	2,169,855

Payer	Formulary Name	Plan Type	Tiers Available	Covered Lives*
Health Care Service Corporation (HCSC)	BCBS of Illinois Basic 6 Tier	Commercial	1 - Preferred Generic 2 - Non-Preferred Generic 3 - Preferred Brand 4 - Non-Preferred Brand 5 - Preferred Specialty 6 - Non-Preferred Specialty	1,163,606
Highmark, Inc.	Highmark Blue Cross Blue Shield 3 Tier	Commercial	1 - Generic 2 - Preferred Brand 3 - Non-Preferred Brand	1,420,620
Blue Shield of California (Blue Shield of CA)	Blue Shield California Plus Formulary	Commercial	1 - Generic/Low-cost 2 - Preferred Brand 3 - Non-Preferred Brand 4 - Specialty/High Cost	1,110,753
Veterans' Health Administration (VHA)	VHA National Formulary	Federal	*The VHA has three categories: formulary, formulary with prior authorization, and non-formulary but covered with clinical justification. There is a flat cost-sharing regardless of the category.*	5,123,794

BCBS: Blue Cross Blue Shield, HMO: Health Maintenance Organization, PBM: Pharmacy Benefit Manager

*Covered lives as of 08/01/2024 according to MMIT

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

As with the 2023 report, the 2024 report evaluated formulary concordance with fair access criteria related to cost sharing, clinical eligibility, step therapy, and restrictions on prescriber qualifications. In addition to core analyses of concordance with fair access criteria for cost sharing and the content of prior authorization policies, we conducted exploratory analyses on a select set of drugs and formularies on criteria related to the transparency of cost sharing and clinical eligibility criteria prior to plan enrollment. 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	**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
All medications identified by the Internal Revenue Service as high-value therapies should receive pre-deductible coverage within high deductible health plans.	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**
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.	**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**
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

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	**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
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
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
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**
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**
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.	**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.	**Yes**

FDA: U.S. Food and Drug Administration

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

Step Therapy and Required Switching	
Fair Access Criteria	**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
• 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** – 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. • 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

FDA: U.S. Food and Drug Administration

For the 2024 report we continued to use a maximum threshold of 3 step therapies, which would cumulatively represent a failure to meet reasonable standards for fair access. Any step therapy policy requiring 4 or more steps will be judged to not meet concordance with step therapy fair access criteria.

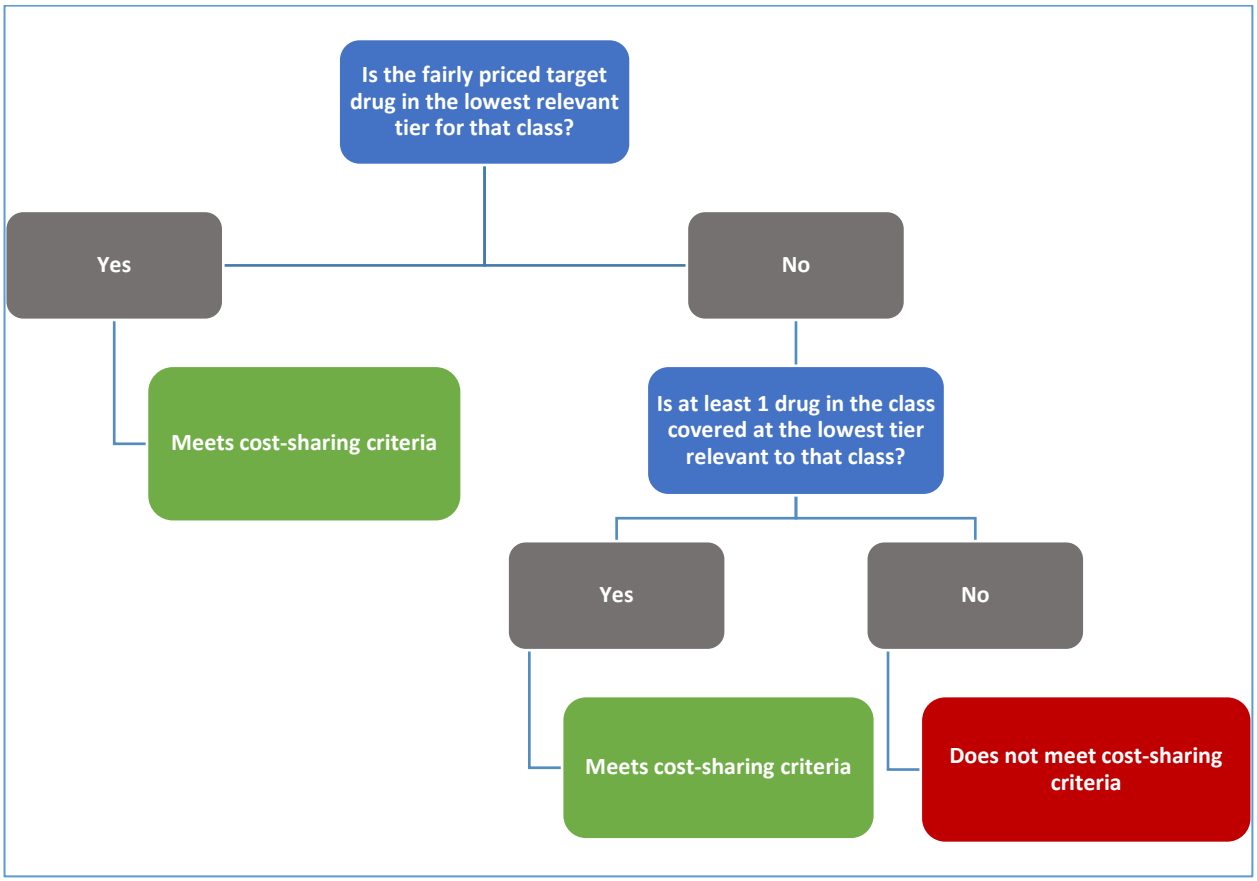
Table A5.4. Provider Qualifications Fair Design Criteria

Provider Qualifications	
Fair Access Criteria	**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**
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**

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.	**Yes**
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.	No
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 non-medical 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

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.

Supporting documents provided by each payer in scope was used as the primary source for cost-sharing and prior authorization information. Any outstanding gaps in policy details were supplemented by using the MMIT database. 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. 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.

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 linkage to 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 a clinician on the ICER staff (GL, who is a practicing internist). When the ICER clinician felt that clinical expert input was needed to determine whether a coverage policy met the fair design criterion, she discussed the question with an expert involved in the original ICER report on that drug. Finally, payers were able to send updated policies if the policy changed after the data abstraction cutoff date {July 12, 2024). While updated policies after the cutoff date did not affect concordance ratings, the changes were assessed on whether the updated policy would change the concordance rating and summarized in Table 19 in the main report.

B. Results

B1. Policy Brief: Mounjaro (tirzepatide), glucose-dependent insulinotropic polypeptide receptor and glucagon-like peptide-1 receptor agonist (subcutaneous)

B1.1. Condition: Type 2 Diabetes Mellitus

Cost-Effective at Current Prices: Yes

Other Drugs in Class: Bydureon BCise (exenatide extended-release), Byetta (exenatide), Ozempic (semaglutide), Rybelsus (semaglutide), Trulicity (dulaglutide), Victoza (liraglutide)

B1.2. Clinical Guidelines

American Diabetes Association Standards of Care (2024)

American Association of Clinical Endocrinologists (2023)

B1.3. Background

FDA Label Information

Indication: Indicated as an **adjunct to diet and exercise** to improve glycemic control in **adults with type 2 diabetes mellitus**.

Dosing: Injection: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, or 15 mg per 0.5 mL in single-dose pen or single-dose vial. The recommended starting dosage is 2.5 mg injected subcutaneously once weekly. After 4 weeks, increase to 5 mg injected subcutaneously once weekly. If additional glycemic control is needed, increase the dosage in 2.5 mg increments after at least 4 weeks on the current dose. The maximum dosage is 15 mg subcutaneously once weekly. Administer once weekly at any time of day, with or without meals. Inject subcutaneously in the abdomen, thigh, or upper arm. Rotate injection sites with each dose.

Warning:
-**Pancreatitis**: Has been reported in clinical trials. Discontinue promptly if pancreatitis is suspected.
-**Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin**: Concomitant use with an insulin secretagogue or insulin may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing dose of insulin secretagogue or insulin may be necessary.
-**Hypersensitivity Reactions**: Serious hypersensitivity reactions (e.g., anaphylaxis and angioedema) have been reported. Discontinue MOUNJARO if suspected and promptly seek medical advice.
-**Acute Kidney Injury**: Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions.

-**Severe Gastrointestinal Disease**: Use may be associated with gastrointestinal adverse reactions, sometimes severe. Has not been studied in patients with severe gastrointestinal disease and is not recommended in these patients.
-**Diabetic Retinopathy Complications in Patients with a History of Diabetic Retinopathy**: Has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy, or diabetic macular edema. Monitor patients with a history of diabetic retinopathy for progression.
-**Acute Gallbladder Disease**: Has occurred in clinical trials. If cholelithiasis is suspected, gallbladder studies and clinical follow- up are indicated.

Contraindications:
-Personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2.
-Known serious hypersensitivity to tirzepatide or any of the excipients in MOUNJARO.

Interactions:
- Concomitant Use with Insulin Secretagogues or Insulin
- When initiating MOUNJARO, consider reducing the dose of concomitantly administered insulin secretagogues such as sulfonylureas or insulin to mitigate hypoglycemia risk.
- Oral Medications: MOUNJARO delays gastric emptying, potentially affecting the absorption of concomitantly administered oral medications. Exercise caution when administering oral medications with MOUNJARO. For patients on oral medications dependent on threshold concentrations for efficacy or those with a narrow therapeutic index such as warfarin, monitor closely when administered concomitantly with MOUNJARO. For patients using oral hormonal contraceptives, advise switching to a non-oral contraceptive method or adding a barrier method for 4 weeks after initiation and each dose escalation of MOUNJARO. Non-orally administered hormonal contraceptives should not be affected.

Clinical Trial Eligibility:
SURPASS-1 and 5:
- Have been diagnosed with T2DM.
- Have HbA1c between ≥7.0% and ≤10.5%
- Be on stable treatment with unchanged dose of metformin >1500 mg/day for at least 3 months prior to screening
- Be of stable weight (±5%) for at least 3 months before screening

Link to Full FDA Label

ICER Policy Recommendations from the 2022 Review of Tirzepatide for Type 2 Diabetes

A comprehensive set of policy recommendations regarding coverage policies, prior authorization criteria, and step therapy considerations for type 2 diabetes medications in the United States were outlined in the ICER February 2022 diabetes review.

B1.4. Findings: Coverage Policies

Mounjaro was covered by 11 payers (CVS Health, Express Scripts, UnitedHealth, Cigna, OptumRx, Kaiser, Elevance, HCSC, Highmark, Blue Shield of CA**,** VHA).

- Ten payers cover Mounjaro under the pharmacy benefit: CVS Health, Cigna, UnitedHealth, OptumRx, Kaiser, Elevance, HCSC, Highmark, Blue Shield of CA, VHA.
- One payer indicated that benefit type was up to the client: Express Scripts

Coverage policies were provided by all but two payers (CVS Health, Kaiser). These payers cover the medication without a specific written policy.

Cost Sharing

Total number of assessed payers: 10/11

Nine payers (CVS Health, Express Scripts, UnitedHealth, Cigna, OptumRx, Elevance, HCSC, Highmark, Blue Shield of CA) placed Mounjaro on the lowest relevant tier. This meets our cost-sharing criteria.

VHA provides coverage at a low, fixed cost-sharing amount which is concordant with these criteria.

Table B1.1 Mounjaro Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	2 (Preferred Brand)	Y	N/A	Y
Express Scripts PBM	2 (Preferred Brand)	Y	N/A	Y
UnitedHealth Group, Inc.	2 (Preferred Brand)	Y	N/A	Y
Cigna Corporation	2 (Preferred Brand)	Y	N/A	Y
OptumRx	2 (Mid-Range Cost)	Y	N/A	Y
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	2 (Preferred Brand)	Y	N/A	Y
Health Care Service Corporation (HCSC)	2 (Preferred Brand)	Y	N/A	Y
Highmark, Inc.	2 (Preferred Brand)	Y	N/A	Y
Blue Shield of California (Blue Shield of CA)	2 (Preferred Brand)	Y	N/A	Y
VHA National Formulary (VHA)	Non-formulary	N/A	N/A	Y

N/A: not applicable, Y: yes

Clinical Eligibility

Total number of assessed payers: 11/11

Two payers (CVS Health, Kaiser) have no clinical eligibility criteria for coverage. This meets our clinical eligibility criteria.

Eight payers (UnitedHealth, Elevance, Express Scripts, Cigna, HCSC, Highmark, Blue Shield of CA, OptumRx) required some version of the following eligible population: Type 2 Diabetes Mellitus. This meets our criteria because it is in line with the label indication.

One payer (VHA) required that individuals have inadequate glycemic control on at least 1mg of semaglutide injection plus two or more glucose lowering drugs (metformin, empagliflozin, insulin, pioglitazone, sulfonylurea) for at least 6 months AND that the change needed to achieve goal A1C is less than 1%. This does not meet our criteria because these requirements are more restrictive than clinical guidelines.

Step Therapy

Total number of assessed payers: 11/11

Step therapy was not required by five payers (UnitedHealth, CVS Health, Express Scripts, Highmark, OptumRx). This meets our criteria for step therapy.

Three payers (Cigna, Elevance, Blue Shield of CA) require individuals to have previous use, failure with, or intolerance to metformin. This meets our criteria step therapy because it does not exceed the 3-step limit and is clinically appropriate.

The following payers have additional step therapy requirements:

- HCSC requires previous or current use of a diabetic agent (e.g., metformin, insulin, DPP-4 inhibitors, SGLT2 inhibitors). This meets our criteria step therapy because it does not exceed the 3-step limit.
- VHA requires individuals to have had inadequate glycemic control on at least 1mg of semaglutide injection plus two or more glucose lowering drugs (metformin, empagliflozin, insulin, pioglitazone, sulfonylurea) for at least 6 months. This meets our criteria step therapy because it does not exceed the 3-step limit.

Kaiser does not implement utilization management so does not require policies for coverage. This meets our criteria for step therapy.

Table B1.2. Mounjaro Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	0	No step therapy policy	Y
Express Scripts PBM	0	No step requirement	Y
UnitedHealth Group, Inc.	0	No step requirement	Y
Cigna Corporation	1	Trial/failure of metformin	Y
OptumRx	0	No step requirement	Y
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	1	Trial/failure of metformin	Y
Health Care Service Corporation (HCSC)	1	Trial/failure of a diabetic agent (i.e., agents containing metformin, agents containing insulin, agents containing DPP-4 inhibitors, agents containing SGLT2 inhibitors, sulfonylureas, dopamine receptor agonists-ergot derivatives (e.g., bromocriptine), d-phenylalanine derivatives, meglitinide analogues, alpha-glucosidase inhibitors)	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	1	Inadequate response, intolerable side effect, or contraindication with metformin	Y
VHA National Formulary (VHA)	3	Inadequate glycemic control on at least 1mg of semaglutide injection plus two or more glucose lowering drugs (metformin, empagliflozin, insulin, pioglitazone, sulfonylurea) for at least 6 months	Y

SGLT2: sodium-glucose contransporter-2, Y: yes

Provider Qualifications

Total number of assessed payers: 11/11

All payers (Express Scripts, UnitedHealth, CVS Health, Cigna, OptumRx, Elevance, HCSC, Highmark, Blue Shield of CA, Kaiser, VHA) did not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

B1.5. Summary of Findings

Table B1.3. Mounjaro Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	Y	Y	Y	Y
Express Scripts PBM	Y	Y	Y	Y
UnitedHealth Group, Inc.	Y	Y	Y	Y
Cigna Corporation	Y	Y	Y	Y
OptumRx	Y	Y	Y	Y
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	Y	Y	Y	Y
Health Care Service Corporation (HCSC)	Y	Y	Y	Y
Highmark, Inc.	Y	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	Y	Y	Y	Y
VHA National Formulary (VHA)	Y	N	Y	Y

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

B2. Policy Brief: Wegovy (semaglutide), glucagon-like peptide-1 receptor agonist (GLP-1 RA, subcutaneous)

B2.1. Condition: Obesity

Cost-Effective at Current Prices: Yes

Other Drugs in Class: Saxenda (liraglutide), Wegovy (semaglutide), Zepbound (tirzepatide), Qsymia (phentermine/topiramate), Contrave (naltrexone/bupropion)

B2.2. Clinical Guidelines

American Gastroenterological Association: Pharmacological interventions for adults with obesity (2022)

Veterans Affairs/Department of Defense: Management of Adult Overweight and Obesity (2020)

B2.3. Background

FDA Label Information

Indication: WEGOVY is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated in combination with a reduced calorie diet and increased physical activity:
• To reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight.
• To reduce excess body weight and maintain weight reduction long term in:
- Adults and pediatric patients aged 12 years and older with obesity
- Adults with overweight in the presence of at least one weight-related comorbid condition.

