11 April 2022

Xagrid (anagrelide hydrochloride): Risk of thrombosis, including cerebral infarction, if treatment discontinued abruptly. [also applicable to generic forms]

Dear Healthcare Professional,

The marketing authorisation holders for anagrelide, in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Authority (MHRA) would like to inform you the following:

Summary

- **There is an increased risk of thrombotic complications, including cerebral infarction, if anagrelide treatment is discontinued abruptly.**
- **Abrupt treatment discontinuation should be avoided due to the risk of sudden increase in platelet counts and potentially fatal thrombotic complications, such as cerebral infarction.**
- **In the event of dosage interruption or treatment withdrawal, monitor platelet counts frequently (refer to SmPC Section 4.4).**
- **Advise patients how to recognise early signs and symptoms suggestive of thrombotic complications, such as cerebral infarction, and to seek medical assistance if symptoms occur.**

Background on the safety concern

Anagrelide is indicated for the reduction of elevated platelet counts in at-risk patients with essential thrombocythemia who are intolerant to their current therapy or whose elevated platelet counts are not reduced to an acceptable level by their current therapy.

A cumulative analysis of the Takeda company safety database for Xagrid up to 6 August 2021 showed 15 events of thrombotic complications, including cerebral infarction, after a recent discontinuation of anagrelide. It was concluded that cerebral infarction, along with other thrombotic complications, while being part of the pre-existing condition/indication, may also occur upon abrupt anagrelide discontinuation, inadequate dosing, or lack of effect.

The mechanism of cerebral infarction following abrupt treatment discontinuation is related to the rebound in platelet count. Platelet count typically will start to rise within 4 days after discontinuation and return to baseline levels in one to two weeks, possibly rebounding above baseline values.

Based upon the available information, the safety information under Section 4.4 "Special Warnings and Precautions for Use" and section 4.8 "Undesirable Effects of Summary of Product Characteristics (SmPC) will be updated to reflect the latest data and recommendations.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

It is easiest and quickest to report ADRs online via the Yellow Card website - https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store. Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

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Yours faithfully,

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