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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Topical Products	**Original Policy Date:**	July 28, 2023
Subject:	Litfulo	**Page:**	1 of 6

Last Review Date: March 8, 2024

Litfulo

Description

Litfulo (ritlecitinib)

Background
Litfulo (ritlecitinib) irreversibly inhibits Janus kinase 3 (JAK3) and the tyrosine kinase expressed in hepatocellular carcinoma (TEC) kinase family by blocking the adenosine triphosphate (ATP) binding site. In cellular settings, Litfulo inhibits cytokine induced STAT phosphorylation mediated by JAK3-dependent receptors. Additionally, Litfulo inhibits signaling of immune receptors dependent on TEC kinase family members. The relevance of inhibition of specific JAK or TEC family enzymes to therapeutic effectiveness is not currently known (1).

Regulatory Status
FDA-approved indication: Litfulo is a kinase inhibitor indicated for the treatment of severe alopecia areata in adults and adolescents 12 years and older (1).

Limitations of Use: Not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, cyclosporine or other potent immunosuppressants (1).

Litfulo carries several boxed warnings: (1)

1. Serious infections
    a. Increased risk for serious bacterial, fungal, viral, and opportunistic infections that may lead to hospitalization or death, including tuberculosis (TB). Interrupt treatment if serious infection occurs until the infection is controlled. Litfulo should not be given to patients with active tuberculosis. Test for latent TB before and during therapy; start treating latent TB prior to use. Monitor all patients for active

TB during treatment, even patients with initial negative, latent TB test. Monitor all patients for signs and symptoms of infection during and after treatment with Litfulo.

2. Mortality
    a. Higher rate of all-cause mortality, including sudden cardiovascular death with another JAK inhibitor vs. TNF blockers in rheumatoid arthritis (RA) patients. Litfulo is not approved for use in RA patients.
3. Malignancy
    a. Malignancies were reported in patients treated with Litfulo. Higher rate of lymphomas and lung cancers with another JAK inhibitor vs. TNF blockers in RA patients.
4. Major adverse cardiovascular events (MACE)
    a. Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs. TNF blockers in RA patients.
5. Thrombosis
    a. Thrombosis has occurred in patients treated with Litfulo. Increased incidence of pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs TNF blockers.

The safety and effectiveness of Litfulo in pediatric patients less than 12 years of age have not been established (1).

Related policies
Olumiant

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Litfulo may be considered **medically necessary** if the conditions indicated below are met.

Litfulo may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 12 years of age or older

Diagnosis

Patient must have the following:

Severe alopecia areata

AND ALL of the following:

1. Patient has ≥50% scalp hair loss
2. Patient does **NOT** have age-related/androgenetic hair loss
3. Inadequate treatment response, intolerance, or contraindication to corticosteroids
4. Prescribed by or recommended by a dermatologist
5. Prescriber has considered the risks for malignancy and major adverse cardiovascular events (MACE) (e.g., advanced age, smoking history, cardiovascular risk factors etc.) and determined that Litfulo therapy is appropriate
6. Result for latent TB infection is negative **OR** result was positive for latent TB and patient completed treatment (or is receiving treatment) for latent TB

AND NONE of the following:

1. Severe hepatic impairment (Child-Pugh Class C)
2. Absolute lymphocyte count (ALC) < 500 cells/mm3
3. Platelet count < 100,000 cells/mm3
4. Active bacterial, invasive fungal, viral, and other opportunistic infections
5. History of thrombotic events including deep vein thrombosis (DVT) or pulmonary embolism (PE)
6. Used in combination with any other biologic DMARD or targeted synthetic DMARD (see Appendix 1)
7. Used in combination with potent immunosuppressants azathioprine or cyclosporine
8. Given concurrently with live vaccines

Prior–Approval *Renewal* Requirements

Age 12 years of age or older

Diagnosis

Patient must have the following:

Severe alopecia areata

AND ALL of the following:

1. Condition has improved or stabilized
2. Prescriber has considered the risks for malignancy and major adverse cardiovascular events (MACE) (e.g., advanced age, smoking history, cardiovascular risk factors etc.) and determined that continuation of Litfulo therapy is appropriate

AND NONE of the following:

1. Active bacterial, invasive fungal, viral, and other opportunistic infections
2. Development of thrombotic events (including DVTs or PEs)
3. Used in combination with any other biologic DMARD or targeted synthetic DMARD (see Appendix 1)
4. Used in combination with potent immunosuppressants azathioprine or cyclosporine
5. Given concurrently with live vaccines

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Quantity 84 capsules per 84 days

Duration 12 months

Prior–Approval *Renewal* Limits

Quantity 84 capsules per 84 days

Duration 18 months

Rationale

Summary
Litfulo is a JAK inhibitor indicated for the treatment of severe alopecia areata in adults and adolescents 12 years and older. It contains boxed warnings regarding serious infections, mortality, malignancy, MACE, and thrombosis. The safety and effectiveness of Litfulo in pediatric patients less than 12 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Litfulo while maintaining optimal therapeutic outcomes.

References

1. Litfulo [package insert]. New York, NY: Pfizer Inc.; June 2023.

Policy History

Date	Action
July 2023	Addition to PA
December 2023	Annual review
March 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.

Appendix 1 - List of DMARDS

Biological disease-modifying antirheumatic drugs (DMARDs)

Generic Name	Brand Name
abatacept	Orencia
adalimumab	Humira
anakinra	Kineret
brodalumab	Siliq
certolizumab	Cimzia
etanercept	Enbrel
golimumab	Simponi/Simponi Aria
guselkumab	Tremfya
infliximab	Remicade/Avsola/Inflectra/Renflexis
ixekizumab	Taltz
risankizumab-rzaa	Skyrizi
rituximab	Rituxan/Riabni/Ruxience/Truxima
sarilumab	Kevzara
secukinumab	Cosentyx
spesolimab-sbzo	Spevigo
tildrakizumab-asmn	Ilumya
tocilizumab	Actemra
ustekinumab	Stelara
vedolizumab	Entyvio

Targeted synthetic disease-modifying antirheumatic drugs (DMARDs)

Generic Name	Brand Name
apremilast	Otezla
baricitinib	Olumiant
deucravacitinib	Sotyktu
ritlecitinib	Litfulo
tofacitinib	Xeljanz/XR
upadactinib	Rinvoq