

Litfulo[▼] (Ritlecitinib)

Healthcare Professional Guide

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

- Risk of Infections (including herpes zoster and serious infections and opportunistic infections)
 - Risk of venous thromboembolism (VTE)
 - Risk of major adverse cardiovascular event (MACE)
 - Risk of malignancy
 - Risk of neurotoxicity
 - Risk of embryo-foetal toxicity following exposure in utero
 - Use in patients over 65 years of age and older
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Please read this brochure in full along with the Summary of Product Characteristics (SmPC) for Litfulo.

Litfulo should only be used if no suitable treatment alternatives are available in patients:

- **65 years of age and older;**
- **patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers);**
- **patients with malignancy risk factors (e.g. current malignancy or history of malignancy)**

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 of age and older.

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.

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

Important points to remember - Patient Card

Prior to starting treatment with Litfulo:

- Provide the Patient Card to patients and explain that the Patient 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 Card and the safe use of Litfulo.
 - Advise patients about the importance of the Patient Card and to keep it with them and to have any doctor or pharmacist involved in their care review the Patient Card.
 - Advise patients that they should read the Patient Card along with the Patient Information Leaflet.
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Use in patients 65 years of age and older:

- Considering the increased risk of MACE, malignancies, serious infections, and all-cause mortality in patients 65 years of age and older, as observed in a large randomised study of tofacitinib (another JAK inhibitor), Litfulo should only be used in these patients if no suitable treatment alternatives are available.
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Infections (including herpes zoster and serious and opportunistic 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. In patients 65 years of age and older Litfulo should only be used if no suitable treatment alternatives are available.
- 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.

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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.

Venous thromboembolism (VTE):

- Events of deep vein thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving Litfulo.
- In a large randomised active-controlled study of tofacitinib (another JAK inhibitor) in rheumatoid arthritis patients 50 years and older with at least one additional cardiovascular risk factor, a dose dependent higher rate of VTE including DVT and PE was observed with tofacitinib compared to TNF inhibitors.
- In patients with cardiovascular or malignancy risk factors Litfulo should only be used if no suitable treatment alternatives are available.
- In patients with known VTE risk factors other than cardiovascular or malignancy risk factors, Litfulo should be used with caution.
- VTE risk factors other than cardiovascular or malignancy risk factors include previous VTE, patients undergoing major surgery, immobilisation, use of combined hormonal contraceptives or hormone replacement therapy, inherited coagulation disorder.
- Patients should be re-evaluated periodically during Litfulo treatment to assess for changes in VTE risk.
- If signs and symptoms of VTE occur:
Promptly evaluate patients and discontinue Litfulo in patients with suspected VTE, regardless of dose.

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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 [including but not limited to MMR (for measles, mumps, rubella), vaccines for rubella, yellow fever, oral vaccines for typhoid fever and poliomyelitis] are not recommended during Litfulo treatment, or just before starting Litfulo treatment.
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Malignancy:

- Malignancies, including non-melanoma skin cancer (NMSC) have been reported in patients receiving Litfulo.
 - 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 patients 65 years of age and older, patients who are current or past long-time smokers, or with other malignancy risk factors (e.g., current malignancy or history of malignancy), Litfulo should only be used if no suitable treatment alternatives are available.
 - Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer.
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Major Adverse Cardiovascular Events (MACE):

- Events of MACE, have been reported in patients receiving Litfulo.
 - 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 MACE, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke was observed with tofacitinib compared to TNF inhibitors.
 - Therefore, in patients 65 years of age and older, patients who are current or past long-time smokers, and patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors, Litfulo should only be used if no suitable treatment alternatives are available.
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Neurotoxicity:

- Ritlecitinib-related axonal dystrophy has been observed in chronic Beagle dog toxicity studies at systemic exposures of at least 7.4-times the expected exposure in patients treated with Litfulo 50 mg per day. At a systemic exposure that was 33-times above the expected exposure in patients treated with Litfulo 50 mg per day, 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.
- 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.

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▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get.

Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form, which is available online at <https://medicinesauthority.gov.mt/adrportal>, and sent by post or email to;

P: Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN 3000

E: postlicensing.medicinesauthority@gov.mt

Alternatively, you may also report such events promptly to Pfizer Hellas Pharmacovigilance Department contact details: +30 210 67 85 908 and +30 210 67 85 808 (24hour line), via the webportal: <https://genaes.pfizersafetyreporting.com/en> (Pfizersafetyreporting.com) or contact the local representative Vivian Corporation Ltd. Tel. +356 2134 4610/ +356 2258 8600.

- All the educational materials including the patient alert card and the prescriber guide are available at: <https://medicinesauthority.gov.mt/rmm>.
- In case you need more copies of the Prescriber Guide or the Patient Card, please call Pfizer's Local Representative, Vivian Corporation Ltd.: 00356 21344610/00356 22588600.