Litfulo™ (ritlecitinib) capsules 50mg

Litfulo (Ritlecitinib)

Prescriber Guide

This Prescriber Guide contains important safety information that you need to consider when prescribing and maintaining patients on Litfulo therapy, namely:

- Potential risk of Infections (including herpes zoster and serious infections and opportunistic infections)
- Potential risk of thromboembolic events (including deep vein thrombosis, pulmonary embolism, and arterial thrombosis)
- Potential risk of MACE
- Potential risk of malignancy
- Potential risk of neurotoxicity, including audiological events
- Potential risk of embryo-foetal toxicity following exposure in utero

About Litfulo

Litfulo works by reducing the activity of the enzymes, JAK3 and the TEC family kinases, which are involved in inflammation at the hair follicle. This reduces the inflammation, leading to hair regrowth in patients with alopecia areata.

Litfulo is indicated for the treatment of severe alopecia areata in adults and adolescents 12 years and older.

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

Posology

Treatment should be initiated and supervised by a healthcare professional experienced in the diagnosis and treatment of alopecia areata.

The recommended dose is 50 mg once daily.

The benefit-risk of treatment should be re-assessed at regular intervals on an individual basis.

Consideration should be given to discontinuing patients who show no evidence of therapeutic benefit after 36 weeks.

Important points to remember - Patient Safety Information Card

Prior to starting treatment with Litfulo:

- Provide the Patient Safety Information Card to patients and explain that the Patient Safety Information Card contains important safety information that patients should be aware of before, during, and after treatment with Litfulo.
- Discuss the important safety information for Litfulo treatment mentioned at the start of this document and ensure patient understanding of this important safety information as well as ways to minimize risks. Encourage patients to ask questions about the Patient Safety Information Card and the safe use of Litfulo.
- Advise patients about the importance of the Patient Safety Information Card and to keep it with them and to have any doctor or pharmacist involved in their care review the Patient Safety Information Card.

- Advise patients that they should read the Patient Safety Information Card along with the Patient Information Leaflet.

Infections/serious infections:

- Litfulo must not be used in patients with active serious systemic infections, including tuberculosis (TB). The most frequent serious infections have been appendicitis, COVID-19 infection (including pneumonia), and sepsis.
- As there is a higher incidence of infections in elderly and in the diabetic population in general, caution should be exercised when treating the elderly and patients with diabetes, and particular attention paid with respect to occurrence of infections.
- Patients should be closely monitored for the development of signs and symptoms of infection, including viral reactivation, during and after treatment with Litfulo.
- It is important to tell patients to get immediate medical attention if they have symptoms suggesting infection. This is to ensure rapid evaluation and appropriate treatment.

The risks and benefits of treatment should be considered in patients:

- with chronic or recurrent infection
- who have been exposed to tuberculosis (TB)
- with a history of serious or an opportunistic infection
- who have resided or travelled in areas of endemic TB or mycoses, or
- with underlying conditions that may predispose them to infection.

- Patients should be screened for TB before starting treatment.
- Anti-TB therapy should be started prior to initiating therapy with Litfulo in patients with a new diagnosis of latent TB or previously untreated latent TB.
- In patients with a negative latent TB test, anti-TB therapy should still be considered before initiating treatment with Litfulo
- If a patient develops herpes zoster, temporary interruption of treatment may be considered until the episode resolves.

- Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with Litfulo.
- Monitoring for reactivation of viral hepatitis according to clinical guidelines is recommended during Litfulo treatment. If there is evidence of reactivation, a liver specialist should be consulted.

Vaccines:

- No data are available on the response to vaccination in patients receiving Litfulo. Use of live attenuated vaccines should be avoided during or immediately prior to Litfulo treatment. Prior to initiating Litfulo, it is recommended that patients are brought up to date with all immunisations, including prophylactic herpes zoster vaccinations, in agreement with current immunisation guidelines.
- Live vaccines are not recommended during Litfulo treatment, or just before starting Litfulo treatment.