Dosing: Injection: pre-filled, single-dose pen that delivers doses of 0.25 mg, 0.5 mg, 1 mg, 1.7 mg, 2.4 mg

Warning:
• In rodents, semaglutide causes thyroid C-cell tumors at clinically relevant exposures. It is unknown whether WEGOVY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.
• WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors.
Acute Pancreatitis: Has occurred in clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed.
• Acute Gallbladder Disease: Has occurred in clinical trials. If cholelithiasis is suspected, gallbladder studies and clinical follow-up are indicated.
• Hypoglycemia: Concomitant use with insulin or an insulin secretagogue may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing the dose of insulin or insulin secretagogue may be

necessary. Inform all patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.
• Acute Kidney Injury: Has occurred. Monitor renal function when initiating or escalating doses of WEGOVY in patients reporting severe adverse gastrointestinal reactions or in those with renal impairment reporting severe adverse gastrointestinal reactions.
• Hypersensitivity Reactions: Anaphylactic reactions and angioedema have been reported postmarketing. Discontinue WEGOVY if suspected and promptly seek medical advice.
• Diabetic Retinopathy Complications in Patients with Type 2 Diabetes: Has been reported in trials with semaglutide. Patients with a history of diabetic retinopathy should be monitored.
• Heart Rate Increase: Monitor heart rate at regular intervals.
• Suicidal Behavior and Ideation: Monitor for depression or suicidal thoughts. Discontinue WEGOVY if symptoms develop.

Contraindications:
• Personal or family history of MTC or in patients with MEN2.
• Known hypersensitivity to semaglutide or any of the excipients in WEGOVY

Interactions:
WEGOVY delays gastric emptying. May impact absorption of concomitantly administered oral medications. Use with caution.

Clinical Trial Eligibility:
STEP 1 Study
In this double-blind trial, adults with a body-mass index (the weight in kilograms divided by the square of the height in meters) of 30 or greater (≥27 in persons with ≥1 weight-related coexisting condition), who did not have diabetes, and randomly assigned, in a 2:1 ratio, to 68 weeks of treatment with once-weekly subcutaneous semaglutide (at a dose of 2.4 mg) or placebo, plus lifestyle intervention.

Link to Full FDA Label

ICER Policy Recommendations from the 2022 Review of Treatments for Obesity Management

A comprehensive set of policy recommendations regarding coverage policies, prior authorization criteria, and step therapy considerations for obesity medications in the United States were outlined in the ICER October 2022 obesity review.

B2.4. Findings: Coverage Policies

Wegovy was covered by nine payers (CVS Health, Express Scripts, Cigna, OptumRx, Kaiser, Elevance, Highmark, Blue Shield of CA, VHA). VHA describes Wegovy as "non-formulary with criteria for use" and provided us with a coverage policy so we assessed it as if covered. An additional three payers allowed the option for groups to opt-in to coverage of obesity medications (UnitedHealth, HCSC, Blue Shield of CA) and will be evaluated on all criteria as if it is a covered benefit.

- Nine payers cover Wegovy under the pharmacy benefit: CVS Health, Cigna, OptumRx, Kaiser, Elevance, HCSC, Highmark, Blue Shield of CA, VHA
- Two payers indicated that benefit type was up to the client: Express Scripts, UnitedHealth

Two payers (CVS Health, Kaiser) cover the medication without a specific written policy so had no policies to provide.

Cost Sharing

Total number of assessed payers: 10/11

Five payers (CVS Health, Express Scripts, Cigna, Elevance, OptumRx) placed Wegovy on the lowest relevant tier. This meets our cost-sharing criteria.

One payer (Blue Shield of CA) did not place Wegovy on the lowest relevant tier available, but they have other drugs in class on the lowest relevant tier. This meets our cost-sharing criteria.

Three payers (UnitedHealth, HCSC, Highmark) do not place Wegovy or other drugs in class on the lowest relevant tier. This does not meet our cost-sharing criteria because a (lower) preferred tier is available and Wegovy is not the only drug in its class. Since ICER determined that Wegovy is cost-effective, our cost-sharing criteria state that it or a therapeutic alternative (Saxenda, Qsymia, Contrave, or Zepbound) must be placed on the lowest relevant tier (i.e., Preferred Brand tier). While we agree that lifestyle modifications, such as diet and exercise, are the recommended first-line approach, these are non-pharmacologic modalities and thus not considered therapeutic alternatives to Wegovy.

VHA provides coverage at a low, fixed cost-sharing amount which is concordant with these criteria.

Table B2.1. Wegovy Cost Sharing by Payer

Payer	Tier (Description)	Lowest Relevant Tier?	If N, Lowest Relevant Tier; Drug(s) in Class Covered	Cost-Sharing Criteria Met?
CVS Health (Aetna)	2 (Preferred Brand)	Y	N/A	Y
Express Scripts PBM	2 (Preferred Brand)	Y	N/A	Y
UnitedHealth Group, Inc.	3 (Non-Preferred Brand)*	N	2 (Preferred Brand): None	N
Cigna Corporation	2 (Preferred Brand)	Y	N/A	Y
OptumRx	2 (Mid-Range Cost)	Y	N/A	Y
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	2 (Preferred Brand)	Y	N/A	Y
Health Care Service Corporation (HCSC)	4 (Non-Preferred Brand)*	N	3 (Preferred Brand): None	N
Highmark, Inc.	3 (Non-Preferred Brand)	N	2 (Preferred Brand): None	N
Blue Shield of California (Blue Shield of CA)	4 (Specialty/High Cost)*	N	2 (Preferred Brand): Qsymia	Y
VHA National Formulary (VHA)	Non-formulary	N/A	N/A	Y

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

* When groups opt-in to coverage of obesity medications, Wegovy is placed on this tier

Clinical Eligibility

Total number of assessed payers: 11/11

Two payers (CVS Health, Kaiser) do not have written policies stating clinical eligibility criteria. This meets our clinical eligibility criteria.

Eight payers (Express Scripts, UnitedHealth, Cigna, OptumRx, Elevance, HCSC, Highmark, Blue Shield of CA) required some version of the following eligible population: Individuals with a documented BMI of 30 kg/m^2 or greater (obese), or 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g. hypertension, type 2 diabetes mellitus, or dyslipidemia). This meets our criteria because it is in line with the label indication and clinical guidelines.

One payer (VHA) included more restrictive criteria:

- One or more VA National Formulary agents for chronic weight management (e.g., phentermine/topiramate; orlistat) at therapeutic or maximally tolerated doses are documented to be not tolerated, not adequate (e.g., < 5 % reduction body weight), or medically inadvisable (with rationale)

- Type 2 diabetes treated with semaglutide (OZEMPIC) AND requires additional weight loss to achieve ≥5% reduction in initial body weight
- BMI greater than or equal to 40
- BMI 35 to < 40 with a significant or difficult to manage weight-related condition or is unable to achieve weight loss goals required for surgery
- BMI 27 to < 40 with previous myocardial infarction, previous stroke, or symptomatic peripheral arterial disease

This does not meet our criteria due to the requirements of step therapy through other obesity medications, as well as additional segmentation of BMI categories beyond what is outlined in the FDA label and clinical guideline.

Step Therapy

Total number of assessed payers: 11/11

One payer (VHA) requires individuals to have stepped through one or more VA National Formulary agents for chronic weight management. This meets our criteria step therapy because it does not exceed the 3-step limit.

Step therapy was not required by any other payers. This meets our criteria for step therapy.

Table B2.2. Wegovy Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	0	No step therapy policy	Y
Express Scripts PBM	0	No step requirement	Y
UnitedHealth Group, Inc.	0	No step requirement	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	0	No step requirement	Y
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	0	No step requirement	Y
Health Care Service Corporation (HCSC)	0	No step requirement	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	0	No step requirement	Y
VHA National Formulary (VHA)	1	Requirement of use, inadequate response to, or intolerance at least one chronic weight management on the VA formulary (phentermine/topiramate; orlistat) Type 2 diabetes treated with semaglutide (OZEMPIC) AND requires additional weight loss to achieve ≥5% reduction in initial body weight	Y

Y: yes

Provider Qualifications

Total number of assessed payers: 11/11

Nine payers (Express Scripts, UnitedHealth, Cigna, OptumRx, Elevance, HCSC, Highmark, Blue Shield of CA, VHA) did not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Two payers (CVS Health, Kaiser) do not have specific written policies for provider qualifications for coverage and as such are rated concordant with these criteria.

B2.5. Summary of Findings

Table B2.3. Wegovy Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	Y	Y	Y	Y
Express Scripts PBM	Y	Y	Y	Y
UnitedHealth Group, Inc.	N	Y	Y	Y
Cigna Corporation	Y	Y	Y	Y
OptumRx	Y	Y	Y	Y
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	Y	Y	Y	Y
Health Care Service Corporation (HCSC)	N	Y	Y	Y
Highmark, Inc.	N	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	Y	Y	Y	Y
VHA National Formulary (VHA)	Y	N	Y	Y

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

B3. Policy Brief: Qsymia (phentermine/topiramate), sympathomimetic amine anorectic/antiepileptic anticonvulsant combination (oral)

B3.1. Condition: Obesity

Cost-Effective at Current Prices: Yes

Other Drugs in Class: Saxenda (liraglutide), Wegovy (semaglutide), Zepbound (tirzepatide), Contrave (naltrexone/bupropion)

B3.2. Clinical Guidelines

American Gastroenterological Association: Pharmacological interventions for adults with obesity (2022)

Veterans Affairs/Department of Defense: Management of Adult Overweight and Obesity (2020)

B3.3. Background

FDA Label Information

Indication: QSYMIA is a combination of phentermine, a sympathomimetic amine anorectic, and topiramate, indicated as an **adjunct to a reduced-calorie diet and increased physical activity** for **chronic weight management** in:

Adults with an initial body mass index (BMI) of:

- 30 kg/m2 or greater (obese)
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Pediatric patients aged 12 years and older with:

- BMI in the 95th percentile or greater standardized for age and sex.

Limitations of Use: The effect of QSYMIA on cardiovascular morbidity and mortality has not been established. The safety and effectiveness of QSYMIA in combination with other products intended for weight loss, including prescription and over-the-counter drugs, and herbal preparations, have not been established

Dosing:
Take orally once daily in morning. Avoid administration in evening to prevent insomnia. Recommended starting dosage is 3.75 mg/23 mg (phentermine mg/topiramate mg) daily for 14 days; then increase to 7.5 mg/46 mg daily. Escalate dosage based on weight loss in adults or BMI reduction in pediatric patients. Gradually discontinue 15 mg/92 mg dosage to prevent possible seizure. Do not exceed 7.5 mg/46 mg dosage for patients with moderate or severe renal impairment or patients with moderate hepatic impairment.

Warning:
- **Embryo-Fetal Toxicity**: Can cause fetal harm. In patients who can become pregnant, a negative pregnancy test is recommended before initiating QSYMIA and monthly during therapy; advise use of effective contraception. QSYMIA is available through a limited program under a Risk Evaluation and Mitigation Strategy (REMS)
- **Increase in Heart Rate**: Monitor heart rate, especially in those with cardiac or cerebrovascular disease

- **Suicidal Behavior and Ideation**: Monitor for depression or suicidal thoughts. Discontinue QSYMIA if symptoms develop
- **Risk of Ophthalmologic Adverse Reactions**: Acute myopia and secondary angle closure glaucoma have been reported. Immediately discontinue QSYMIA if symptoms develop. Consider QSYMIA discontinuation if visual field defects occur
- **Mood and Sleep Disorders**: Consider dosage reduction or discontinuation for clinically significant or persistent mood or sleep disorder symptoms
- **Cognitive Impairment**: May cause disturbances in attention or memory, or speech/language problems. Caution patients about operating automobiles or hazardous machinery when starting treatment
- **Slowing of Linear Growth**: Consider dosage reduction or discontinuation if pediatric patients are not growing or gaining height as expected
- **Metabolic Acidosis**: Measure electrolytes before and during treatment. If persistent metabolic acidosis develops, reduce dosage or discontinue QSYMIA
- **Decrease in Renal Function**: Measure creatinine before and during treatment. For persistent creatinine elevations, reduce dosage or discontinue QSYMIA
- **Serious Skin Reactions**: QSYMIA should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related

Contraindications: Pregnancy; Glaucoma; Hyperthyroidism; Taking or within 14 days of stopping monoamine oxidase inhibitors; Known hypersensitivity to any component of QSYMIA or idiosyncrasy to sympathomimetic amines

Interactions: **Oral Contraceptives**: Altered exposure of progestin and estrogen may cause irregular bleeding, but not increased risk of pregnancy. Advise patients not to discontinue oral contraceptives if spotting occurs. **CNS Depressants Including Alcohol**: May potentiate CNS depressant effects. Avoid excessive use of alcohol. **Non-potassium Sparing Diuretics**: May potentiate hypokalemia. Measure potassium before and during treatment

Clinical Trial Eligibility:
Study 1: Obese patients (BMI greater than or equal to 35 kg/m^2). Patients with diabetes were excluded.
Study 2: overweight and obese patients (BMI greater than or equal to 27 kg/m^2 and less than or equal to 45 kg/m^2). No lower limit on BMI for patients with type 2 diabetes) and two or more of the following obesity-related co-morbid conditions: Elevated blood pressure (greater than or equal to 140/90 mmHg, or greater than or equal to 130/85 mmHg for diabetics) or requirement for greater than or equal to 2 antihypertensive medications; Triglycerides greater than 200-400 mg/dL or were receiving treatment with 2 or more lipid-lowering agents; Elevated fasting blood glucose (greater than 100 mg/dL) or diabetes; and/or Waist circumference greater than or equal to 102 cm for men or greater than or equal to 88 cm for women.

Link to Full FDA Label

ICER Policy Recommendations

A comprehensive set of policy recommendations to payers regarding coverage policies, prior authorization criteria, and step therapy considerations for obesity medications in the United States were outlined in the October 2022 Review of *Treatments for Obesity Management.*

B3.4. Findings: Coverage Policies

Qsymia was covered by seven payers (CVS Health, Express Scripts, Cigna, OptumRx, Kaiser, Highmark, VHA). An additional three payers allowed the option for groups to opt-in to coverage of obesity medications (UnitedHealth, HCSC, Blue Shield of CA) and will be evaluated on all criteria as if it is a covered benefit. These ten payers were covered under the following benefit designs:

- Pharmacy benefit: CVS Health, Cigna, OptumRx, Kaiser, HCSC, Highmark, Blue Shield of CA, VHA
- Benefit type up to the client: Express Scripts, UnitedHealth

One payer (Elevance) listed Qsymia as non-formulary. This payer was only assessed on our cost-sharing criteria.

Coverage policies were provided by all payers who cover Qsymia with a written policy. Two payers (CVS Health, Kaiser) cover the medication without a specific written policy so had no policies to provide.

Cost Sharing

Total number of assessed payers: 11/11

Four payers (CVS Health, Blue Shield of CA, Kaiser, OptumRx) placed Qsymia on the lowest relevant tier. This meets our cost-sharing criteria.

Three payers (Express Scripts, Cigna, Elevance) did not place Qsymia on the lowest relevant tier, but they have one other drugs in class (Wegovy) on the lowest relevant tier. This meets our cost-sharing criteria.

VHA provides coverage at a low, fixed cost-sharing amount. This meets our cost-sharing criteria.

Three payers (HCSC, Highmark, UnitedHealth) do not place Qsymia or other weight loss drugs in class on the lowest relevant tier when a lower tier was available. This does not meet our cost-sharing criteria because a preferred tier is available and no other weight loss drugs were placed on a lower tier. We received feedback suggesting coverage of generic phentermine or coverage of the components of Qsymia separately should be considered to meet cost-sharing criteria. However, since phentermine is not indicated for chronic use and it is not possible to replicate the dosages of Qsymia through the generic components, we judged that neither option would allow Qsymia to meet cost-sharing criteria.

Table B3.1. Qsymia Cost Sharing by Payer

Payer	Tier (Description)	Lowest Relevant Tier?	If N, Lowest Relevant Tier; Drug(s) covered	Cost-Sharing Criteria Met?
CVS Health (Aetna)	2 (Preferred Brand)	Y	N/A	Y
Express Scripts PBM	3 (Non-Preferred Brand)	N	2 (Preferred Brand): Wegovy	Y
UnitedHealth Group, Inc.	3 (Non-Preferred Brand)*	N	2 (Preferred Brand): None	N
Cigna Corporation	3 (Non-Preferred Brand)	N	2 (Preferred Brand): Wegovy	Y
OptumRx	2 (Mid-Range Cost)	Y	N/A	Y
Kaiser Foundation Health Plans, Inc.	2 (Preferred Brand)	Y	N/A	Y
Elevance Health, Inc.	Non-formulary	N	2 (Preferred Brand): Wegovy	Y
Health Care Service Corporation (HCSC)	4 (Non-Preferred Brand)*	N	2 (Preferred Brand): None	N
Highmark, Inc.	3 (Non-Preferred Brand)	N	2 (Preferred Brand): None	N
Blue Shield of California (Blue Shield of CA)	2 (Preferred Brand)*	Y	N/A	Y
VHA National Formulary (VHA)	Formulary	N/A	N/A	Y

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

* When groups opt-in to coverage of obesity medications, Qsymia is placed on this tier

Clinical Eligibility

Total number of assessed payers: 10/11

One payer (Elevance) listed Qsymia as non-formulary. This payer was not assessed on our clinical eligibility criteria.

