Treatment Options for Plaque Psoriasis: Effectiveness, Value, and Value-Based Price Benchmarks

Background and Scope

Background

Psoriasis is a common disease that causes itchy, red, scaly, raised lesions on the skin, most commonly on the elbows, knees, scalp, and back.[1] Psoriasis affects about 2% of the population and significantly decreases health-related quality of life, particularly if lesions are in areas that can affect daily functioning (e.g., the hands or soles of the feet) or social functioning (e.g., the face).[2-4] Psoriasis is a chronic inflammatory condition that is associated with systemic diseases including psoriatic arthritis, other autoimmune diseases, the metabolic syndrome, and cardiovascular disease.[5]

Cutaneous psoriasis types include plaque psoriasis, guttate psoriasis, pustular psoriasis, inverse psoriasis, nail psoriasis, and erythrodermic psoriasis. Chronic plaque psoriasis accounts for about 80% to 90% of all patients with psoriasis. Up to 30% of patients with plaque psoriasis have at least some manifestations of psoriatic arthritis.[6]

Plaque psoriasis is caused by dysregulation of innate and adaptive immunity in genetically susceptible people.[5] This dysregulation produces an overabundance of inflammatory mediators such as tumor necrosis factor (TNF)-α and interleukins (IL)-12, 23, and 17A. Activated immune cells and inflammatory mediators lead to overgrowth, scaling, redness, and other changes in psoriatic skin.

Roughly 70% to 80% of patients with plaque psoriasis have mild disease that can be adequately managed with topical therapy. Definitions of “moderate-to-severe” plaque psoriasis vary, but generally consist of psoriasis that affects at least 3% of a patients’ body surface; produces lesions that have significant redness, thickness, and scale; or significantly reduces quality of life.[7,8]

Treatments for psoriasis can be grouped within 4 broad categories: 1) topical therapies such as steroids, vitamin D analogues, retinoids, and calcineurin inhibitors; 2) older systemic therapies, such as cyclosporine and methotrexate; 3) phototherapy such as psoralen and ultraviolet A radiation (PUVA); and 4) biologics or “targeted immunomodulators.” Clinical interest in this last category is high, as many patients with chronic plaque psoriasis do not see adequate or durable benefit from older systemic therapies or phototherapy. Additionally, targeted immunomodulators are associated with a high financial cost, some of which is passed on to patients. Targeted immunomodulators approved, or nearing approval, for the treatment of moderate-to-severe

plaque psoriasis in the United States consist of medications with activity against the following targets:

- ***TNF-α:*** adalimumab (Humira®), etanercept (Enbrel®), infliximab (Remicade®)
- ***IL-17A:*** secukinumab (Cosentyx®), ixekizumab (Taltz®), brodalumab (investigational)
- ***IL-12/23:*** ustekinumab (Stelara®)
- ***Phosphodiesterase (PDE)-4:*** apremilast (Otezla®) Although not technically a biologic, apremilast is a novel, targeted, oral agent also approved for treatment of patients with moderate-to-severe plaque psoriasis.

[Note: Certolizumab pegol (Cimzia®) and golimumab (Simponi®, Simponi ARIA) are anti-TNF agents that have been approved for the treatment of psoriatic arthritis, but not plaque psoriasis.]

Treatment of plaque psoriasis can be challenging for patients. It can be difficult to apply topical therapies, especially when the affected area involves the scalp or covers a large part of the body. Therapies can be inconvenient to use; some require multiple injections on a daily or weekly basis. Insurance plans generally mandate "step therapy," which requires patients and clinicians to first try a list of preferred medications and, only after repeated treatment failures, progress to non-preferred treatments.

Studies have found that up to half of patients are dissatisfied with psoriasis treatment.[3,9] Dissatisfaction may be due to the unpredictable effectiveness of agents, poor tolerability, lack of durable response, and lack of access to medications because of coverage restrictions or costs.[3] The newer targeted immunomodulators are generally more expensive than older medications and there are questions regarding how these costs align with the clinical value brought to patients.

Report Aims

This project will evaluate the comparative clinical effectiveness and value of targeted immunomodulators (biologics plus apremilast) for adults with moderate-to-severe plaque psoriasis. Note that, while many of these agents are FDA approved for the treatment of both plaque psoriasis and psoriatic arthritis, these conditions involve distinctly different sets of measures, outcomes, and clinical audiences. As such, our scope will be limited to the available evidence for plaque psoriasis, the more prevalent manifestation of the disease.

