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Direct Healthcare Professional Communication

Human epoetins: new warnings on severe cutaneous adverse reactions

Dear Healthcare Professional

In agreement with the European Medicines Agency and the Malta Medicines Authority, the Marketing Authorisation Holders (MAHs) of all Epoetins would like to inform you of the risk of severe cutaneous adverse reactions in patients treated with the epoetins: **darbepoetin alfa** (Aranesp), **epoetin alfa** (Abseamed, Binocrit, Epoetin Alfa Hexal, Eprex, Erypo and Erypo FS), **epoetin beta** (NeoRecormon), **epoetin theta** (Biopoin and Eporatio), **epoetin zeta** (Retacrit and Silapo) and **methoxy polyethylene glycol-epoetin beta** (Mircera)

Summary

- Severe cutaneous adverse reactions (SCARs) have been reported in patients treated with epoetins. These included cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) some of which have been fatal.
- Severe cutaneous adverse reactions are considered to be a class effect of all epoetins.
- The reactions have been more severe with long-acting epoetins.
- The frequency of these severe cutaneous reactions could not be calculated but they occur very rarely.
- **Patients should be advised of the following signs and symptoms of severe skin reactions when starting treatment with an epoetin product:**
    - **widespread rash with reddening and blistering of the skin and oral mucosa, eyes, nose, throat, or genital area, which follow flu-like symptoms including fever, tiredness, muscle and joint pain. This often leads to peeling and shedding of the affected skin which looks like a severe burn.**
- **Patients who develop these signs and symptoms should be instructed to contact their doctor immediately and stop epoetin treatment.**
- If the patient has developed severe cutaneous adverse reactions such as SJS or TEN which is considered to be related to the use of an epoetin, the patient **must never** be given an epoetin again.

Background of the safety concern

Following post-marketing reports of severe cutaneous adverse reactions in particular SJS, TEN and blistering and exfoliative reactions with some epoetins, a detailed analysis of all cases (including data from the EudraVigilance database and data from the MAHs) has been performed for all epoetin-containing medicines.

This analysis has revealed that severe cutaneous reactions including SJS and TEN can be considered a class risk for all epoetins. The more severe reactions were reported with long-acting epoetins and included cases with positive de-challenge and positive re-challenge.

The frequency of these severe cutaneous reactions could not be calculated but they occur very rarely.

The product information of all epoetin-containing products, including darbepoetin alfa, epoetin alfa, epoetin beta, epoetin theta, epoetin zeta and methoxy polyethylene glycol-epoetin beta is being updated to reflect the risk of severe cutaneous adverse reactions.

Call for reporting

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with this product in accordance with the national spontaneous reporting system. Any suspected adverse reactions and medication errors can be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta or sent by email to postlicensing.medicinesauthority@gov.mt

Companies contact points

If you have further questions or require additional information please contact:

Company	Product name	Email	Phone
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V.J.Salomone Pharma Ltd	Binocrit Epoetin alfa Hexal	pharma@vjsalomone.com	+35621220174
AM Mangion Ltd on behalf of Janssen - Cilag NV	Eprex	gganado@its.jnj.com	+35623976000
AM Mangion Ltd on behalf of Janssen – Cilag Pharma GmBH	Erypo Erypo FS	gganado@its.jnj.com	+35623976000
Roche Registration Ltd	NeoRecormon Mircera	*Additional Information* medinfo.uk@roche.com *Suspected adverse reactions* welwyn.uk_dsc@roche.com	+44(0)1707361010 +44(0)1707367554
Actavis International Ltd	Biopoin Eporatio	PHVMALTA@actavis.com	+302118805166
Hospira UK Limited, now a Pfizer company	Retacrit	safety@drugsalesltd.com	+35621419070/1/2
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Yours faithfully,

Post-Licensing Directorate
Medicines Authority

Disclaimer

This Direct Healthcare Professional Communication has been submitted to you on behalf of Amgen Europe B.V, Medice Arzneimittel Pütter GmbH & Co. KG, Sandoz GmbH, Hexal AG, Janssen-Cilag NV, Janssen-Cilag Pharma GmbH, Roche Registration Limited, Actavis International Ltd, Hospira UK Limited, now a Pfizer company and STADA Arzneimittel AG together with their local representatives.