Two payers (CVS Health, Kaiser) do not have clinical eligibility criteria for coverage. This meets our clinical eligibility criteria.

Eight payers (Express Scripts, Cigna, HCSC, Highmark, Blue Shield of CA, OptumRx, VHA, UnitedHealth) required some version of the following eligible populations: Pediatric patients or adults who will use Qsymia as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management. Pediatric patients must be ages 12 years and older with an initial body mass index (BMI) in at least the 95th percentile for age and sex. Adult patients must be considered obese (BMI of 30 kg/m^2 or greater) or overweight (BMI of 27 kg/m^2 or greater in the presence of at least one weight-related comorbidity). This meets our criteria because it is in line with the label indication.

Some of the above eight payers included more specific criteria:

- Five payers additionally required patients to fail to limit weight gain through lifestyle modifications over at least 3 months (Express Scripts, Cigna, Highmark) or at least 6 months (HCSC, Blue Shield of CA). This meets our criteria as guidelines recommend behavioral and dietary modifications as first line of treatment.
- One payer (VHA) additionally required that patients taking topiramate for another condition (e.g., seizure disorder, migraines) must have the dose of topiramate adjusted so the cumulative dose does not exceed 400 mg/day. Although not part of the label indication, this requirement aligns with maximum safe dosing of topiramate and is not restrictive. This meets our criteria.
- One payer (Blue Shield of CA) additionally required that a patient has not undergone bariatric surgery within 12 months of receiving Qsymia. This does not meet our criteria as it is not part of the label indication or clinical guidelines.

Step Therapy

Total number of assessed payers: 10/11

One payer (Elevance) listed Qsymia as non-formulary. This payer was not assessed on our step therapy criteria.

Step therapy was not required by any other payer. This meets our criteria for step therapy.

Table B3.2. Qsymia Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	0	No step therapy policy	Y
Express Scripts PBM	0	No step requirement	Y
UnitedHealth Group, Inc.	0	No step requirement	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	0	No step requirement	Y
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	N/A	N/A	N/A*
Health Care Service Corporation (HCSC)	0	No step requirement	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	0	No step requirement	Y
VHA National Formulary (VHA)	0	No step requirement	Y

N/A: not applicable; Y: yes

* No rating issued as this payer does not cover Qsymia

Provider Qualifications

Total number of assessed payers: 10/11

One payer (Elevance) listed Qsymia as non-formulary. This payer was not assessed on our provider qualifications criteria.

No payers with coverage policies mentioned requiring specialist prescribing or consultation for Qsymia. This meets our provider qualifications criteria.

Two payers (CVS Health, Kaiser) do not have written policies for coverage and as such are rated concordant with these criteria.

B3.5. Summary of Findings

Table B4.3. Qsymia Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	Y	Y	Y	Y
Express Scripts PBM	Y	Y	Y	Y
UnitedHealth Group, Inc.	N	Y	Y	Y
Cigna Corporation	Y	Y	Y	Y
OptumRx	Y	Y	Y	Y
Kaiser Foundation Health Plans, Inc.	Y	Y	Y	Y
Elevance Health, Inc.	Y	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N	Y	Y	Y
Highmark, Inc.	N	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	Y	N	Y	Y
VHA National Formulary (VHA)	Y	Y	Y	Y

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

B4. Policy Brief: Saxenda (liraglutide), glucagon-like peptide-1 receptor agonist (GLP-1 RA, subcutaneous)

B4.1. Condition: Obesity

Cost-Effective at Current Prices: No

Other Drugs in Class: Wegovy (semaglutide), Zepbound (tirzepatide), Qsymia (phentermine/topiramate), Contrave (naltrexone/bupropion)

B4.2. Clinical Guidelines

American Gastroenterological Association: Pharmacological interventions for adults with obesity (2022)

Veterans Affairs/Department of Defense: Management of Adult Overweight and Obesity (2020)

B4.3. Background

FDA Label Information

Indication: SAXENDA is a glucagon like peptide 1 (GLP-1) receptor agonist indicated as **an adjunct to a reduced-calorie diet and increased physical activity** for chronic weight management in:
Adult patients with an initial body mass index (BMI) of:
• 30 kg/m2 or greater (obese), or
• 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g. hypertension, type 2 diabetes mellitus, or dyslipidemia).
Pediatric patients aged 12 years and older with:
• body weight above 60 kg and
• an initial BMI corresponding to 30 kg/m2 for adults (obese) by international cut-offs.

Dosing: Injection: 6 mg/mL solution in a 3 mL pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg.

Warning:
• Thyroid C-cell Tumors: Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether SAXENDA causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.
• SAXENDA is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC with use of SAXENDA and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early
detection of MTC in patients treated with SAXENDA.
• Acute Pancreatitis: Discontinue promptly if pancreatitis is suspected. Do

not restart if pancreatitis is confirmed.
• Acute Gallbladder Disease: If cholelithiasis or cholecystitis are suspected, gallbladder studies are indicated.
• Hypoglycemia: Can occur in adults when SAXENDA is used with an insulin secretagogue (e.g. a sulfonylurea) or insulin. The risk may be lowered by a reduction in the dose of concomitantly administered insulin secretagogues or insulin. In the pediatric clinical trial, patients did not have type 2 diabetes. Hypoglycemia occurred in SAXENDA-treated pediatric patients. Inform all patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.
• Heart Rate Increase: Monitor heart rate at regular intervals.
• Renal Impairment: Has been reported post-marketing, usually in association with nausea, vomiting, diarrhea, or dehydration which may sometimes require hemodialysis. Use caution when initiating or escalating doses of SAXENDA in patients with renal impairment.
• Hypersensitivity Reactions: Post-marketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema). Discontinue SAXENDA and other suspect medications and promptly seek medical advice.
• Suicidal Behavior and Ideation: Monitor for depression or suicidal thoughts. Discontinue SAXENDA if symptoms develop.

Contraindications:
• Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2.
• Hypersensitivity to liraglutide or any excipients in SAXENDA.
• Pregnancy.

Interactions:
SAXENDA delays gastric emptying. May impact absorption of concomitantly administered oral medications. Use with caution.

Clinical Trial Eligibility:
SCALE Maintenance Study
Obese/overweight participants (⩾18 years, body mass index ⩾30 kg m−2 or ⩾27 kg m−2 with comorbidities) who lost ⩾5% of initial weight during a LCD run-in were randomly assigned to liraglutide 3.0 mg per day or placebo (subcutaneous administration) for 56 weeks.

Link to Full FDA Label

ICER Policy Recommendations from the 2022 Review of Treatments for Obesity Management

A comprehensive set of policy recommendations regarding coverage policies, prior authorization criteria, and step therapy considerations for obesity medications in the United States were outlined in the ICER October 2022 obesity review.

B4.4. Findings: Coverage Policies

Saxenda was covered by eight payers (CVS Health, Express Scripts, Cigna, OptumRx, Kaiser, Elevance, Highmark, VHA). An additional three payers allowed the option for groups to opt-in to coverage of obesity medications (UnitedHealth, HCSC, Blue Shield of CA) and will be evaluated on all criteria as if it is a covered benefit.

- Nine of the above eleven payers cover Saxenda under the pharmacy benefit: CVS Health, Cigna, OptumRx, Kaiser, Elevance, HCSC, Highmark, Blue Shield of CA, VHA
- Two payers indicated that benefit type was up to the client: Express Scripts, UnitedHealth

Coverage policies were provided by all payers who cover Saxenda with a written policy. Because some clients of the PBM may opt to add coverage of obesity medications, the PBM has a coverage policy written for those circumstances, but for this formulary assessed it was not a covered benefit, and therefore not rated.

Two payers (CVS Health, Kaiser) cover the medication without a specific written policy so had no policies to provide.

Cost Sharing

Because Saxenda was deemed unfairly priced at its current price, we did not issue a rating on cost-sharing criteria for any payer.

Table B4.1. Saxenda Cost Sharing by Payer

Payer	Tier (Description)	Lowest Relevant Tier?	If N, Lowest Relevant Tier; Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	2 (Preferred Brand)	N/A	N/A	N/A
Express Scripts PBM	3 (Non-Preferred Brand)	N/A	N/A	N/A
UnitedHealth Group, Inc.*	3 (Non-Preferred Brand)*	N/A	N/A	N/A
Cigna Corporation	3 (Non-Preferred Brand)	N/A	N/A	N/A
OptumRx	2 (Mid-Range Cost)	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	3 (Non-Preferred Brand)	N/A	N/A	N/A
Health Care Service Corporation (HCSC)*	4 (Non-Preferred Brand)*	N/A	N/A	N/A
Highmark, Inc.	3 (Non-Preferred Brand)	N/A	N/A	N/A
Blue Shield of California (Blue Shield of CA) *	4 (Specialty/High Cost)*	N/A	N/A	N/A
VHA National Formulary (VHA)	Non-formulary	N/A	N/A	N/A

N/A: not applicable

* When groups opt-in to coverage of obesity medications, Saxenda is placed on this tier

Clinical Eligibility

Total number of assessed payers: 11/11

One payer (CVS Health) does not have a specific policy stating clinical eligibility criteria. This meets our clinical eligibility criteria.

Kaiser does not implement utilization management so does not require policies for coverage. This meets our clinical eligibility criteria.

Eight payers (Express Scripts, UnitedHealth, Cigna, OptumRx, Elevance, HCSC, Highmark, Blue Shield of CA) required some version of the following eligible population:

Individuals with a documented BMI of 30 kg/m2 or greater (obese), or 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g. hypertension, type 2 diabetes mellitus, or dyslipidemia).

This meets our criteria because it is in line with the label indication.

One payer (VHA) included more restrictive criteria, requesting that individuals meet ONE of the following:

- All VA National Formulary agents for chronic weight management (e.g., phentermine/topiramate; orlistat) at therapeutic or maximally tolerated doses are documented to be not tolerated, not adequate (e.g., < 5 % reduction body weight), or medically inadvisable (with rationale)
- Meets diagnostic criteria for prediabetes
- Type 2 diabetes AND is eligible for or treated with semaglutide (OZEMPIC) as per the Criteria for Use for management of diabetes, but is unable to use (e.g., due to intolerance)

This does not meet our criteria because the requirement for prior use of other obesity medications and meeting diagnostic criteria for prediabetes is not consistent with the drug's FDA label and is more restrictive than clinical guidelines.

Step Therapy

Total number of assessed payers: 11/11

One payer (VHA) required patients to have either:

1) Documented intolerance, inadequate response (< 5% weight loss), or medical unsuitability (with rationale) to all VA National Formulary chronic weight management medications (e.g., phentermine/topiramate; orlistat) at therapeutic or maximum tolerated doses.
2) Eligibility for or previous treatment with semaglutide but inability to use

This meets our criteria step therapy because it is in line with the FDA label and does not exceed the 3-step limit.

Step therapy was not required by any other payer. This meets our criteria for step therapy.

Table B4.2. Saxenda Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	0	No step therapy policy	Y
Express Scripts PBM	0	No step requirement	Y
UnitedHealth Group, Inc.	0	No step requirement	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	0	No step requirement	Y
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	0	No step requirement	Y
Health Care Service Corporation (HCSC)	0	No step requirement	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	0	No step requirement	Y
VHA National Formulary (VHA)	1-2	Requires individuals have stepped through phentermine/topiramate and orlistat OR Diagnosis of type 2 diabetes and be eligible for or treated with semaglutide but is unable to use	Y

Y: yes

Provider Qualifications

Total number of assessed payers: 11/11

Ten payers (CVS Health, Express Scripts, UnitedHealth, Cigna, OptumRx, Elevance, HCSC, Highmark, Blue Shield of CA, VHA) did not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Kaiser does not implement utilization management so does not require policies for coverage. This meets our provider qualifications criteria.

B4.5. Summary of Findings

Table B4.3. Saxenda Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	N/A	Y	Y	Y
Express Scripts PBM	N/A	Y	Y	Y
UnitedHealth Group, Inc.	N/A	Y	Y	Y
Cigna Corporation	N/A	Y	Y	Y
OptumRx	N/A	Y	Y	Y
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	N/A	Y	Y	Y
Health Care Service Corporation (HCSC)	N/A	Y	Y	Y
Highmark, Inc.	N/A	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	N/A	Y	Y	Y
VHA National Formulary (VHA)	N/A	N	Y	Y

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

B5. Policy Brief: Contrave (naltrexone/bupropion), opioid antagonist/ aminoketone antidepressant (oral)

B5.1. Condition: Obesity

Cost-Effective at Current Prices: No

Other Drugs in Class: Saxenda (liraglutide), Wegovy (semaglutide), Zepbound (tirzepatide), Qsymia (phentermine/topiramate)

B5.2. Clinical Guidelines

American Gastroenterological Association: Pharmacological interventions for adults with obesity (2022)

Veterans Affairs/Department of Defense: Management of Adult Overweight and Obesity (2020)

B5.3. Background

FDA Label Information

Indication: adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m2 or greater (obese) or
- 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbidity (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia).

Dosing: CONTRAVE dose escalation schedule

	Morning Dose	Evening Dose
Week 1	1 tablet	None
Week 2	1 tablet	1 tablet
Week 3	2 tablets	1 tablet
Week 4 – Onward	2 tablets	2 tablets

Warning:

- Suicidal Behavior and Ideation: Monitor for depression or suicidal thoughts. Discontinue CONTRAVE if symptoms develop.
- Risk of seizure may be minimized by adhering to the recommended dosing schedule and avoiding coadministration with high-fat meal.
- Increase in Blood Pressure and Heart Rate: Monitor blood pressure and heart rate in all patients, especially those with cardiac or cerebrovascular disease.
- Hepatotoxicity: Cases of hepatitis and clinically significant liver dysfunction observed with naltrexone exposure.
- Angle-closure glaucoma: Angle-closure glaucoma has occurred in patients with untreated anatomically narrow angles treated with antidepressants.
- Use of Antidiabetic Medications: Weight loss may cause hypoglycemia. Monitor blood glucose.

Contraindications:
- Uncontrolled hypertension
- Seizure disorders, anorexia nervosa or bulimia, or undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs
- Use of other bupropion-containing products
- Chronic opioid use
- During or within 14 days of taking monoamine oxidase inhibitors (MAOI)
- Known allergy to any of the ingredients in CONTRAVE
- Pregnancy

Interactions:
- MAOIs: Increased risk of hypertensive reactions can occur when used concomitantly.
- Drugs Metabolized by CYP2D6: Bupropion inhibits CYP2D6 and can increase concentrations of: antidepressants, (e.g., selective serotonin reuptake inhibitors and many tricyclics), antipsychotics (e.g., haloperidol, risperidone and thioridazine), beta-blockers (e.g., metoprolol) and Type 1C antiarrhythmics (e.g., propafenone and flecainide): Consider dose reduction when using with CONTRAVE.
- Concomitant Treatment with CYP2B6 Inhibitors (e.g., ticlopidine or clopidogrel) can increase bupropion exposure. Do not exceed one tablet twice daily when taken with CYP2B6 inhibitors.
- CYP2B6 Inducers (e.g., ritonavir, lopinavir, efavirenz, carbamazepine, phenobarbital, and phenytoin) may reduce efficacy by reducing bupropion exposure, avoid concomitant use.
- Drugs that Lower Seizure Threshold: Dose CONTRAVE with caution.
- Dopaminergic Drugs (levodopa and amantadine): CNS toxicity can occur when used with CONTRAVE.
- Drug-Laboratory Test Interactions: CONTRAVE can cause false-positive urine test results for amphetamines.

Clinical Trial Eligibility:
Trial Name: COR-I, COR-II, COR-DMOB
- Patients with obesity (BMI 30 kg/m^2 or greater) or overweight (BMI 27 kg/m^2 or greater) and at least one comorbidity (hypertension or dyslipidemia).