Scope of the Evidence Review Focusing on Comparative Clinical Effectiveness

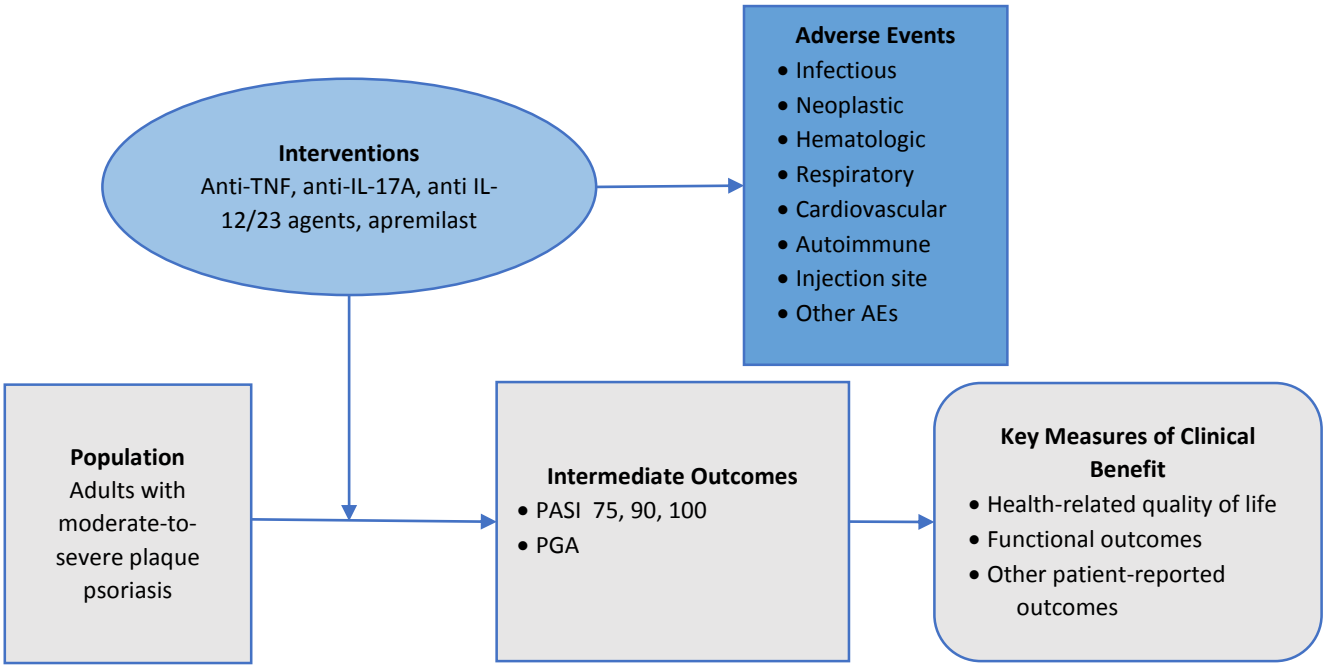
The proposed scope for this assessment is described below using the PICOTS (Population, Intervention, Comparators, Outcomes, Timing, and Settings) framework. Evidence will be collected from available randomized controlled trials as well as high-quality systematic reviews; higher-quality comparative cohort studies will also be evaluated as necessary. We will not restrict studies according to study duration or study setting; however, we will limit our review to those that capture the key outcomes of interest. We will supplement our review of published studies with data from conference proceedings, regulatory documents, information submitted by

manufacturers, and other grey literature when the evidence meets ICER standards (for more information, see https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework/grey-literature-policy/).

Analytic Framework

The general analytic framework for assessment of anti-plaque psoriasis medications is depicted in Figure 1 below.

Figure 1. Analytic Framework: Management of Moderate-to-Severe Chronic Plaque Psoriasis



PASI = psoriasis area severity index; PGA = physician global assessment

Populations

The population of focus for this review is adults with moderate-to-severe chronic plaque psoriasis. Although not a focus of the review, we will not exclude patient populations with other concomitant psoriasis types or psoriatic arthritis, and will evaluate psoriasis outcomes in these subgroups if data are available. Additionally, we will attempt to distinguish outcomes for patients who have and have not been previously treated with a targeted immunomodulator.

