Ref: 22/10003/TAK/PV/SAHPRA

IMPORTANT
MEDICINE SAFETY INFORMATION

05 August 2022

Anagrelide hydrochloride: Risk of thrombosis including cerebral infarction upon abrupt treatment discontinuation

Dear Healthcare Professional,

Takeda (Pty) Ltd, as directed by the South African Health Products Regulatory Authority (SAHPRA), wish to inform you about the risk of thrombosis including cerebral infarction upon abrupt treatment discontinuation of anagrelide hydrochloride.

The Professional Information (PI) and Patient Information Leaflet (PIL) of anagrelide hydrochloride containing medicines will be amended to reflect the above safety information. The updated PI/PIL will also include information on the weaning process to prevent the risk of thrombosis associated with abrupt discontinuation of anagrelide treatment.

Summary

- **Abrupt treatment discontinuation should be avoided due to the risk of a sudden increase in the platelet count with potentially fatal thrombotic complications.**
- **Platelet count should be monitored frequently during dosage interruption or treatment withdrawal.**

Background information on the safety concern

Agrylin® 0.5 mg (anagrelide hydrochloride) is indicated to reduce the platelet count in patients with essential thrombocythemia, polycythemia vera and other myeloproliferative disorders.

A cumulative analysis of Takeda's safety database for Agrylin® 0,5 mg, till 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.

Advice to healthcare professionals

- Healthcare professionals are advised to avoid abrupt treatment discontinuation as it is associated with the risk of a sudden increase in platelet counts resulting in potentially fatal thrombotic complications.
- In the event of dosage interruption or treatment withdrawal, monitor platelet counts frequently.
- Patients should be advised on how to recognize early signs and symptoms suggestive of thrombotic complications, such as cerebral infarction, and if symptoms occur, to seek medical assistance.

Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality issues (including batch details) related to anagrelide hydrochloride to Takeda (Pty) Ltd via the following email address: AE.SouthAfricaSSA@takeda.com. Alternatively, please complete the ADR reporting form accessible via the SAHPRA website and email it to adr@sahpra.org.za.
Healthcare professionals may also use the eReporting link available on the SAHPRA website (www.sahpra.org.za), or the National Department of Health Mobile Application accessible from the Essential Medicines List (EML) Clinical Guide to report ADRs or product quality issues. For more information on ADR reporting of products listed below, please contact the SAHPRA vigilance unit at pvqueries@sahpra.org.za

For further information, please contact the company listed in the table below:

Product	Active ingredient	Company	Registration Number	Contact Details
AGRYLIN® 0,5 mg	Anagrelide hydrochloride	Takeda (Pty) Ltd	A33/8/0288	**Tel:** 082 525 3040 **Fax:** 086 558 7816 **Email**: AE.SouthAfricaSSA@takeda.com

Yours Sincerely

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