Trial Name: COR-Diabetes
- Patients with BMI greater than 27 kg/m^2 with type 2 diabetes with or without hypertension and/or dyslipidemia

Link to Full FDA Label

ICER Policy Recommendations

A comprehensive set of policy recommendations to payers regarding coverage policies, prior authorization criteria, and step therapy considerations for obesity medications in the United States were outlined in the October 2022 Review of *Treatments for Obesity Management.*

B5.4. Findings: Coverage Policies

Contrave was covered by five payers (Express Scripts, Cigna, Kaiser, Highmark, VHA). An additional three payers allowed the option for groups to opt-in to coverage of obesity medications (UnitedHealth, HCSC, Blue Shield of CA) and will be evaluated on all criteria as if it is a covered benefit. These eight payers had coverage under the following benefit designs:

- Pharmacy benefit only: Cigna, Kaiser, Elevance, HCSC, Highmark, Blue Shield of CA, VHA
- Benefit type up to the client: Express Scripts, UnitedHealth

Three payers (CVS Health, Elevance, OptumRx) listed Contrave as excluded or non-formulary. Thus, this drug was only assessed on our cost-sharing criteria for these payers.

We received policies from seven payers who cover Contrave with a written policy. One payer (Kaiser) does not implement utilization management and does not require policies for coverage and so had no policy to review.

Cost Sharing

Because Contrave was deemed unfairly priced at its current price, we did not issue a rating on cost-sharing criteria for any payer.

Table B5.1. Contrave Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	3 (Non-Preferred Brand)	N/A	N/A	N/A
Express Scripts PBM	3 (Non-Preferred Brand)	N/A	N/A	N/A
UnitedHealth Group, Inc.	3 (Non-Preferred Brand)*	N/A	N/A	N/A
Cigna Corporation	3 (Non-Preferred Brand)	N/A	N/A	N/A
OptumRx	Excluded	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	Non-formulary	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	4 (Non-Preferred Brand)*	N/A	N/A	N/A
Highmark, Inc.	3 (Non-Preferred Brand)	N/A	N/A	N/A
Blue Shield of California (Blue Shield of CA)	3 (Non-Preferred Brand)*	N/A	N/A	N/A
VHA National Formulary (VHA)	N/A	N/A	N/A	N/A

N/A: not applicable

* When groups opt-in to obesity management coverage, Contrave is placed on this tier

Clinical Eligibility

Total number of assessed payers: 8/11

Kaiser does not implement utilization management so does not require policies for coverage. This meets our clinical eligibility criteria.

Seven payers (Express Scripts, UnitedHealth, Cigna, HCSC, Highmark, Blue Shield of CA, VHA) required some version of the following eligible population: the patient is ≥ 18 years of age; BMI ≥ 30 kg/m2, or a BMI ≥ 27 kg/m2 for those with comorbidities besides obesity; engaged in behavioral modification and dietary restriction and failed to achieve desired weight loss. This meets our criteria because it is in line with the label indication.

Three payers (CVS Health, Elevance, OptumRx) listed Contrave as excluded or non-formulary. These payers were not assessed on our clinical eligibility criteria for Contrave.

Step Therapy

Total number of assessed payers: 8/11

Step therapy was not required by seven of the assessed payers and one payer (Kaiser) has no written step therapy policy for coverage. This meets our criteria for step therapy.

Three payers (CVS Health, Elevance, OptumRx) listed Contrave as excluded or non-formulary. These payers were not assessed on our step therapy criteria for Contrave.

Table B5.2. Contrave Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A
Express Scripts PBM	0	No step requirement	Y
UnitedHealth Group, Inc.	0	No step requirement	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	0	No step requirement	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	0	No step requirement	Y
VHA National Formulary (VHA)	0	No step requirement	Y

N/A: not applicable, Y: yes

Provider Qualifications

Total number of assessed payers: 8/11

Three payers (CVS Health, Elevance, OptumRx) listed Contrave as excluded or non-formulary. These payers were not assessed on our provider qualifications criteria.

Kaiser does not implement utilization management so does not require policies for coverage. This meets our provider qualifications criteria.

Specialist prescribing or consultation was not required by any of the remaining payers. This meets our provider qualifications criteria.

B5.5. Summary of Findings

Table B5.3. Contrave Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	N/A	Y	Y	Y
UnitedHealth Group, Inc.	N/A	Y	Y	Y
Cigna Corporation	N/A	Y	Y	Y
OptumRx	N/A	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	N/A	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N/A	Y	Y	Y
Highmark, Inc.	N/A	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	N/A	Y	Y	Y
VHA National Formulary (VHA)	N/A	Y	Y	Y

N/A: not applicable, Y: yes

B6. Policy Brief: Cosela (trilaciclib), CDK4/6 inhibitor (intravenous injection)

B6.1. Condition: Chemotherapy-induced myelosuppression

Cost-Effective at Current Prices: No

Other Drugs in Class: None

B6.2. Clinical Guidelines

NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Growth Factors Version 3.2024

B6.3. Background

FDA Label Information

Indication: COSELA is a kinase inhibitor indicated to decrease the incidence of **chemotherapy-induced myelosuppression** in **adult patients** when administered **prior to a platinum/etoposide-containing regimen or topotecan-containing regimen** for **extensive-stage small cell lung cancer (ES-SCLC)**.

Dosing: COSELA is for intravenous use only. The recommended dose of COSELA is 240 mg/m^2 as a 30-minute intravenous infusion completed within 4 hours prior to the start of chemotherapy on each day chemotherapy is administered. Reduce dose in patients with moderate or severe hepatic impairment.

Warning:
- **Injection-Site Reactions, Including Phlebitis and Thrombophlebitis**: Monitor for signs and symptoms of injection-site reactions, including phlebitis and thrombophlebitis during infusion. Stop infusion and permanently discontinue COSELA for severe or life-threatening reactions.
- **Acute Drug Hypersensitivity Reactions**: Monitor for signs and symptoms of acute drug hypersensitivity reactions, including edema (facial, eye, and tongue), urticaria, pruritus, and anaphylactic reactions. Withhold COSELA for moderate reactions, and permanently discontinue for severe or life-threatening reactions.
- **Interstitial Lung Disease (ILD)/Pneumonitis**: Patients treated with CDK4/6 inhibitors should be monitored for pulmonary symptoms indicative of ILD/pneumonitis. Interrupt and evaluate patients with new or worsening symptoms suspected to be due to ILD/pneumonitis. Permanently discontinue COSELA in patients with recurrent symptomatic or severe/life-threatening ILD/pneumonitis.
- **Embryo-Fetal Toxicity**: Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.

Contraindications: Patients with a history of serious hypersensitivity reactions to COSELA.

Interactions: Certain OCT2, MATE1, and MATE-2K substrates: Avoid concomitant use with certain OCT2, MATE1, and MATE-2K substrates where minimal concentration changes may lead to serious or life-threatening toxicities.

Clinical Trial Eligibility:

Study 1: In patients with newly diagnosed ES-SCLC not previously treated with chemotherapy. COSELA or placebo administered prior to treatment with etoposide, carboplatin, and atezolizumab (E/P/A).
Study 2: COSELA or placebo administered prior to treatment with etoposide and carboplatin (E/P) for patients with newly diagnosed ES-SCLC not previously treated with chemotherapy.
Study 3: COSELA or placebo administered prior to treatment with topotecan for patients with ES-SCLC previously treated with chemotherapy

Link to Full FDA Label

ICER Policy Recommendations

No policy recommendations were established as no public meeting was held for the review of Cosela.

B6.4. Findings: Coverage Policies

Cosela was covered by seven payers under the following benefit designs:

- Medical benefit only: UnitedHealth, Cigna, HCSC, Highmark, Blue Shield of CA, Kaiser
- Benefit type up to the client: Express Scripts

Two payers excluded Cosela from coverage (CVS Health, OptumRx). These payers were not assessed on any of our criteria and excluded from analysis for this drug. Two payers listed Cosela as non-formulary (Elevance, VHA). These payers were only assessed on our cost-sharing criteria for this drug.

Three payers cover the medication without a specific written policy so had no policies to provide (UnitedHealth, Blue Shield of CA, Kaiser). Coverage policies were provided by all four remaining payers who cover Cosela with a written policy (Cigna, Express Scripts, HCSC, Highmark).

Cost Sharing

Because Cosela was deemed unfairly priced at its current price, we did not issue a rating on cost-sharing criteria for any payer.

Table B6.1. Cosela Cost Sharing by Payer

Payer	Tier (Description)	Lowest Relevant Tier?	If N, Lowest Relevant Tier; Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	Excluded	N/A	N/A	N/A
Express Scripts PBM	3 (Non-Preferred Brand)	N/A	N/A	N/A
UnitedHealth Group, Inc.	N/A	N/A	N/A	N/A
Cigna Corporation	N/A	N/A	N/A	N/A
OptumRx	Excluded	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	Non-formulary	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N/A	N/A	N/A	N/A
Highmark, Inc.	N/A	N/A	N/A	N/A
Blue Shield of California (Blue Shield of CA)	N/A	N/A	N/A	N/A
VHA National Formulary (VHA)	Non-formulary	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Total number of assessed payers: 7/11

Four payers (UnitedHealth, HCSC, Kaiser, Blue Shield of CA) do not require clinical eligibility criteria for coverage. This meets our clinical eligibility criteria.

Three payers (Express Scripts, Cigna, Highmark) required some version of the following eligible population: Adults 18 years of age or older with extensive-small cell lung cancer (ES-SCLC) who will receive Cosela to decrease the incidence of chemotherapy-induced myelosuppression while taking platinum and etoposide-containing chemotherapy regimens OR topotecan-containing regiments. This meets our criteria because it is in line with the label indication.

Four payers (Elevance, VHA, CVS Health, OptumRx) listed Cosela as excluded or non-formulary. These payers were not assessed on our clinical eligibility criteria for Cosela.

Step Therapy

Total number of assessed payers: 7/11

Of the seven payers that cover Cosela, three (Express Scripts, Cigna, Highmark) do not require step therapy and the remaining four (UnitedHealth, Kaiser, Blue Shield of CA, HSCS) cover the drug without a specific written policy on step therapy. This meets our criteria for step therapy.

Four payers (Elevance, VHA, CVS Health, OptumRx) listed Cosela as excluded or non-formulary. These payers were not assessed on our step therapy criteria for Cosela.

Table B6.2. Cosela Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A
Express Scripts PBM	0	No step requirement	Y
UnitedHealth Group, Inc.	0	No step therapy policy	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	0	No step therapy policy	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	0	No step therapy policy	Y
VHA National Formulary (VHA)	N/A	N/A	N/A

N/A: not applicable, Y: yes

Provider Qualifications

Total number of assessed payers: 7/11

Four payers (UnitedHealth, Kaiser, Blue Shield of CA, HCSC) covered the drug without a specific coverage policy. One payer (Highmark) did not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Two payers (Express Scripts, Cigna) required prescribing by or in consultation with an oncologist. This meets our criteria because specialist clinician diagnosis is appropriate for this condition.

Four payers (CVS Health, OptumRx, Elevance, VHA) listed Cosela as excluded or non-formulary. These payers were not assessed on our provider qualifications criteria for Cosela.

B6.5. Summary of Findings

Table B6.3. Cosela Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	N/A	Y	Y	Y
UnitedHealth Group, Inc.	N/A	Y	Y	Y
Cigna Corporation	N/A	Y	Y	Y
OptumRx	N/A	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	N/A	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N/A	Y	Y	Y
Highmark, Inc.	N/A	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	N/A	Y	Y	Y
VHA National Formulary (VHA)	N/A	N/A	N/A	N/A

N/A: not applicable, Y: yes

B7. Policy Brief: Veozah (fezolinetant), neurokinin 3 receptor (oral tablet)

B7.1. Condition: Menopause (Vasomotor Symptoms)

Cost-Effective at Current Prices: No

Other Drugs in Class: None

B7.2. Clinical Guidelines

The North American Menopause Society (NAMS) 2023

The National Institute for Health and Care Excellence (NICE) 2019 and 2024 summary

B7.3. Background

FDA Label Information

Indication: VEOZAH is a neurokinin 3 (NK3) receptor antagonist indicated for the treatment of **moderate to severe vasomotor symptoms due to menopause**.

Dosing: One 45 mg tablet orally once daily with or without food. Perform baseline bloodwork to evaluate for hepatic function and injury before beginning VEOZAH. While using VEOZAH, perform follow-up bloodwork at 3 months, 6 months, and 9 months after initiation of therapy and when symptoms suggest liver injury.

Warning:
- **Hepatic Transaminase Elevation**: Elevations in serum transaminase concentrations greater than three times the upper limit of normal (ULN) occurred in the clinical trials. Perform bloodwork prior to initiation of VEOZAH to evaluate for hepatic function and injury. Do not start therapy if serum transaminase concentration is equal to or exceeds two times the ULN. Perform follow-up evaluations of hepatic transaminase concentration at 3 months, 6 months, and 9 months after initiation of therapy.

Contraindications: Known cirrhosis, severe renal impairment or end-stage renal disease, and concomitant use with CYP1A2 inhibitors.

Interactions: CYP1A2 Inhibitors Concomitant use of VEOZAH with drugs that are weak, moderate, or strong CYP1A2 inhibitors, increase the plasma C_{max} and AUC of VEOZAH. VEOZAH is contraindicated in individuals using CYP1A2 inhibitors.

Clinical Trial Eligibility:
Trials 1 & 2: women who had a minimum average of 7 moderate to severe vasomotor symptoms per day

Link to Full FDA Label

ICER Policy Recommendations

A comprehensive set of policy recommendations to payers regarding coverage policies, prior authorization criteria, and step therapy considerations for vasomotor symptoms associated with menopause in the United States were outlined in the January 2023 Review of *Fezolinetant for Moderate to Severe Vasomotor Symptoms Associated with Menopause.*

B7.4. Findings: Coverage Policies

Veozah was covered by eight payers under the following benefit designs:

- Pharmacy benefit: UnitedHealth, Cigna, Kaiser, HCSC, Highmark, Blue Shield of CA, VHA
- Benefit type up to the client: Express Scripts

Two payers excluded Veozah from coverage (CVS Health, OptumRx). These payers were not assessed on any of our criteria and excluded from analysis for this drug. One payer (Elevance) listed Cosela as non-formulary, this payer was only assessed on our cost-sharing criteria for this drug.

Three payers (Express Scripts, Cigna, Kaiser) cover the medication without a specific written policy so had no policies to provide. Coverage policies were provided by all five remaining payers who cover Cosela with a written policy (UnitedHealth, HCSC, Highmark, Blue Shield of CA, VHA).

Cost Sharing

Because Veozah was deemed unfairly priced at its current price, we did not issue a rating on cost-sharing criteria for any payer.

Table B7.1. Veozah Cost Sharing by Payer

Payer	Tier (Description)	Lowest Relevant Tier?	If N, Lowest Relevant Tier; Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	Excluded	N/A	N/A	N/A
Express Scripts PBM	3 (Non-Preferred Brand)	N/A	N/A	N/A
UnitedHealth Group, Inc.	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna Corporation	3 (Non-Preferred Brand)	N/A	N/A	N/A
OptumRx	Excluded	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	Non-formulary	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	4 (Non-Preferred Brand)	N/A	N/A	N/A
Highmark, Inc.	3 (Non-Preferred Brand)	N/A	N/A	N/A
Blue Shield of California (Blue Shield of CA)	3 (Non-Preferred Brand)	N/A	N/A	N/A
VHA National Formulary (VHA)	Non-formulary*	N/A	N/A	N/A

N/A: not applicable

* Although marked as non-formulary, VHA has a written policy for Veozah and will be considered as "covered"

Clinical Eligibility

Total number of assessed payers: 8/11

Three payers (Express Scripts, Cigna, Kaiser) cover Veozah without written coverage policies specific to the medication. This is concordant with our clinical eligibility criteria.

All five payers covering Veozah (UnitedHealth, HCSC, Highmark, Blue Shield of CA, VHA) with coverage policies required some version of the following eligible population: Patients with moderate to severe vasomotor symptoms due to menopause. This meets our criteria because it is in line with the label indication.

Additionally, all of the above payers required patients to have tried and failed, be contraindicated or intolerant to at least one menopausal hormone therapy. One payer (UnitedHealth) required either trial and failure, contraindication or intolerance to hormone OR non-hormonal therapy. One payer (HCSC) required patients step through hormone therapy OR be over 60 years of age or have onset of menopause greater than 10 years prior. These requirements meet our clinical eligibility criteria because they are in line with treatment guidelines and clinician recommendations.

Three payers (HCSC, Blue Shield of CA, VHA) required patients to have tried and failed, be contraindicated, or intolerant to both hormonal therapy and non-hormonal therapy. These requirements meet our clinical eligibility criteria because they are in line with treatment guidelines and clinician recommendations.

One payer (Highmark) included an age requirement of 18 years of age. Although not included in the label indication, an age requirement of 18 years or older is appropriate given the onset of the condition. This meets our criteria.

Two payers (HCSC, VHA) require patients to have hepatic transaminase levels less than two times the upper limit of normal and total bilirubin within the normal range. These requirements match recommendations in the Warnings and Precautions section of the label recommending Veozah be used only under these conditions of hepatic function. This meets our criteria. VHA additionally lists the following exclusion criteria for coverage: known cirrhosis, severe renal impairment, and concomitant use of CYP1A2 inhibitors. As all three of these requirements are listed in the label's Contraindications section, these requirements also meet our criteria.

