<Date>

Litfulo▼ (ritlecitinib): Updated recommendations to minimise the risks of major adverse cardiovascular events, malignancy, venous thromboembolism, serious infections, and mortality

Dear Healthcare Professional,

{Pfizer Europe}, in agreement with the European Medicines Agency (EMA) and the <National Competent Authority>, would like to inform you of the following:

Summary

- **Based on the review of latest available data, risks of JAK inhibitors, i.e. major adverse cardiovascular events (MACE), malignancy, serious infections, and venous thromboembolism (VTE) are relevant for Litfulo in its approved indication.**
- **Litfulo should only be used if no suitable treatment alternatives are available in patients:**
    - **65 years of age and older;**
    - **with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers);**
    - **with malignancy risk factors (e.g., current malignancy or history of malignancy).**
- **Litfulo should be used with caution in patients with VTE risk factors other than those listed above.**
- **Periodic skin examinations are recommended for all patients.**

Background on safety concerns and updated risk minimisation measure

Litfulo (ritlecitinib) is a selective JAK3 and TEC family kinase inhibitor, authorised in September 2023 for the treatment of severe alopecia areata (AA) in adults and adolescents 12 years of age and older.

In February 2023, a DHPC[1] for Cibinqo (abrocitinib), Jyseleca (filgotinib), Olumiant (baricitinib), Rinvoq (upadacitinib) and Xeljanz (tofacitinib) was disseminated to healthcare professionals, informing them that an increased incidence of malignancy, major adverse cardiovascular events (MACE), serious

[1] https://www.ema.europa.eu/en/documents/dhpc/direct-healthcare-professional-communication-dhpc-updated-recommendations-minimise-risks-malignancy-major-adverse-cardiovascular-events-serious-infections-venous-thromboembolism-and-mortality-use_en.pdf

infections, venous thromboembolism (VTE) and mortality was observed in patients with rheumatoid arthritis (RA) with certain risk factors using JAK inhibitor treatment compared to TNFα inhibitor[2]. These risks were considered class effects and relevant across all approved indications for JAK inhibitors in inflammatory and dermatologic diseases; class-wide risk minimisation measures were therefore implemented to minimise these risks[3].

As part of EMA's routine assessment of the benefit-risk balance of Litfulo, based on cumulative evidence from clinical trials and post-marketing data, and in the absence of definitive data establishing that JAK3/TEC selectivity abrogates these risks, it was concluded that the precautionary measures recommended in the Article 20 procedure for JAKis used in chronic inflammatory disorders are also relevant for Litfulo. Measures to minimise these risks have therefore been implemented, as outlined in the summary above.

The product information of Litfulo will be updated accordingly. Overall, EMA concluded that the benefit-risk profile of Litfulo remains positive. The updated recommendations are intended to support and reinforce risk minimisation measures.

Call for reporting

Healthcare professionals and patients are encouraged to report any suspected adverse reactions. Please report adverse events in accordance with your national spontaneous reporting system:

Country specific reporting information

Company contact point

If you have any questions or require further information, please contact Pfizer Medical Information:

- Telephone:
- Email:
- Website:
- Postal Address:

Sincerely,

[2] Ytterberg SR, Bhatt DL, Mikuls TR, et al. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. N Engl J Med. 2022;386(4):316-326.

[3] European Medicines Agency. EMA confirms measures to minimise risk of serious side effects with Janus kinase inhibitors for chronic inflammatory disorders. EMA/142279/2023. Published March 10, 2023. Accessed July 2, 2026. https://www.ema.europa.eu.

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	**Litfulo(ritlecitinib) 50 mg hard capsules**
Marketing authorisation holder(s)	Pfizer Europe MA EEIG
Safety concern and purpose of the communication	Inform about updated recommendations to minimise the risk of malignancy, major adverse cardiovascular events, serious infections, venous thromboembolism and mortality
DHPC recipients	Dermatologists, Paediatricians. The target group should be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU/EEA Member states

Timetable *Delete steps which are not applicable*	**Date**
DHPC and communication plan (in English) agreed by PRAC	**09 July 2026**
DHPC and communication plan (in English) agreed by CHMP/CMDh	**23 July 2026**
Submission of translated DHPCs to the national competent authorities for review	**28 July 2026**
Agreement of translations by national competent authorities	**04 August 2026**
Dissemination of DHPC	**10 August 2026**