Thromboembolic events including deep vein thrombosis, pulmonary embolism and arterial thrombosis:

- Events of venous and arterial thromboembolism, including MACE, have been reported in patients receiving Litfulo.
- It is not known whether selective JAK3 inhibition may be associated with adverse reactions of JAK inhibition predominantly involving JAK1 and JAK2. In a large randomised active-controlled study of tofacitinib (another JAK inhibitor) in RA patients 50 years and older with at least one additional cardiovascular risk factor, a higher rate of b, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke, and a dose-dependent higher rate of venous thromboembolism including DVT and PE were observed with tofacitinib compared to TNF inhibitors.
- In this study, current or past, long-time smokers and patients 65 years of age and older had an additional increased risk for major adverse cardiovascular events (MACE).
- Long-term safety evaluations for Litfulo are ongoing.

- The risks and benefits of Litfulo treatment should be considered prior to initiating therapy in patients.
- In patients with a suspected thromboembolic event, discontinuation of Litfulo and prompt re-evaluation is recommended.

If signs and symptoms occur:

- Promptly evaluate patients and discontinue Litfulo in patients with suspected thromboembolic events.

Malignancy:

- Malignancies, including non-melanoma skin cancer (NMSC) have been reported in patients receiving Litfulo.
- It is not known whether selective JAK3 inhibition may be associated with adverse reactions of JAK inhibition predominantly involving JAK1 and JAK2.
- In a large randomised active-controlled study of tofacitinib (another JAK inhibitor) in rheumatoid arthritis (RA) patients 50 years and older with at least one additional cardiovascular risk factor, a higher rate of malignancies, particularly lung cancer, lymphoma and NMSC, was observed with tofacitinib compared to tumour necrosis factor (TNF) inhibitors.
- In this study, current or past, long-time smokers and patients 65 years of age and older had an additional increased risk of overall malignancies.
- Limited clinical data are available to assess the potential relationship of exposure to Litfulo and the development of malignancies.
- Long-term safety evaluations are ongoing. The risks and benefits of Litfulo treatment should be considered prior to initiating or continuing therapy in patients with a known malignancy other than a successfully treated NMSC or cervical cancer.
- Periodic skin examination is recommended for patients at increased risk for skin cancer.

Neurotoxicity, including audiological events:

- Ritlecitinib-related axonal dystrophy has been observed in chronic Beagle dog toxicity studies. Axonal dystrophy was associated with neurological hearing loss. While these findings proved to reverse after dosing cessation of ritlecitinib in dogs, a risk to patients at a chronic dosing regimen cannot be fully excluded.
- Routine audiological testing (including pure tone audiometry, speech audiometry, and immittance audiometry) was implemented in the trials at specified time points to assess for potential changes in hearing status.
- In the placebo-controlled trials, for up to 24 weeks, sensorineural hearing loss occurred in less than 1% of participants in the ritlecitinib group (1 case) and the rate in placebo was 0.
- Across clinical trials, including the long-term trial, the majority of audiological events were mild in severity, did not demonstrate a dose response, were considered unrelated to ritlecitinib, and resolved without change to Ritlecitinib treatment.
- Available clinical data has not indicated an effect on neurological or audiological outcomes.
- Treatment with Litfulo should be discontinued in case unexplained neurological symptoms occur.

Embryofoetal toxicity following exposure in utero:

There is limited amount of data on the use of Litfulo in pregnant women. Studies in animals have shown reproductive toxicity.

- Litfulo is contraindicated during pregnancy.
- Women of reproductive potential should be advised to use effective contraception during and for 1 month following the final dose of Litfulo. Pregnancy planning and prevention for females of reproductive potential should be encouraged.
- Advise patients to inform their healthcare provider immediately if they think they could be pregnant or if pregnancy is confirmed.

Further information:

- As a healthcare professional, it is important that you report any suspected adverse reactions. It allows continued monitoring of the benefit/risk balance of the medicinal product. Adverse events can be reported directly to the Ministry of Health using the adverse events reporting portal which is available on the home page of the Ministry of Health website:

  www.health.gov.il or by this link: **https://sideeffects.health.gov.il**

  Side effects can also be reported to Pfizer by email: **isr.aereporting@pfizer.com**

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Pfizer

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