Three payers (CVS Health, OptumRx, Elevance) listed Veozah as excluded or non-formulary. These payers were not assessed on our clinical eligibility criteria for Veozah.

Step Therapy

Total number of assessed payers: 8/11

Three payers (Express Scripts, Cigna, Kaiser) cover Veozah without written coverage policies specific to the medication and so have no step therapy requirements. This is concordant with our step therapy criteria.

Five payers listed at least one step requirement: Highmark listed one step requirement of a trial and failure, contraindication, or intolerance to hormone therapy prior to Veozah, or prescriber attestation that hormone therapy is not appropriate. UnitedHealth required either trial and failure, contraindication or intolerance to hormone or non-hormonal therapy. HCSC required patients to step through hormone therapy or be either over the age of 60 or have onset of menopause 10 or more years prior. HCSC additionally required patients to step through nonhormonal therapy or show documentation that nonhormonal therapy would not be appropriate or ineffective. Blue Shield of CA requires patients to be contraindicated, intolerant, or have insufficient response to hormonal therapy and nonhormonal therapy. VHA requires patients to be contraindicated or intolerant to one hormonal therapy (or have a preference to avoid) and be contraindicated, intolerant, or have insufficient response to one nonhormonal therapy. These requirements meet our step therapy criteria because they are in line with clinical guidelines and do not exceed the 3-step limit.

Three payers (CVS Health, OptumRx, Elevance) listed Veozah as excluded or non-formulary. These payers were not assessed on our step therapy criteria for Veozah.

Table B7.2. Veozah Step Therapy by Payer

Payer	Steps	Summarized Details	Step Therapy Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A
Express Scripts PBM	0	No step therapy policy	Y
UnitedHealth Group, Inc.	1	Must have tried and failed menopausal hormone therapy OR Non-hormonal therapy	Y
Cigna Corporation	0	No step therapy policy	Y
OptumRx	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	2	Must have tried and failed menopausal hormone therapy AND one nonhormonal therapy	Y
Highmark, Inc.	1	Must have tried and failed one generic hormone therapy	Y
Blue Shield of California (Blue Shield of CA)	2	Must have tried and failed one agent from each of the following classes: a. Hormone therapy b. Non-hormonal therapy	Y
VHA National Formulary (VHA)	2	Must have tried and failed menopausal hormone therapy (MHT) and one nonhormonal treatment for VMS	Y

N/A: not applicable, VMS: vasomotor symptoms, Y: yes

Provider Qualifications

Total number of assessed payers: 8/11

Three payers (Express Scripts, Cigna, Kaiser) cover Veozah without written coverage policies specific to the medication and so have no prescriber qualification requirements. This is concordant with our provider qualifications criteria.

None of the remaining five payers with written coverage policies mentioned require specialist prescribing or consultation. This meets our provider qualifications criteria.

Three payers (CVS Health, OptumRx, Elevance) listed Veozah as excluded or non-formulary. These payers were not assessed on our provider qualifications criteria for Veozah.

B7.5. Summary of Findings

Table B7.3. Veozah Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	N/A	Y	Y	Y
UnitedHealth Group, Inc.	N/A	Y	Y	Y
Cigna Corporation	N/A	Y	Y	Y
OptumRx	N/A	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	N/A	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N/A	Y	Y	Y
Highmark, Inc.	N/A	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	N/A	Y	Y	Y
VHA National Formulary (VHA)	N/A	Y	Y	Y

N/A: not applicable, Y: yes

B8. Policy Brief: Radicava ORS (oral edaravone), free radical scavenger and antioxidant (oral)

B8.1. Condition: Amyotrophic Lateral Sclerosis (ALS)

Cost-Effective at Current Prices: No

Other Drugs in Class: None

B8.2. Clinical Guidelines

American Academy of Neurology 2009, reaffirmed 2023

European Federation of Neurological Societies 2024

Canadian ALS Research Network Guideline 2020

B8.3. Background

FDA Label Information

Indication: treatment of ALS

Dosing: Oral suspension: the recommended dosage is 105 mg (5 mL) taken orally or via feeding tube in the morning after overnight fasting. Food should not be consumed for 1 hour after administration except water.

Warning:
- Hypersensitivity Reactions: Advise patients to seek immediate medical care.
- Sulfite Allergic Reactions: RADICAVA and RADICAVA ORS contain sodium bisulfite, which may cause allergic type reactions, including anaphylactic symptoms and asthmatic episodes in susceptible people.

Contraindications: Patients with a history of hypersensitivity to edaravone or any of the inactive ingredients in RADICAVA and/or RADICAVA ORS

Interactions: None

Clinical Trial Eligibility:
Trial Name: Study 19/MCI186-19
- Patients whose conditions are defined as "definite ALS" or "probable ALS" diagnostic criteria El Escorial and revised Airlie House.
- Patients who can eat a meal, excrete, or move with oneself alone, and do not need assistance in everyday life.
- Patients of less than 2 years after the onset of ALS.
- Patients whose progress of the condition during 12 weeks before administration meet other requirements.

Link to Full FDA Label

ICER Policy Recommendations from the 2022 Review of AMX0035 and Oral Edaravone for Amyotrophic Lateral Sclerosis

A comprehensive set of policy recommendations regarding coverage policies, prior authorization criteria, and step therapy considerations for ALS medications in the United States were outlined in the ICER September 2022 ALS review.

B8.4. Findings: Coverage Policies

Radicava ORS was covered by 10 payers (CVS Health, Express Scripts, UnitedHealth, Cigna, OptumRx, Kaiser, HCSC, Highmark, Blue Shield of CA, VHA).

- Nine payers cover Radicava ORS under the pharmacy benefit: CVS Health, UnitedHealth, Cigna, OptumRx, Kaiser, HCSC, Highmark, Blue Shield of CA, VHA
- One payer indicated that benefit type was up to the client: Express Scripts

One payer (Elevance) listed Radicava ORS as non-formulary. This drug was only assessed on our cost-sharing criteria.

One payer (Kaiser) covers the medication without a specific written policy so had no policies to provide.

Cost Sharing

Because Radicava ORS was deemed unfairly priced at its current price, we did not issue a rating on cost-sharing criteria for any payer.

Table B8.1. Radicava ORS Cost Sharing by Payer

Payer	Tier (Description)	Lowest Relevant Tier?	If N, Lowest Relevant Tier; Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	2 (Preferred Brand)	N/A	N/A	N/A
Express Scripts PBM	2 (Preferred Brand)	N/A	N/A	N/A
UnitedHealth Group, Inc.	3 (Non-Preferred Brand)	N/A	N/A	N/A
Cigna Corporation	3 (Non-Preferred Brand)	N/A	N/A	N/A
OptumRx	2 (Mid-Range Cost)	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	N/A (Specialty)	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	6 (Non-Preferred Specialty)	N/A	N/A	N/A
Highmark, Inc.	3 (Non-Preferred Brand)	N/A	N/A	N/A
Blue Shield of California (Blue Shield of CA)	4 (Specialty/High Cost)	N/A	N/A	N/A
VHA National Formulary (VHA)	N/A (Formulary)	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Nine payers (CVS Health, Express Scripts, UnitedHealth, Cigna, OptumRx, HCSC, Highmark, Blue Shield of CA, VHA) required some version of the following eligible population:

- Functionality retained most activities of daily living (defined as scores of 2 points or better on each individual item of the ALS Functional Rating Scale)
- Normal respiratory function (defined as percent-predicted forced vital capacity values of ≥ 80%)
- Definite or Probable ALS based on El Escorial revised criteria
- Disease duration of 2 years or less

The eligibility criteria outlined above are more restrictive than the FDA-approved labeling for this drug, reflecting the inclusion criteria used in the pivotal Phase 3 clinical trial. The Fair Access protocol permits the use of trial eligibility for clinical eligibility when a drug is not cost-effective, as is the case here. Thus, these policies are concordant with clinical eligibility criteria.

Kaiser does not implement utilization management so does not require policies for coverage. This meets our clinical eligibility criteria.

One payer (Elevance) listed Radicava ORS as non-formulary. This drug/payer combination was not assessed on our clinical eligibility criteria.

Step Therapy

Total number of assessed payers: 10/11

Step therapy was not required by seven payers (CVS Health, UnitedHealth, Cigna, OptumRx, Highmark, Kaiser, VHA). This meets our criteria for step therapy.

Three payers (Express Scripts, HCSC, Blue Shield of CA) require patients to have concurrent, prior treatment with, or intolerance to riluzole. This meets our criteria step therapy because it does not exceed the 3-step limit.

One payer (Elevance) listed Radicava ORS as non-formulary. This drug/payer combination was not assessed on our step therapy criteria.

Table B8.2. Radicava ORS Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	0	No step requirement	Y
Express Scripts PBM	1	Patient has received or is currently receiving riluzole	Y
UnitedHealth Group, Inc.	0	No step requirement	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	0	No step requirement	Y
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	1	Current or previous use of, or intolerance to riluzole	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	1	Patient has received concurrent or prior treatment with riluzole OR patient is unable to take riluzole	Y
VHA National Formulary (VHA)	0	No step requirement	Y

N/A: not applicable, Y: yes

Provider Qualifications

Total number of assessed payers: 10/11

The following payers required prescribing by or in consultation with an ALS specialist: (CVS Health, Express Scripts, UnitedHealth, Cigna, OptumRx, HCSC, Highmark, Blue Shield of CA, VHA). This meets our criteria because specialist clinician diagnosis and monitoring are appropriate for this condition.

One payer (Elevance) listed Radicava ORS as non-formulary. This drug/payer combination was not assessed on our provider qualifications criteria.

Kaiser does not implement utilization management so does not require policies for coverage. This meets our provider qualifications criteria.

B8.5. Summary of Findings

Table B8.3. Radicava ORS Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	N/A	Y	Y	Y
Express Scripts PBM	N/A	Y	Y	Y
UnitedHealth Group, Inc.	N/A	Y	Y	Y
Cigna Corporation	N/A	Y	Y	Y
OptumRx	N/A	Y	Y	Y
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	N/A	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N/A	Y	Y	Y
Highmark, Inc.	N/A	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	N/A	Y	Y	Y
VHA National Formulary (VHA)	N/A	Y	Y	Y

N/A: not applicable, Y: yes

B9. Policy Brief: Zynteglo (drug name), gene therapy (intravenous infusion)

B9.1. Condition: Beta Thalassemia (transfusion-dependent)

Cost-Effective at Current Prices: No

Other Drugs in Class: Casgevy (exagamglogene autotemcel)

B9.2. Clinical Guidelines

2021 Thalassaemia International Federation Guidelines

B9.3. Background

FDA Label Information

Indication: ZYNTEGLO is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of **adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusions.**

Dosing: For autologous use only. For intravenous use only. Patients are required to undergo hematopoietic stem cell (HSC) mobilization followed by apheresis to obtain CD34+ cells for ZYNTEGLO manufacturing. Dosing of ZYNTEGLO is based on the number of CD34+ cells in the infusion bag(s) per kg of body weight. The **minimum recommended dose is 5.0 × 10^6 CD34+ cells/kg**. Full myeloablative conditioning must be administered before infusion of ZYNTEGLO. Prophylaxis for hepatic veno-occlusive disease (VOD) is recommended. Prophylaxis for seizures should be considered.

Preparation Before ZYNTEGLO Infusion

- Before mobilization, apheresis, and myeloablative conditioning are initiated, confirm that hematopoietic stem cell (HSC) transplantation is appropriate for the patient.
- It is recommended that patients be maintained at a hemoglobin (Hb) ≥ 11 g/dL for at least 30 days prior to mobilization and 30 days prior to myeloablative conditioning.
- Granulocyte-colony stimulating factor (G-CSF) and plerixafor were used for mobilization and busulfan was used for myeloablative conditioning. Refer to the prescribing information for the mobilization agent(s) and the myeloablative conditioning agent(s) prior to treatment.
- Perform screening for hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2), and human immunodeficiency virus 1 & 2 (HIV-1/HIV-2) in accordance with clinical guidelines before collection of cells for manufacturing.

Warning:

- **Delayed Platelet Engraftment**: Monitor platelet counts until platelet engraftment and recovery are achieved. Patients should be monitored for thrombocytopenia and bleeding.
- **Risk of Neutrophil Engraftment Failure**: Monitor absolute neutrophil counts (ANC) after ZYNTEGLO infusion. If neutrophil engraftment does not occur administer rescue cells.
- **Risk of Insertional Oncogenesis**: Monitor patients at least annually for hematologic malignancies for at least 15 years after ZYNTEGLO infusion.

- **Hypersensitivity Reactions**: Monitor for hypersensitivity reactions during infusion.

Contraindications: None.

Interactions:
- Anti-retrovirals and Hydroxyurea: Do not take anti-retroviral medications or hydroxyurea for one month prior to mobilization, or for the expected duration for elimination of the medications, and until all cycles of apheresis are completed.
- **Iron Chelation**: Discontinue iron chelators 7 days prior to initiation of myeloablative conditioning. Avoid use of myelosuppressive iron chelators for 6 months after ZYNTEGLO infusion.

Clinical Trial Eligibility:
Two Phase 3 Trials:
- β-thalassemia requiring regular transfusions.
- Had a history of transfusions of at least 100 mL/kg/year of packed red blood cells (pRBCs) or with 8 or more transfusions of pRBCs per year in the 2 years preceding enrollment.
- Patients who had severely **elevated iron in the heart** (i.e., patients with cardiac T2* less than 10 msec by magnetic resonance imaging [MRI]) or **advanced liver disease** were not accepted into the studies.
- Patients younger than 18 years with MRI results demonstrating liver iron content ≥ 15 mg/g were excluded from the studies unless a liver biopsy could provide additional data to confirm eligibility.
- Patients with a liver biopsy demonstrating bridging fibrosis, cirrhosis, or active hepatitis, were also excluded.

The safety and efficacy of ZYNTEGLO in children less than 4 years of age have not been established. No data are available. ZYNTEGLO has not been studied in patients > 65 years of age.

Link to Full FDA Label

ICER Policy Recommendations

A comprehensive set of policy recommendations to payers regarding coverage policies, prior authorization criteria, and step therapy considerations for vasomotor symptoms associated with menopause in the United States were outlined in the July 2022 Review of *Zynteglo for Beta Thalassemia*.

B9.4. Findings: Coverage Policies

Zynteglo was covered by 10 payers under the following benefit designs:

- Medical benefit only: CVS Health, UnitedHealth, Cigna, OptumRx, Elevance, HCSC, Highmark, Blue Shield of CA, Kaiser
- Benefit type up to the client: Express Scripts

One payer (VHA) listed Zynteglo as "non-formulary but covered with clinical justification" with no criteria for coverage provided. This payer was only assessed on our cost-sharing criteria for this drug.

Three payers covering Zynteglo are PBMs and since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria, even if a policy for coverage was provided.

One payer (Kaiser) covers the medication without a specific written policy so had no policy to provide. Coverage policies were provided by all seven remaining payers who cover Zynteglo with a written policy (Express Scripts, UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA).

Cost Sharing

Because Zynteglo was deemed unfairly priced at its current price, we did not issue a rating on cost-sharing criteria for any payer.

Table B9.1. Zynteglo Cost Sharing by Payer

Payer	Tier (Description)	Lowest Relevant Tier?	If N, Lowest Relevant Tier; Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	2 (Preferred Brand)	N/A	N/A	N/A
UnitedHealth Group, Inc.	N/A	N/A	N/A	N/A
Cigna Corporation	N/A	N/A	N/A	N/A
OptumRx	N/A	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	N/A	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N/A	N/A	N/A	N/A
Highmark, Inc.	N/A	N/A	N/A	N/A
Blue Shield of California (Blue Shield of CA)	N/A	N/A	N/A	N/A
VHA National Formulary (VHA)	Non-formulary	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Total number of assessed payers: 7/11

One payer (Kaiser) does not implement utilization management so does not have coverage policies specific to Zynteglo; drugs that are deemed medically appropriate by the prescribing physician are covered. This meets our clinical eligibility criteria.

Six payers (UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA) required some version of the following eligible population: adults and pediatric patients with beta-thalassemia requiring regular red blood cell transfusions (at least 100 mL/kg/year or 8 units/year of packed red blood cell transfusions). This meets our criteria because it is in line with the label indication and clinical definitions of transfusion dependence.

All six payers also listed the following requirements aligning with clinical trial exclusion criteria that meet our criteria: No evidence of severe iron overload, advanced liver disease, or current or prior malignancies. In addition to the above, other payers also included exclusion criteria from the clinical trials:

- Four payers (UnitedHealth, Cigna, HCSC, Blue Shield of CA) also required patients to be negative for human immunodeficiency virus type 1 or 2 (HIV-1 or 2). This meets our criteria as it aligns with clinical trial exclusion criteria and language in the label suggesting a negative serology test for HIV is necessary to ensure acceptance of apheresis material for Zynteglo.
- Three payers (UnitedHealth, Cigna, Blue Shield of CA) additionally required negative results for hepatitis B virus (HBV), hepatitis C virus (HCV). UnitedHealth and Cigna required negative results for human T-lymphotropic virus 1 & 2 (HTLV-1/HTLV-2) as well. This also meets our criteria as it aligns with clinical trial exclusion criteria.
- Four payers (Cigna, HCSC, Highmark, Blue Shield of CA) also required patients to have a white blood cell (WBC) count above 3×10^9/liter, and/or platelet count above 100×10^9/liter. This meets our criteria as it aligns with clinical trial exclusion criteria.

