Opzelura® 15 mg/g cream (ruxolitinib phosphate): Important information regarding presence of particles in Opzelura cream

Dear Healthcare Professional,

The marketing authorisation holder Incyte Biosciences Distribution B.V. ("Incyte"), in agreement with the European Medicines Agency (EMA) and *(insert NCA),* would like to inform you of the following:

Summary

- **Complaints about the presence of small, visible crystal-like particles in Opzelura (ruxolitinib) cream have been reported. The particles might form out of the active ingredient (ruxolitinib, as the dihydrate).**
- **While these crystal-like particles may cause some discomfort to patients when they apply the cream, they do not pose any significant safety risk to patients, nor are expected to impact the product's efficacy.**
- **Patients should be advised that small, visible crystal-like particles may be present in Opzelura.**
- **If a patient observes crystals in Opzelura cream they should stop treatment with the affected tube, return the tube to the pharmacy where they obtained it and request a replacement tube as soon as possible.**
- **A pharmacist who receives a tube of Opzelura containing visible crystal-like particles should contact Incyte's Medical Information Team at eumedinfo@incyte.com, and Incyte will arrange for a replacement tube to be sent to them, free of charge.**

Background
Opzelura is indicated for the treatment of non-segmental vitiligo with facial involvement in adults and adolescents from 12 years of age.

Quality complaints and non-serious events reporting
Since the availability of Opzelura in the European Union/EEA in May 2023, the frequency of complaints received regarding the presence of crystal-like particles has ranged from 6 in 10,000 for all distributed batches to an estimated 1 in 10,000 for batches subject to the latest monitoring controls aimed at limiting the distribution of tubes containing crystal-like particles. From May 2023 until 5 March 2025, the incidence of patient-reported non-serious events after application of the cream due to presence of crystal-like particles has been very rare (< 1/10,000). These events include pain, scratches, paraesthesia or erythema at the application site.

The crystal formation is not expected to result in significant loss of efficacy over a short period of time.

Root cause
The precise root cause of the crystal formation is not clear. During manufacturing of Opzelura, particles might form out of the active ingredient (ruxolitinib phosphate). If formation of ruxolitinib dihydrate takes place, this could present as small particles in the cream.

Measures taken by the marketing authorisation holder Incyte
Incyte has implemented measures including conducting additional testing for crystal formation of every product batch before release to prevent releasing tubes with crystal formations. In addition, Incyte is developing an alternative formulation to prevent the formation of crystals in the cream going forward. Product quality complaints and adverse events will be monitored continuously.

Call for reporting
Please report suspected adverse reactions or product quality complaints in patients treated with Opzelura® 15 mg/g cream to *eumedinfo@incyte.com* and, in accordance with the national requirements, to <*local agency*> through <*email, website, address*>including batch/Lot number if available.

Company contact point
If you have any questions, please contact Incyte at eumedinfo@incyte.com.
Alternatively, you can contact us via telephone. Please visit https://incyte.com/contact-us to find your local number.

DHPC Communication Plan	
Medicinal product(s)/active substance(s)	Opzelura® 15 mg/g Cream (ruxolitinib phosphate)
Marketing authorisation holder	Incyte Biosciences Distribution B.V.
Safety concern and purpose of the communication	There is a quality concern due to the potential presence of small, visible crystal-like particles of the active ingredient ruxolitinib in the cream. While these particles may create grainy texture to the cream which may cause some discomfort during application, they do not pose any significant safety risk to patients. With a prompt replacement of the tube, it is unlikely that the vitiligo treatment will be affected. The purpose of the communication is to advise HCPs to instruct each patient receiving a tube of Opzelura that if their dispensed product contains visible particles, they are recommended to bring their tube back to the dispensing pharmacy to secure a replacement tube of Opzelura at no cost.
DHPC recipients	Dermatologists and pharmacists. In countries where the prescription and dispensing of Opzelura is restricted to hospital setting, hospital-based dermatologists and pharmacists. 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	The DHPC will be distributed to recipients in the EU countries where the product has been launched: Austria, Croatia, Cyprus, France, Germany, Greece, Italy, Luxembourg, Malta, Slovenia, Spain and Sweden.

Timetable	Date
DHPC and communication plan (in English) agreed by CHMP	27 March 2025
Submission of translated DHPCs to the national competent authorities for review	03 April 2025
Agreement of translations by national competent authorities	10 April 2025
Dissemination of DHPC	24 April 2025