Interventions

The interventions of interest are the targeted immunomodulators (biologics and apremilast) all but one of which have been approved for the treatment of moderate-to-severe plaque psoriasis:

- ***Anti-TNF-α agents:*** adalimumab, etanercept, infliximab (approved only for severe plaque psoriasis)
- ***Anti IL-17A agents:*** secukinumab, ixekizumab, brodalumab (not yet approved)
- ***Anti IL-12/23 agent:*** ustekinumab
- ***Anti PDE-4 agent:*** apremilast

Comparators

Wherever possible, we will evaluate head-to-head trials of these interventions. Other comparators may include placebo or other active treatments not listed above.

Outcomes

This review will examine key clinical outcomes, including outcomes common to plaque psoriasis trials. Discussions with patients, patient groups, clinicians, industry, and publications from academic research groups indicate that people with psoriasis have symptoms and burdens that are not well-captured by standard trial outcomes.[3,10] Standard trial outcomes are generally not used or feasible to employ in actual clinical practice. We will examine available data for evidence about the comparative effectiveness of targeted immunomodulators in affecting domains such as itch, scaling, pain, quality-of-life, work productivity, and satisfaction with treatment.

Clinical Trial and Study Outcomes

- Psoriasis Area and Severity Index (PASI): 75, 90, 100
- Physician Global Assessment (PGA)
- Treatment-related adverse events

Patient-Reported Outcomes

- Dermatology Life Quality Index (DLQI)
- Other measures of health-related quality of life
- Symptom control
- Treatment tolerability

We will develop evidence tables for each selected study and results will be summarized in a qualitative fashion; meta-analysis will be used to quantitatively summarize outcomes for the therapies of interest. We will perform a network meta-analysis for PASI scores and consider network meta-analysis to combine direct and indirect evidence of effectiveness as available data permit.

Timing

Evidence on intervention effectiveness and harms will be derived from studies of any duration. Because psoriasis is a chronic condition with no cure, we are particularly interested in evidence of durability of response to medications, as well as long-term safety.

Settings

Plaque psoriasis is generally treated in outpatient and/or clinic settings, which will be the focus of our review.

Simulation Models Focusing on Comparative Value

As a complement to the evidence review, we will develop a simulation model to assess the cost-effectiveness of the regimens of interest. The model structure will be based in part on previously developed economic models assessing treatments for psoriasis and be conducted from a health system perspective over a lifetime time horizon.[11] The model will focus attention on regimens most likely to be used for adults with moderate-to-severe chronic plaque psoriasis who have failed topical and/or phototherapy.

Proposed regimens include:

- ***Anti-TNF-α agents:*** adalimumab, etanercept, infliximab
- ***Anti IL-17A agents:*** secukinumab, ixekizumab, brodalumab (not yet approved)
- ***Anti IL-12/23 agent:*** ustekinumab
- ***Anti PDE-4 agent:*** apremilast

Effectiveness will be estimated based on network meta-analyses of randomized controlled trials conducted in this patient population.

Key model inputs will include disease-specific measures such as the PASI, symptom improvement, treatment-related adverse events, health-related quality of life, and systemic manifestations, as feasible. Costs will include those of current and subsequent treatment, management of adverse events, and ongoing care. If sufficient data are available, the model will incorporate effects on productivity as a scenario analysis. Results will be expressed primarily in terms of the incremental cost per quality-adjusted life year (QALY) gained.

We will also assess the potential budgetary impact of each regimen over a 5-year time horizon, utilizing information on treatment costs and any cost offsets from reductions in use of other health care resources. Potential budgetary impact analyses will assume a product “uptake” rate over the 5-year period based on ICER criteria. Finally, we will develop a “value-based price benchmark” for each treatment reflecting prices aligned with long-term cost-effectiveness thresholds and below a threshold for potential budgetary impact that would exceed growth targets for national health care costs.

More information on ICER's methods for estimating product uptake and calculating value-based price benchmarks can be found at: http://www.icer-review.org/wp-content/uploads/2014/01/Slides-on-value-framework-for-national-webinar1.pdf.

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