Several payers included more specific criteria:

- Four payers (Cigna, HCSC, Highmark, Blue Shield of CA) specified an upper age limit of 50 years of age. Three payers (UnitedHealth, Highmark, Blue Shield of CA) specified a lower age limit of 4 years of age or a minimum weight of 6 kilograms and able to provide the minimum number of cells required for treatment. This meets our criteria because it is consistent with clinical trial enrollment and lack of data in patients younger than 4 years of age.
- Three payers (UnitedHealth, Cigna, Highmark) require documentation of either a β0/β0 or non-β0/β0 genotype. This meets our criteria because it is consistent with clinical trials enrollment criteria and guideline recommendations.
- Three payers (UnitedHealth, Cigna, Elevance) required that patients be candidates for an allogeneic hematopoietic cell transplantation but be ineligible due to the absence of a donor. This meets our criteria as it is consistent with clinical guideline recommendations.

One payer (VHA) listed Zynteglo as "non-formulary but covered with clinical justification" and did not provide criteria for coverage. This payer was not assessed on our clinical eligibility criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

Step Therapy

Total number of assessed payers: 7/11

Step therapy was not required by any of the six payers with coverage policies (UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA) and one payer (Kaiser) does not have a written step policy to gain coverage. This meets our criteria for step therapy.

One payer (VHA) listed Zynteglo as "non-formulary but covered with clinical justification" and did not provide criteria for coverage. This payer was not assessed on our step therapy criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

Table B9.2. Zynteglo Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A
Express Scripts PBM	N/A	N/A	N/A
UnitedHealth Group, Inc.	0	No step requirement	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	0	No step therapy policy	Y
Elevance Health, Inc.	0	No step requirement	Y
Health Care Service Corporation (HCSC)	0	No step requirement	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	0	No step requirement	Y
VHA National Formulary (VHA)	N/A	N/A	N/A

N/A: not applicable, Y: yes

Provider Qualifications

Total number of assessed payers: 7/11

Three payers (Elevance, HCSC, Blue Shield of CA) did not mention requiring specialist prescribing or consultation. One payer (Kaiser) does not have a written policy to gain coverage. This meets our provider qualifications criteria.

Three payers (UnitedHealth, Cigna, Highmark) required prescribing by or in consultation with a specialist: UnitedHealth required clinical eligibility evaluations by hepatology and oncology. Cigna and Highmark required consultation with a hematologist or specialist. This meets our criteria because specialist clinician diagnosis and monitoring is appropriate for this condition.

One payer (VHA) listed Zynteglo as "non-formulary but covered with clinical justification" and did not provide criteria for coverage. This payer was not assessed on our provide qualifications criteria for Zynteglo.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

B9.5. Summary of Findings

Table B9.3. Zynteglo Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	N/A	N/A	N/A	N/A
UnitedHealth Group, Inc.	N/A	Y	Y	Y
Cigna Corporation	N/A	Y	Y	Y
OptumRx	N/A	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	N/A	Y	Y	Y
Health Care Service Corporation (HCSC)	N/A	Y	Y	Y
Highmark, Inc.	N/A	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	N/A	Y	Y	Y
VHA National Formulary (VHA)	N/A	N/A	N/A	N/A

N/A: not applicable, Y: yes

B10. Policy Brief: Hemgenix (etranacogene dezaparvovec-drlb), viral gene therapy (IV infusion)

B10.1. Condition: Hemophilia B

Cost-Effective at Current Prices: No

Other Drugs in Class: None

B10.2. Clinical Guidelines

National Bleeding Disorders Foundation (NBDF): Medical and Scientific Advisory Council (MASAC) recommendations concerning products licensed for the treatment of hemophilia and selected disorders of the coagulation system (2024)

National Bleeding Disorders Foundation (NBDF): Medical and Scientific Advisory Council (MASAC) Recommendation Concerning Prophylaxis for Hemophilia A and B with and without Inhibitors (2022)

B10.3. Background

FDA Label Information

Indication: treatment of adults with Hemophilia B (congenital Factor IX deficiency) who:

- Currently use Factor IX prophylaxis therapy, or
- Have current or historical life-threatening hemorrhage, or
- Have repeated, serious spontaneous bleeding episodes.

Dosing: For single-use intravenous infusion only.

- Perform baseline testing to select patients, including testing for Factor IX inhibitor presence and liver health tests.
- The recommended dose of HEMGENIX is 2 x 10^{13} genome copies (gc) per kg of body weight.
- Administer HEMGENIX as an intravenous infusion after dilution with 0.9% normal saline at a constant infusion rate of 500 ml/hour (8 mL/min).

Warning:

- Infusion reactions: Monitor during administration and for at least 3 hours after end of infusion. If symptoms occur, slow or interrupt administration. Re-start administration at a slower infusion once resolved.
- Hepatotoxicity: Closely monitor transaminase levels once per week for 3 months after HEMGENIX administration to mitigate the risk of potential hepatotoxicity. Continue to monitor transaminases in all patients who developed liver enzyme elevations until liver enzymes return to baseline. Consider corticosteroid treatment should elevations occur.
- Hepatocellular carcinogenicity: For patients with preexisting risk factors (e.g., cirrhosis, advanced hepatic fibrosis, hepatitis B or C, non-alcoholic fatty liver disease (NAFLD), chronic alcohol consumption,

non-alcoholic steatohepatitis (NASH), and advanced age), perform regular (e.g., annual) liver ultrasound and alpha-fetoprotein testing following administration.
- Monitoring Laboratory tests: Monitor for Factor IX activity and Factor IX inhibitors.

Contraindications: None

Interactions: None

Clinical Trial Eligibility:
Trial Name: HOPE-B
- Adult male subjects aged 19 to 75 years, with severe or moderately severe Hemophilia B, who received a single intravenous dose of 2×10^{13} gc/kg body weight of HEMGENIX
- Completed a lead-in period of at least six months with the intent to receive standard of care routine Factor IX prophylaxis.

Link to Full FDA Label

ICER Policy Recommendations

A comprehensive set of policy recommendations to payers regarding coverage policies, prior authorization criteria, and step therapy considerations for Hemgenix in the United States were outlined in the ICER December 2022 Hemophilia Review.

B10.4. Findings: Coverage Policies

Hemgenix was covered by ten payers. These payers had coverage under the following benefit designs:

- Medical benefit only: Nine payers (CVS Health, UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA, OptumRx, Kaiser)
- Benefit type up to the client: One payer (Express Scripts)

One payer (VHA) listed Hemgenix as "non-formulary but covered with clinical justification" with no criteria for coverage provided, this drug was only assessed on our cost-sharing criteria.

Coverage policies were provided by all seven payers who cover Hemgenix with a written policy. The remaining three payers (CVS Health, OptumRx, Kaiser) cover the medication without a specific written policy so had no policies to provide.

Cost Sharing

Because Hemgenix was deemed unfairly priced at its current price, we did not issue a rating on cost-sharing criteria for any payer.

Table B10.1. Hemgenix Cost Sharing by Payer

Payer	Tier (Description)	Lowest Relevant Tier?	If N, Lowest Relevant Tier; Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	2 (Preferred Brand)	N/A	N/A	N/A
UnitedHealth Group, Inc.	N/A	N/A	N/A	N/A
Cigna Corporation	N/A	N/A	N/A	N/A
OptumRx	3 (Higher Cost)	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	N/A	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N/A	N/A	N/A	N/A
Highmark, Inc.	N/A	N/A	N/A	N/A
Blue Shield of California (Blue Shield of CA)	N/A	N/A	N/A	N/A
VHA National Formulary (VHA)	N/A	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Total number of assessed payers: 7/11

Kaiser does not implement utilization management so does not require policies for coverage. This meets our clinical eligibility criteria.

Six payers (UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA) required some version of the following eligible population: patient is ≥ 18 years of age; diagnosis of moderate-to-severe hemophilia B; received routine prophylaxis with factor replacement therapy. This meets our criteria because it is in line with the inclusion/exclusion criteria from clinical trials.

Some payers included more specific criteria:

- Three payers (UnitedHealth, Highmark, Blue Shield of CA) required documentation that patient has been evaluated for presence of preexisting neutralizing antibodies to the adenovirus vector (AAV-5) which may be associated with a lack of treatment response. This meets our criteria because it is appropriate to screen patients who are suitable for viral gene therapy.

One payer (VHA) listed Hemgenix as excluded or non-formulary. This payer was not assessed on our clinical eligibility criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

Step Therapy

Total number of assessed payers: 7/11

Step therapy was not required by any payer covering Hemgenix. This meets our criteria for step therapy.

One payer (VHA) listed Hemgenix as excluded or non-formulary. This payer was not assessed on our step therapy criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

Table B10.2. Hemgenix Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A
Express Scripts PBM	N/A	N/A	N/A
UnitedHealth Group, Inc.	0	No step requirement	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	0	No step requirement	Y
Elevance Health, Inc.	0	No step requirement	Y
Health Care Service Corporation (HCSC)	0	No step requirement	Y
Highmark, Inc.	0	No step requirement	Y
Blue Shield of California (Blue Shield of CA)	0	No step requirement	Y
VHA National Formulary (VHA)	N/A	N/A	N/A

N/A: not applicable, Y: yes

Provider Qualifications

Total number of assessed payers: 7/11

Three payers (Elevance, HCSC, Blue Shield of CA) did not mention requiring specialist prescribing or consultation. Kaiser does not implement utilization management so does not require policies for coverage. These meet our provider qualifications criteria.

The following payers required prescribing by or in consultation with a specialist: (UnitedHealth, Cigna, Highmark) required that the prescriber be a specialist. This meets our criteria because specialist clinician diagnosis and monitoring are appropriate for this condition.

One payer (VHA) listed Hemgenix as excluded or non-formulary. This payer was not assessed on our provider qualifications criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

B10.5. Summary of Findings

Table B10.3. Hemgenix Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	N/A	N/A	N/A	N/A
UnitedHealth Group, Inc.	N/A	Y	Y	Y
Cigna Corporation	N/A	Y	Y	Y
OptumRx	N/A	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	N/A	Y	Y	Y
Health Care Service Corporation (HCSC)	N/A	Y	Y	Y
Highmark, Inc.	N/A	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	N/A	Y	Y	Y
VHA National Formulary (VHA)	N/A	N/A	N/A	N/A

N/A: not applicable, Y: yes

B11. Policy Brief: Roctavian (valoctocogene roxaparvovec-rvox), viral gene therapy (IV infusion)

B11.1. Condition: Hemophilia A

Cost-Effective at Current Prices: No

Other Drugs in Class: None

B11.2. Clinical Guidelines

National Bleeding Disorders Foundation (NBDF): Medical and Scientific Advisory Council (MASAC) recommendations concerning products licensed for the treatment of hemophilia and selected disorders of the coagulation system (2024)

National Bleeding Disorders Foundation (NBDF): Medical and Scientific Advisory Council (MASAC) Recommendation Concerning Prophylaxis for Hemophilia A and B with and without Inhibitors (2022)

B11.3. Background

FDA Label Information

Indication: treatment of adults with severe hemophilia A (congenital factor VIII deficiency with factor VIII activity < 1 IU/dL) without pre-existing antibodies to adeno-associated virus serotype 5 detected by an FDA-approved test.

Dosing: For one-time single-dose intravenous use only.

- Perform baseline testing to select patients, including testing for pre-existing antibodies to adeno-associated virus serotype 5 (AAV5), factor VIII inhibitor presence, and liver health assessments.
- The recommended dose of ROCTAVIAN is 6×10^{13} vector genomes (vg) per kg of body weight.
- Start the infusion at 1 mL/min. If tolerated, the rate may be increased every 30 minutes by 1 mL/min up to a maximum rate of 4 mL/min.

Warning:

- Infusion-related reactions: Infusion reactions, including hypersensitivity reactions and anaphylaxis, have occurred. Monitor during and for at least 3 hours after ROCTAVIAN administration. If symptoms occur, slow or interrupt administration and give appropriate treatment. Restart infusion at slower rate once symptoms resolve. Discontinue infusion for anaphylaxis.
- Hepatotoxicity: Monitor alanine aminotransferase (ALT) weekly for at least 26 weeks and institute corticosteroid treatment in response to ALT elevations as required. Continue to monitor ALT until it returns to baseline. Monitor factor VIII activity levels since ALT elevation may be accompanied by a decrease in factor VIII activity. Monitor for and manage adverse reactions from corticosteroid use.
- Thromboembolic events: Thromboembolic events may occur in the setting of elevated factor VIII activity above the upper limit of normal (ULN). Factor VIII activity above ULN has been reported following

ROCTAVIAN infusion. Evaluate for risk factors for thrombosis including cardiovascular risk factors prior to and after ROCTAVIAN use and advise patients accordingly.
- Monitoring laboratory tests: Monitor for factor VIII activity and factor VIII inhibitors.
- Malignancy: Monitor for hepatocellular malignancy in patients with risk factors for hepatocellular carcinoma (e.g., hepatitis B or C, non-alcoholic fatty liver disease, chronic alcohol consumption, non-alcoholic steatohepatitis, advanced age). Perform regular liver ultrasound (e.g., annually) and alpha-fetoprotein testing following administration. In the event that any malignancy occurs after treatment with ROCTAVIAN, contact BioMarin Pharmaceutical Inc. at 1-866-906-6100.

Contraindications:
- Active infections, either acute or uncontrolled chronic.
- Known significant hepatic fibrosis (stage 3 or 4), or cirrhosis.
- Known hypersensitivity to mannitol.

Interactions: None

Clinical Trial Eligibility:
Trial Name: GENEr8-1, GENEr8-2
- adult males (18 years of age and older) with severe hemophilia A, who received a single intravenous dose of ROCTAVIAN
- previously treated with prophylactic factor VIII replacement therapy, but not emicizumab
- patients without detectable, pre-existing antibodies to AAV5 capsid

Link to Full FDA Label

ICER Policy Recommendations

A comprehensive set of policy recommendations regarding coverage policies, prior authorization criteria, and step therapy considerations for Roctavian in the United States were outlined in the ICER December 2022 Hemophilia Review.

B11.4. Findings: Coverage Policies

Roctavian was covered by 10 payers. These payers had coverage under the following benefit designs:

- Medical benefit only: nine payers (CVS Health, UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA, OptumRx, Kaiser)
- Benefit type up to the client: One payer (Express Scripts)

Three payers (CVS Health, OptumRx, Kaiser) cover the medication without a specific written policy so had no policy to provide. Coverage policies were provided by all seven remaining payers who cover Roctavian with a written policy (UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA, Express Scripts).

One payer (VHA) listed Roctavian as "non-formulary but covered with clinical justification" with no criteria for coverage provided, this drug was only assessed on our cost-sharing criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on this criteria.

Cost Sharing

Because Roctavian was deemed unfairly priced at its current price, we did not issue a rating on cost-sharing criteria for any payer.

Table B11.1. Roctavian Cost Sharing by Payer

Payer	Tier (Description)	Best Relevant Tier?	If N, Best Tier and Drug(s)	Cost-Sharing Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	2 (Preferred Brand)	N/A	N/A	N/A
UnitedHealth Group, Inc.	N/A	N/A	N/A	N/A
Cigna Corporation	N/A	N/A	N/A	N/A
OptumRx	3 (Higher Cost)	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	N/A	N/A	N/A
Elevance Health, Inc.	N/A	N/A	N/A	N/A
Health Care Service Corporation (HCSC)	N/A	N/A	N/A	N/A
Highmark, Inc.	N/A	N/A	N/A	N/A
Blue Shield of California (Blue Shield of CA)	N/A	N/A	N/A	N/A
VHA National Formulary (VHA)	Non-formulary	N/A	N/A	N/A

N/A: not applicable

Clinical Eligibility

Total number of assessed payers: 7/11

Kaiser does not implement utilization management so does not require policies for coverage. This meets our clinical eligibility criteria.

Six payers (UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA) required some version of the following eligible population: patient is ≥ 18 years of age; diagnosis of severe hemophilia A; received routine prophylaxis with factor replacement therapy. This meets our criteria because it is in line with the label indication.

Some payers included more specific criteria:

- Six payers (UnitedHealth, Cigna, Elevance, HCSC, Highmark, Blue Shield of CA) required that patient has been evaluated for presence of preexisting neutralizing antibodies to the adenovirus vector (AAV-5) which may be associated with a lack of treatment response. This meets our criteria because it is appropriate to screen patients who are suitable for viral gene therapy.

