PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Siliq™ (brodalumab for subcutaneous injection – Valeant Pharmaceuticals)

DATE REVIEWED: 04/08/2020

OVERVIEW

Siliq is indicated for treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies.[1] In plaque psoriasis, the recommended dose is 210 mg subcutaneously (SC) at Week 0, 1, and 2 followed by 210 mg once every 2 weeks (Q2W). Consider discontinuing if an adequate response has not been achieved after 12 to 16 weeks; continued treatment is unlikely to result in greater success. Siliq is intended for use under the guidance and supervision of a physician. Those trained in SC injection technique may self-inject when deemed appropriate.

Disease Overview

IL-17A is a naturally occurring cytokine involved in normal inflammatory and immune responses. However, levels of IL-17A are elevated in psoriatic plaques.[1] Siliq is a human monoclonal immunoglobulin G (IgG)2 antibody which selectively binds to interleukin (IL)-17RA and inhibits its interaction with cytokines IL-17A, IL-17-F, IL-17C, IL-17A/F heterodimer, and IL-25. By blocking IL-17RA, Siliq inhibits IL-17 cytokine-induced responses, including the release of pro-inflammatory cytokines and chemokines involved in the inflammatory process.

Guidelines

Joint guidelines from the American Academy of Dermatology (AAD) and National Psoriasis Medical Board (2019) have been published for management of psoriasis with biologics.[2] These guidelines list Siliq as a monotherapy treatment option for patients with moderate to severe plaque psoriasis. Guidelines from the European Dermatology Forum (EDF) [2015] recommend biologics (i.e., etanercept, adalimumab, infliximab, Stelara SC) as second-line therapy for induction and long-term treatment if phototherapy and conventional systemic agents have failed, are contraindicated, or are not tolerated.[3]

Safety

Siliq has a Boxed Warning, Risk Evaluation and Mitigation Strategy (REMS) program, and limited distribution program due to risks of suicidal ideation and behavior. The REMS program requires prescribers and pharmacies to be certified to prescribe and/or dispense Siliq.[4] Patients must sign a patient-prescriber agreement form and be aware of the need to seek medical attention for any new/worsening suicidal thoughts or behavior, depression, anxiety, or mood changes. Siliq is also contraindicated in Crohn's disease.[1] Other Warnings/Precautions include infections, risk for latent tuberculosis reactivation, and vaccinations.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Siliq. Because of the specialized skills required for evaluation and diagnosis of patients treated with Siliq as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Siliq to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Siliq is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Plaque Psoriasis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following criteria (i, ii, and iii):
     - **i.** The patient is ≥ 18 years of age; AND
     - **ii.** The patient meets ONE of the following conditions (a or b):
       - **a)** The patient has tried at least at least one traditional systemic agent for psoriasis for at least 3 months, unless intolerant.
         Note: Examples of traditional systemic agents for psoriasis include methotrexate (MTX), cyclosporine, acitretin tablets, or psoralen plus ultraviolet A light (PUVA). An exception to the requirement for a trial of one traditional systemic agent for psoriasis can be made if the patient has already had a 3-month trial or previous intolerance to at least one biologic. Refer to **Appendix** for examples of biologics used for plaque psoriasis. These patients who have already tried a biologic for psoriasis are not required to "step back" and try a traditional systemic agent for psoriasis; OR
       - **b)** The patient has a contraindication to methotrexate (MTX), as determined by the prescriber; AND
     - **iii.** Siliq is prescribed by or in consultation with a dermatologist.
   - **B)** Patient is Currently Receiving Siliq. Approve for 3 years if the patient has responded, as determined by the prescriber.
     Note: The patient may not have a full response, but there should have been a recent or past response to Siliq.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Siliq has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Concurrent Use with other Biologics or with Targeted Synthetic Disease-Modifying Antirheumatic Drugs (DMARDs).** Siliq should not be administered in combination with a biologic used for an inflammatory condition (see Appendix for examples). Combination therapy with biologics and/or biologics + targeted synthetic DMRADs has a potential for a higher rate of adverse effects and lack controlled trial data in support of additive efficacy.[5-6] Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Siliq.

2. **Crohn's Disease.** Siliq is contraindicated in patients with Crohn's disease.[1] There is a published Phase II study evaluating Siliq in Crohn's disease (n = 130) that was terminated early due to a disproportionate number of worsening Crohn's disease and lack of efficacy.[7]

3. **Rheumatoid Arthritis.** Efficacy has not been established. A published Phase II study (n = 252) did not demonstrate improvement in American College of Rheumatology (ACR) 20/50/70 responses with Siliq vs. placebo for treatment of rheumatoid arthritis in patients who had previously failed methotrexate.[8]

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Siliq® injection [prescribing information]. Bridgewater, NJ: Valeant Pharmaceuticals; February 2017.
2. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019 80(4):1029-1072.
3. Nast A, Gisondi P, Ormerod AD, et al. European S3-Guidelines on the systemic treatment of psoriasis vulgaris – Update 2015 – Short version – EDF in cooperation with EADV and IPC. *J Eur Acad Dermatol Venereol*. 2015;29(12):2277-2294.
4. FDA approves new psoriasis drug [press release]. Silver Springs, MD. US FDA Web site; Updated March 28, 2018. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm541981.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery. Accessed on April 2, 2019.
5. Furst DE, Keystone EC, So AK, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2012. *Ann Rheum Dis*. 2013;72 Suppl 2:ii2-34.
6. Xeljanz® tablets [prescribing information]. New York, NY: Pfizer Inc; May 2014.
7. Targan SR, Feagan B, Vermeire S, et al. A randomized, double-blind, placebo-controlled Phase 2 study of brodalumab in patients with moderate-to-severe Crohn's disease. *Am J Gastroenterol*. 2016;111(11):1599-1607.
8. Pavelka K, Chon Y, Newmark R, et al. A study to evaluate the safety, tolerability, and efficacy of brodalumab in subjects with rheumatoid arthritis and an inadequate response to methotrexate. *J Rheumatol*. 2015;42(6):912-919.

APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications for Products*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, PJIA, PsO, PsA, RA, SJIA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: PJIA, PSA, RA
		IV formulation: PJIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Ilaris (canakinumab SC injection**)**	Inhibition of IL-1β	SJIA
Kineret® (anakinra SC injection)	Inhibition of IL-1	RA, SJIA^
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx™ (secukinumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzza SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AS – Ankylosing spondylitis; CD – Crohn's disease; PJIA – Polyarticular juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; SJIA – Systemic juvenile idiopathic arthritis; UC – Ulcerative colitis; ^ Off-label use of SJIA supported in guidelines.