One payer (VHA) listed Roctavian as excluded or non-formulary. This payer was not assessed on our clinical eligibility criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

Step Therapy

Total number of assessed payers: 7/11

Two payers (UnitedHealth, Highmark) required routine prophylaxis with Hemlibra (emicizumab). This meets our criteria step therapy because it is in line with clinical guidelines and does not exceed the 3-step limit.

Kaiser does not implement utilization management so does not require policies for coverage. This meets our step therapy criteria.

One payer (VHA) listed Roctavian as excluded or non-formulary. This payer was not assessed on our step therapy criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

Table B11.2. Roctavian Step Therapy by Payer

Payer	Steps	Details	Step Therapy Criteria Met ?
CVS Health (Aetna)	N/A	N/A	N/A
Express Scripts PBM	N/A	N/A	N/A
UnitedHealth Group, Inc.	0-1	Trial/failure of routine prophylaxis with Hemlibra (emicizumab) and/or factor replacement	Y
Cigna Corporation	0	No step requirement	Y
OptumRx	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	0	No step requirement	Y
Elevance Health, Inc.	0	No step requirement	Y
Health Care Service Corporation (HCSC)	0	No step requirement	Y
Highmark, Inc.	0-1	Trial/failure of routine prophylaxis with Hemlibra (emicizumab) and/or factor replacement	Y
Blue Shield of California (Blue Shield of CA)	0	No step requirement	Y
VHA National Formulary (VHA)	N/A	N/A	N/A

N/A: not applicable, Y: yes

Provider Qualifications

Total number of assessed payers: 7/11

Two payers (Elevance, HCSC) did not mention requiring specialist prescribing or consultation. This meets our provider qualifications criteria.

Four payers required prescribing by or in consultation with a specialist: (UnitedHealth, Cigna, Highmark, Blue Shield of CA) required that the prescriber be a specialist. This meets our criteria because specialist clinician diagnosis and monitoring are appropriate for this condition.

Kaiser does not implement utilization management so does not require policies for coverage. This meets our provider qualifications criteria.

One payer (VHA) listed Roctavian as excluded or non-formulary. This payer was not assessed on our provider qualifications criteria.

Three payers (CVS Health, Express Scripts, OptumRx) in scope are pharmacy benefit managers (PBMs). Since coverage policies for gene therapies are decided and enforced by health plans, we did not issue ratings on these criteria.

B11.5. Summary of Findings

Table B11.3. Roctavian Fair Access Criteria by Payer

Payer	Cost-Sharing Criteria Met?	Clinical Eligibility Criteria Met?	Step Therapy Criteria Met?	Provider Qualifications Criteria Met?
CVS Health (Aetna)	N/A	N/A	N/A	N/A
Express Scripts PBM	N/A	N/A	N/A	N/A
UnitedHealth Group, Inc.	N/A	Y	Y	Y
Cigna Corporation	N/A	Y	Y	Y
OptumRx	N/A	N/A	N/A	N/A
Kaiser Foundation Health Plans, Inc.	N/A	Y	Y	Y
Elevance Health, Inc.	N/A	Y	Y	Y
Health Care Service Corporation (HCSC)	N/A	Y	Y	Y
Highmark, Inc.	N/A	Y	Y	Y
Blue Shield of California (Blue Shield of CA)	N/A	Y	Y	Y
VHA National Formulary (VHA)	N/A	N/A	N/A	N/A

N/A: not applicable, Y: yes

B12. Supplemental Fair Access Criteria Concordance Ratings

Table B12. Fair Access Criteria Concordance by Drug and Formulary

Drug and Formulary	Dominant Benefit Plan Type*	Cost Sharing Met?	Clinical Eligibility Met?	Step Therapy Met?	Provider Qualifications Met?
Mounjaro					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Pharmacy	Y	Y	Y	Y
Express Scripts National Preferred Formulary	Pharmacy	Y	Y	Y	Y
UnitedHealthcare Advantage Three Tier	Pharmacy	Y	Y	Y	Y
Cigna Standard Three Tier	Pharmacy	Y	Y	Y	Y
OptumRx Premium Formulary	Pharmacy	Y	Y	Y	Y
Kaiser Permanente Southern California 3 Tier HMO	Pharmacy	N/A	Y	Y	Y
Anthem Essential 4 Tier	Pharmacy	Y	Y	Y	Y
BCBS of Illinois Basic 6 Tier	Pharmacy	Y	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Pharmacy	Y	Y	Y	Y
Blue Shield California Plus Formulary	Pharmacy	Y	Y	Y	Y
VHA National Formulary	Pharmacy	Y	N	Y	Y
Cosela					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Medical	N/A	N/A	N/A	N/A
Express Scripts National Preferred Formulary	Medical	N/A	Y	Y	Y
UnitedHealthcare Advantage Three Tier	Medical	N/A	Y	Y	Y
Cigna Standard Three Tier	Medical	N/A	Y	Y	Y
OptumRx Premium Formulary	Medical	N/A	N/A	N/A	N/A
Kaiser Permanente Southern California 3 Tier HMO	Medical	N/A	Y	Y	Y
Anthem Essential 4 Tier	Medical	N/A	N/A	N/A	N/A
BCBS of Illinois Basic 6 Tier	Medical	N/A	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Medical	N/A	Y	Y	Y
Blue Shield California Plus Formulary	Medical	N/A	Y	Y	Y
VHA National Formulary	Medical	N/A	N/A	N/A	N/A

Zynteglo					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Medical	N/A	N/A	N/A	N/A
Express Scripts National Preferred Formulary	Medical	N/A	N/A	N/A	N/A
UnitedHealthcare Advantage Three Tier	Medical	N/A	Y	Y	Y
Cigna Standard Three Tier	Medical	N/A	Y	Y	Y
OptumRx Premium Formulary	Medical	N/A	N/A	N/A	N/A
Kaiser Permanente Southern California 3 Tier HMO	Medical	N/A	Y	Y	Y
Anthem Essential 4 Tier	Medical	N/A	Y	Y	Y
BCBS of Illinois Basic 6 Tier	Medical	N/A	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Medical	N/A	Y	Y	Y
Blue Shield California Plus Formulary	Medical	N/A	Y	Y	Y
VHA National Formulary	Medical	N/A	N/A	N/A	N/A
Radicava ORS					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Pharmacy	N/A	Y	Y	Y
Express Scripts National Preferred Formulary	Pharmacy	N/A	Y	Y	Y
UnitedHealthcare Advantage Three Tier	Pharmacy	N/A	Y	Y	Y
Cigna Standard Three Tier	Pharmacy	N/A	Y	Y	Y
OptumRx Premium Formulary	Pharmacy	N/A	Y	Y	Y
Kaiser Permanente Southern California 3 Tier HMO	Pharmacy	N/A	Y	Y	Y
Anthem Essential 4 Tier	Pharmacy	N/A	N/A	N/A	N/A
BCBS of Illinois Basic 6 Tier	Pharmacy	N/A	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Pharmacy	N/A	Y	Y	Y
Blue Shield California Plus Formulary	Pharmacy	N/A	Y	Y	Y
VHA National Formulary	Pharmacy	N/A	Y	Y	Y
Wegovy					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Pharmacy	Y	Y	Y	Y
Express Scripts National Preferred Formulary	Pharmacy	Y	Y	Y	Y
UnitedHealthcare Advantage Three Tier	Pharmacy	N	Y	Y	Y
Cigna Standard Three Tier	Pharmacy	Y	Y	Y	Y
OptumRx Premium Formulary	Pharmacy	Y	Y	Y	Y

Kaiser Permanente Southern California 3 Tier HMO	Pharmacy	N/A	Y	Y	Y
Anthem Essential 4 Tier	Pharmacy	Y	Y	Y	Y
BCBS of Illinois Basic 6 Tier	Pharmacy	N	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Pharmacy	N	Y	Y	Y
Blue Shield California Plus Formulary	Pharmacy	Y	Y	Y	Y
VHA National Formulary	Pharmacy	Y	N	Y	Y
Saxenda					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Pharmacy	N/A	Y	Y	Y
Express Scripts National Preferred Formulary	Pharmacy	N/A	Y	Y	Y
UnitedHealthcare Advantage Three Tier	Pharmacy	N/A	Y	Y	Y
Cigna Standard Three Tier	Pharmacy	N/A	Y	Y	Y
OptumRx Premium Formulary	Pharmacy	N/A	Y	Y	Y
Kaiser Permanente Southern California 3 Tier HMO	Pharmacy	N/A	Y	Y	Y
Anthem Essential 4 Tier	Pharmacy	N/A	Y	Y	Y
BCBS of Illinois Basic 6 Tier	Pharmacy	N/A	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Pharmacy	N/A	Y	Y	Y
Blue Shield California Plus Formulary	Pharmacy	N/A	Y	Y	Y
VHA National Formulary	Pharmacy	N/A	N	Y	Y
Qsymia					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Pharmacy	Y	Y	Y	Y
Express Scripts National Preferred Formulary	Pharmacy	Y	Y	Y	Y
UnitedHealthcare Advantage Three Tier	Pharmacy	N	Y	Y	Y
Cigna Standard Three Tier	Pharmacy	Y	Y	Y	Y
OptumRx Premium Formulary	Pharmacy	Y	Y	Y	Y
Kaiser Permanente Southern California 3 Tier HMO	Pharmacy	Y	Y	Y	Y
Anthem Essential 4 Tier	Pharmacy	Y	N/A	N/A	N/A
BCBS of Illinois Basic 6 Tier	Pharmacy	N	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Pharmacy	N	Y	Y	Y
Blue Shield California Plus Formulary	Pharmacy	Y	N	Y	Y
VHA National Formulary	Pharmacy	Y	Y	Y	Y

Contrave					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Pharmacy	N/A	N/A	N/A	N/A
Express Scripts National Preferred Formulary	Pharmacy	N/A	Y	Y	Y
UnitedHealthcare Advantage Three Tier	Pharmacy	N/A	Y	Y	Y
Cigna Standard Three Tier	Pharmacy	N/A	Y	Y	Y
OptumRx Premium Formulary	Pharmacy	N/A	N/A	N/A	N/A
Kaiser Permanente Southern California 3 Tier HMO	Pharmacy	N/A	Y	Y	Y
Anthem Essential 4 Tier	Pharmacy	N/A	N/A	N/A	N/A
BCBS of Illinois Basic 6 Tier	Pharmacy	N/A	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Pharmacy	N/A	Y	Y	Y
Blue Shield California Plus Formulary	Pharmacy	N/A	Y	Y	Y
VHA National Formulary	Pharmacy	N/A	Y	Y	Y
Hemgenix					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Medical	N/A	N/A	N/A	N/A
Express Scripts National Preferred Formulary	Medical	N/A	N/A	N/A	N/A
UnitedHealthcare Advantage Three Tier	Medical	N/A	Y	Y	Y
Cigna Standard Three Tier	Medical	N/A	Y	Y	Y
OptumRx Premium Formulary	Medical	N/A	N/A	N/A	N/A
Kaiser Permanente Southern California 3 Tier HMO	Medical	N/A	Y	Y	Y
Anthem Essential 4 Tier	Medical	N/A	Y	Y	Y
BCBS of Illinois Basic 6 Tier	Medical	N/A	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Medical	N/A	Y	Y	Y
Blue Shield California Plus Formulary	Medical	N/A	Y	Y	Y
VHA National Formulary	Medical	N/A	N/A	N/A	N/A
Roctavian					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Medical	N/A	N/A	N/A	N/A
Express Scripts National Preferred Formulary	Medical	N/A	N/A	N/A	N/A
UnitedHealthcare Advantage Three Tier	Medical	N/A	Y	Y	Y
Cigna Standard Three Tier	Medical	N/A	Y	Y	Y
OptumRx Premium Formulary	Medical	N/A	N/A	N/A	N/A

Kaiser Permanente Southern California 3 Tier HMO	Medical	N/A	Y	Y	Y
Anthem Essential 4 Tier	Medical	N/A	Y	Y	Y
BCBS of Illinois Basic 6 Tier	Medical	N/A	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Medical	N/A	Y	Y	Y
Blue Shield California Plus Formulary	Medical	N/A	Y	Y	Y
VHA National Formulary	Medical	N/A	N/A	N/A	N/A
Veozah					
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	Pharmacy	N/A	N/A	N/A	N/A
Express Scripts National Preferred Formulary	Pharmacy	N/A	Y	Y	Y
UnitedHealthcare Advantage Three Tier	Pharmacy	N/A	Y	Y	Y
Cigna Standard Three Tier	Pharmacy	N/A	Y	Y	Y
OptumRx Premium Formulary	Pharmacy	N/A	N/A	N/A	N/A
Kaiser Permanente Southern California 3 Tier HMO	Pharmacy	N/A	Y	Y	Y
Anthem Essential 4 Tier	Pharmacy	N/A	N/A	N/A	N/A
BCBS of Illinois Basic 6 Tier	Pharmacy	N/A	Y	Y	Y
Highmark Blue Cross Blue Shield 3 Tier formulary	Pharmacy	N/A	Y	Y	Y
Blue Shield California Plus Formulary	Pharmacy	N/A	Y	Y	Y
VHA National Formulary	Pharmacy	N/A	Y	Y	Y

BCBS: Blue Cross Blue Shield, HMO: health maintenance organization, N: no, N/A: not applicable, VHA: Veterans Health Administration, Y: yes

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

B13. Supplemental Tables for Exploratory Transparency Analyses

Table B13.1. Results of Exploratory Transparency Analysis for Zynteglo

Formulary	Transparency of Cost Sharing / Tier Info	Transparency of Clinical Criteria	Transparency of Site of Care
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	N/A	N/A	N/A
Express Scripts National Preferred Formulary	N/A	N/A	N/A
UnitedHealthcare Advantage Three Tier	N	Y	N
Cigna Standard Three Tier	Y	Y	N
OptumRx Premium Formulary	N/A	N/A	N/A
Kaiser Permanente Southern California 3 Tier HMO	N/A	N/A	N/A
Anthem Essential 4 Tier	Y	Y	N
BCBS of Illinois Basic 6 Tier	N	Y	N
Highmark Blue Cross Blue Shield 3 Tier formulary	Y	Y	N
Blue Shield California Plus Formulary	N	N	N
VHA National Formulary	N/A	N/A	N/A

BCBS: Blue Cross Blue Shield, HMO: Health Maintenance Organization, N: no, N/A: not applicable, VHA: Veterans Health Administration, Y: yes

Table B13.2. Results of Exploratory Transparency Analysis for Hemgenix

Formulary	Transparency of Cost Sharing / Tier Info	Transparency of Clinical Criteria	Transparency of Site of Care
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	N/A	N/A	N/A
Express Scripts National Preferred Formulary	N/A	N/A	N/A
UnitedHealthcare Advantage Three Tier	N	Y	N
Cigna Standard Three Tier	Y	Y	N
OptumRx Premium Formulary	N/A	N/A	N/A
Kaiser Permanente Southern California 3 Tier HMO	N/A	N/A	N/A
Anthem Essential 4 Tier	Y	Y	N
BCBS of Illinois Basic 6 Tier	N	Y	N
Highmark Blue Cross Blue Shield 3 Tier formulary	N	Y	N
Blue Shield California Plus Formulary	N	N	N
VHA National Formulary	N/A	N/A	N/A

BCBS: Blue Cross Blue Shield, HMO: Health Maintenance Organization, N: no, N/A: not applicable, VHA: Veterans Health Administration, Y: yes

Table B13.3. Results of Exploratory Transparency Analysis for Roctavian

Formulary	Transparency of Cost Sharing / Tier Info	Transparency of Clinical Criteria	Transparency of Site of Care
CVS Caremark Performance Standard Control w/ Advanced Specialty Control	N/A	N/A	N/A
Express Scripts National Preferred Formulary	N/A	N/A	N/A
UnitedHealthcare Advantage Three Tier	N	Y	N
Cigna Standard Three Tier	Y	Y	N
OptumRx Premium Formulary	N/A	N/A	N/A
Kaiser Permanente Southern California 3 Tier HMO	N/A	N/A	N/A
Anthem Essential 4 Tier	Y	Y	N
BCBS of Illinois Basic 6 Tier	N	Y	N
Highmark Blue Cross Blue Shield 3 Tier formulary	N	Y	N
Blue Shield California Plus Formulary	N	N	N
VHA National Formulary	N/A	N/A	N/A

BCBS: Blue Cross Blue Shield, HMO: Health Maintenance Organization, N: no, N/A: not applicable, VHA: Veterans Health Administration, Y: yes

C. Supplemental Information for Consumer Accessibility Analyses

Data source: IQVIA Longitudinal Access and Adjudication Data, which are open source claims written and/or dispensed in the U.S. (50 states and Washington, D.C.). Reports were sourced from the IQVIA Market Access Analytic Library solution from calendar years 2022 and 2023. Data are summarized by calendar year.

C1.1. Definitions

- Commercial line of business: All third-party payers excluding all Medicare, Medicaid, and Cash payments.
- Cash: True cash payments by the patient. Does not include discount cards or coupons. The patient may have been uninsured or insured but chose to pay privately by cash.

C1.2. Prescription Claim Definitions (percentages calculated on normalized New-to-Brand)

- Written Prescriptions: Prescriptions written by a prescriber (includes Rx's that have been filled, rejected, or abandoned). The claim samples included are claims that have been normalized to 30-day supply.
- Dispensed (Paid) Prescriptions: Prescriptions filled. The claim samples included are claims that have been normalized to a 30-day supply.
- New-to-Brand Prescriptions (NBRx): New-to-Brand claims represents a patient's first prescription of a drug. Claims have been normalized to 30-day supply.
- Durable Claim Status: The outcome of the patient's attempt to fill a prescription after the designated look-forward (30 days for this deliverable). Patients that were rejected or reversed a script on their initial claim might have ultimately filled by the end of the look forward period.
- Look-forward Period: A period in which a patient associated with a claim is monitored and their prescription activity is tracked following a rejection or reversed claims.
- Attempts: Number of attempts patient submitted prescription for approval.
- Filled % - The Durable claims where payer has approved and script was filled.
- Rejection - Not Covered %: The Durable claims where payer has indication product in Not Covered or NDC Blocked divided by the sum of the NBRx claims.
- Rejection - Prior Auth/Step %: The Durable rejected claims where payer indicated that product requires physician to submit a prior authorization request to payer or payer requires another product(s) must be tried/failed prior to coverage divided by the sum of the NBRx claims. Step Edit

is a common way for a payer to dictate use of a particular medication or medications in a particular order. Failing to prescribe in the correct order can cause a rejection.

- Rejection - Other %: The Durable rejected claims due to other reasons such as plan/refill limits, distribution limitations or administrative errors, divided by the sum of the NBRx Claims.
- Abandonment- Abandonment %: The Durable reversed claims divided by the sum of the NBRx claims.

C1.3. Patient Out-of-Pocket Definitions

- Final Cost: The actual amount the patient pays in order to fill the product after any buydown.
- Patient OOP Categories: Range of patient cost exposure for final cost.

C1.4. Supplemental Tables

Table C1.1. Commercial Prescription Volume and Rate of New to Brand Prescriptions Filled, Rejected, or Reversed on a Single Attempt – 2022 and 2023

Drug Name	Calendar Year	Total Commercial Prescriptions			Single Attempts				
		Written Prescriptions	Dispensed Prescriptions	New to Brand Dispensed Prescriptions	% Filled	% Rejections			% Reversals
						Not covered	Prior auth/step	Other	
Mounjaro	2022	1,536,182	1,176,264	444,393	74%	11%	8%	3%	4%
	2023	8,712,178	7,323,251	959,308	59%	12%	17%	4%	8%
Wegovy	2022	1,405,003	958,123	137,158	15%	38%	19%	7%	20%
	2023	6,169,210	4,370,675	794,915	17%	37%	19%	6%	21%
Saxenda	2022	908,705	711,048	161,122	23%	39%	18%	4%	17%
	2023	826,347	584,738	127,105	17%	34%	23%	7%	19%
Qsymia	2022	127,629	99,281	16,027	22%	49%	16%	4%	8%
	2023	158,295	120,445	22,925	22%	49%	17%	4%	8%
Contrave	2022	165,224	80,828	20,931	18%	48%	12%	6%	17%
	2023	227,205	106,492	39,161	22%	37%	11%	5%	26%
Radicava ORS	2022	1,616	1,560	424	4%	23%	23%	46%	4%
	2023	5,995	5,870	571	6%	20%	22%	43%	8%
Radicava ORS Starter Kit	2022	421	371	367	-	31%	27%	42%	-
	2023	610	532	522	-	26%	23%	40%	11%
Radicava	2022	149	80	10	-	50%	33%	17%	-
	2023	47	41	6	75%	25%	-	-	-
Veozah	2022	-	-	-	-	-	-	-	-
	2023	50,207	33,375	16,429	46%	32%	5%	3%	15%
Cosela	2022	8	7	2	50%	50%	-	-	-
	2023	11	5	2	25%	50%	-	25%	-
Hemgenix	2022	-	-	-	-	-	-	-	-
	2023	-	-	-	-	-	-	-	-

Table C1.2. Rate of New to Brand Prescriptions Filled, Rejected, or Reversed on Multiple and All Attempts – 2022 and 2023

Drug Name	Calendar Year	Multiple Attempts*					All Attempts*				
		% Filled	% Rejections			% Reversals†	% Filled	% Rejections			% Reversals†
			Not covered	Prior auth/step	Other			Not covered	Prior auth/step	Other	
Mounjaro	2022	30%	35%	27%	4%	3%	43%	28%	22%	3%	4%
	2023	40%	19%	30%	4%	7%	48%	17%	25%	3%	7%
Wegovy	2022	24%	39%	18%	3%	16%	21%	39%	19%	4%	18%
	2023	30%	35%	16%	4%	15%	26%	36%	17%	4%	17%
Saxenda	2022	42%	33%	13%	2%	10%	37%	35%	14%	2%	12%
	2023	39%	28%	14%	3%	16%	31%	30%	17%	4%	17%
Qsymia	2022	24%	53%	16%	2%	4%	23%	52%	16%	3%	5%
	2023	26%	51%	16%	2%	5%	25%	50%	16%	2%	6%
Contrave	2022	18%	52%	16%	4%	11%	18%	50%	14%	4%	13%
	2023	27%	29%	16%	4%	23%	24%	33%	13%	5%	24%
Radicava ORS	2022	24%	18%	24%	21%	12%	15%	20%	24%	33%	8%
	2023	15%	22%	22%	29%	12%	10%	21%	22%	36%	10%
Radicava ORS Starter Kit	2022	18%	29%	18%	24%	12%	7%	30%	23%	35%	5%
	2023	45%	5%	26%	16%	8%	23%	15%	25%	27%	10%
Radicava	2022	10%	40%	20%	10%	20%	4%	46%	29%	15%	7%
	2023	-	100%	-	-	-	60	40%	-	-	-
Veozah	2022	-	-	-	-	-	-	-	-	-	-
	2023	39%	37%	6%	2%	16%	42%	35%	5%	2%	15%
Cosela	2022	-	-	-	-	-	50%	50%	-	-	-
	2023	-	-	-	-	100%	17%	33%	-	17%	33%
Hemgenix	2022	-	-	-	-	-	-	-	-	-	-
	2023	-	-	-	-	-	-	-	-	-	-

*Multiple Attempts and All Attempts categories include all recorded attempts to fill prescriptions, including (but not limited to) administrative errors, test claims to determine whether drug is covered, and test claims to determine if drug has been approved.

† Reversals are defined as prescriptions that were initially filled but then claim was reversed and drug was not dispensed. Reasons for reversals include, for example, prescription abandonment due to drug shortages or rejection by patient due to high out-of-pocket cost.

Table C1.3. Volume of Cash Pay Prescriptions – 2022 and 20

Drug Name	Calendar Year	Total Cash Written Prescriptions	Total Cash Dispensed Prescriptions	Total Cash New to Brand Dispensed
Mounjaro	2022	137,023	102,170	43,539
	2023	153,014	93,518	19,822
Wegovy	2022	33,774	16,093	2,258
	2023	82,270	27,523	13,117
Saxenda	2022	16,255	4,611	2,438
	2023	12,238	3,205	1,432
Qsymia	2022	3,906	2,305	830
	2023	4,468	2,698	1,055
Contrave	2022	26,617	23,040	7,995
	2023	47,673	44,520	14,607
Radicava ORS	2022	-	-	-
	2023	3	-	-
Radicava ORS Starter Kit	2022	-	-	-
	2023	3	-	-
Radicava	2022	74	70	6
	2023	1	1	-
Veozah	2022	-	-	-
	2023	861	363	267
Cosela	2022	-	-	-
	2023	1	-	-
Hemgenix	2022	-	-	-
	2023	-	-	-

D. Additional Patient Input

August 19, 2024

Grace Sternklar
Program and Events Coordinator
Institute for Clinical and Economic Review
14 Beacon Street, 8th floor
Boston, MA 02108

Dear Ms. Sternklar,

Thank you for requesting input from The ALS Association as part of your "Assessment of Barriers to Fair Access" report including Radicava ORS, an important drug in slowing functional decline, extending lifespan, and significantly improving the quality of life for people living with amyotrophic lateral sclerosis (ALS). ALS is a progressive, neurodegenerative, rare disease that harms nerve cells in the brain and spinal cord causing them to degenerate and eventually die. As ALS progresses, people lose the ability to speak, eat, move, and breathe. There is no cure for ALS yet and extremely limited options for drugs that impact ALS. Average life expectancy after diagnosis is two to five years.

The following comments are based on direct feedback from ALS clinicians from across the country and our review of payer coverage detailed in the attached chart.

ICER's "Fair Access" Study is Flawed

Access to treatments for people living with ALS is determined by many factors including: 1) individual out-of-pocket costs, 2) fairness and speed of prior authorization and utilization management techniques, and 3) variations in clinical criteria from the FDA (Food & Drug Administration) approved label.

Many of the drugs in ICER'S 2024 review treat common disorders such as diabetes, obesity, hemophilia, menopause, and problems related to cancer treatment. By contrast, Radicava ORS is approved for people living with ALS. Therefore, it is difficult to ascertain how ICER's analysis of Radicava ORS - which treats a rare disease - will provide an incentive for payers to change their policies.

Additionally, while ICER's assessment of barriers to "Fair Access" focuses on employer plans, the devastating nature of ALS forces most people with the disease out of the workplace. For this reason, most people with ALS who have not served in the military purchase Medicare Fee-for-Service (FFS) or Medicare Advantage plans.

As of July 31, 2024, 67.3 million people were enrolled in Medicare, with approximately half enrolled in Medicare Advantage (MA). It is well-documented that Medicare Advantage plans use prior authorization, utilization review, and/or fail-first policies to routinely deny care and boost profits. Such strategies are blatantly unfair since they deny and/or delay access to Radicava ORS. Therefore, the results of ICER's 2024 assessment of barriers to "Fair Access" provide an incomplete and flawed perspective on access to Radicava ORS and cannot be applied to insurers in general.

FDA Label Versus Clinical Criteria

The FDA label approved for Radicava ORS is for the treatment of amyotrophic lateral sclerosis for everyone without any other clinical criteria. It is important to note that clinical trials are designed to detect efficacy in a very short period – some as short as 6 months. For that reason, a clinical trial will narrow eligibility for participation. However, when the FDA approves a new drug, it looks beyond the narrow clinical trial eligibility and carefully considers who may benefit. This is of particular importance for rare diseases such as ALS where life expectancy is very short and there are extremely limited options for treatment. It is inappropriate for insurance companies and PBMs to narrowly limit their coverage decisions on Radicava ORS to the clinical trial criteria when the FDA has made clear that all people living with ALS can benefit.

Despite a broad FDA label, pharmaceutical companies have developed their own clinical criteria to limit access to Radicava ORS. The variations from the FDA label are substantial. For illustrative purposes we focus here on scores on the ALS Functional Rating Scale - Revised, Forced Vital Capacity, and the onset of symptoms being 2 years or less from the beginning of treatment.

ALS FUNCTIONAL RATING SCALE - REVISED (ALSFRS-R)

The ALSFRS-R measures 12 aspects of physical function. Each function is scored from 4 (normal) to 0 (no ability), with a maximum total score of 48 and a minimum total score of 0. The revised scale measures: speech, salivation, swallowing, handwriting, cutting food, climbing stairs, turning in bed, walking, dressing and hygiene, dyspnea (difficulty breathing), orthopnea (shortness of breath while lying down), and breathing insufficiency.

***Comment ALSFRS-R Score**: Two insurers in the attached Payer Policies for Radicava ORS chart have no required ALSFRS-R score. All the other payors require a minimum score of two in each of the categories listed above. **We recommend that no ALSFRS-R score be required. If a score is required, it should be a composite score not a requirement of two in all categories**.*

The twelve categories measured in the ALSFRS-R are not equal in importance and people who have a reduced function in one or more categories should not be denied Radicava ORS which can slow the decline of ALS.

For example, Bulbar ALS causes neuromuscular disabilities that lead to various symptoms related to speech, swallowing, and breathing. A person living with this condition will score low on the ALSFRS-R in this specific area but be able to complete all the other important activities of daily living measured by that scale. That person should not be denied Radicava ORS.

Comment ALSFRS-R or Japan Severity Score: *As the attached chart notes, Anthem's clinical criteria for people with ALS living in the United States is not based on the ALSFRS-R system and is an outlier for that reason. Instead, Anthem uses the ALS Japan Severity Score. In our estimation, this is not "Fair Access."*

FORCED VITAL CAPACITY

Forced vital capacity (FVC) is a pulmonary function test that measures the maximum amount of air a person can exhale after taking a deep breath in. It is measured in liters during spirometry, a lung function test.

Comment FVC*: As the attached Payer Policies for Radicava ORS chart indicates, several payors have no requirement for FVC while others require FVC below 80%. FVC is only one of several factors taken into consideration by ALS clinicians when they prescribe Radicava. To ensure fair access and respect the expertise of the ALS clinician, we believe that no requirement for FVC should be included in a payer's clinical criteria.*

ONSET OF SYMPTOMS LESS THAN 2 YEARS FROM START OF TREATMENT

Of paramount importance to a person with ALS is denial of Radicava because onset of symptoms is greater than or equal to two years from start of treatment. As you can see from the attached *Payer Policies for Radicava ORS* chart, the clinical criteria of many pharmaceutical companies disqualify a person with ALS from receiving Radicava ORS if their onset of symptoms is greater or equal to two years regardless of ALSFRS-R or FVC scores.

Delays in diagnosis are unfortunately common because other conditions must be ruled out before a neurologist can identify possible ALS. Once a neurologist determines that a person may have ALS, a preliminary diagnosis may be offered. However, that person often must go to an ALS clinic to get a final diagnosis of ALS. Many clinics have long waitlists to secure an initial appointment and/or someone may need to travel to get to a clinic. As you can see from the Payer Policies for Radicava ORS, only four companies have no criteria related to the onset of symptoms while the rest deny Radicava. Onset of symptoms is not related to function and is not valid.

Comment: Time From Onset of Symptoms: *We believe that onset of symptoms equal to or less than 2 years should not be included in clinical criteria because of the variability of ALS. ALS can*

begin in any part of the body and if a person with ALS can benefit from Radicava ORS – the time from onset of symptoms should be irrelevant.

In conclusion, it is inappropriate for insurance companies and PBMs to narrowly limit their coverage decisions on Radicava ORS to the clinical trial criteria when the FDA has made clear that all people living with ALS can benefit.

Thank you for the opportunity to present comments on ICER's "Assessment of Barriers to Fair Access" Report on Radicava ORS. If any follow-up information is needed upon review of this letter, please contact me directly at Kathleen.Sheehan@als.org.

Sincerely,

Kathleen Sheehan
Vice President, Public Policy
The ALS Association

ALS ASSOCIATION

Payer Policies for Radicava ORS

Clinical Criteria Requirements for Radicava ORS®

Payor/Plan	ALSFRS Scoring Requirement	Forced Vital Capacity	Onset of Symptoms beginning less than 2 years from start of treatment	Link to Payor Coverage Resources
Aetna	2 in each category	No Requirement	No Requirement	https://www.aetna.com
Anthem*	2 in each category	80% FVC	Yes	https://www.anthem.com/
Blue Cross Blue Shield Blue Care Network of Michigan	No req Score	No FVC if < 2 yrs	Yes	https://www.bcbsm.com/
BlueCross BlueShield of Alabama	2 in each category	80% FVC	Yes	https://al-policies.exploremyplan.com/
BlueCross BlueShield of North Carolina	No Requirement	Yes	Yes	https://www.bluecrossnc.com/
California Physicians' Service Association	2 in each category	80% FVC	No Requirement	https://www.blueshieldca.com/
CareFirst BlueCross BlueShield	2 in each category	No Requirement	No Requirement	https://member.carefirst.com/
Centene	2 in each category	80% FVC	Yes	https://pharmacy.envolvehealth.com/
Cigna	2 in each category	80% FVC	Yes	https://static.cigna.com/
GuideWell (Florida Blue)	2 in each category	No Requirement	Yes	https://mcgs.bcbsfl.com/
Health Care Service Corporation	2 in each category	80% FVC	Yes	https://www.myprime.com/
Highmark	2 in each category	80% FVC	Yes	https://securecms.highmark.com/
Horizon Blue Cross Blue Shield of New Jersey	2 in each category	80% FVC	Yes	https://www.myprime.com/
Humana	2 in each category	80% FVC	Yes	https://dctm.humana.com/
Kaiser Permanente	2 in each category	80% FVC	Yes	https://healthy.kaiserpermanente.org/
UnitedHealth Group	2 in each category	80% FVC	No Requirement	https://www.uhcprovider.com/

*Anthem is the only payor requiring adherence to JSS (ALS Japan Severity Scale)