September 2017

Direct Healthcare Professional Communication

Recombinant human erythropoietins: Risk of severe cutaneous adverse reactions

Dear Healthcare Professional,

In agreement with the European Medicines Agency and the MHRA, the Marketing Authorisation Holders (MAHs) of all recombinant human erythropoietins (r-HuEPOs) would like to inform you of the risk of severe cutaneous adverse reactions in patients treated with the r-HuEPOs: **darbepoetin alfa, epoetin alfa, epoetin beta, epoetin zeta and methoxy polyethylene glycol-epoetin beta**.

Summary

- Cases of severe cutaneous adverse reactions (SCARs) have been reported in patients treated with r-HuEPOs. 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 r-HuEPOs.
- The reactions have been more severe with long-acting r-HuEPOs.
- 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 r-HuEPO 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 r-HuEPO, the patient **must never** be given an r-HuEPO 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 r-HuEPOs, a detailed analysis of all cases (including data from the EudraVigilance database and data from the MAHs) has been performed for all r-HuEPOs.

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

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

The product information of all r-HuEPOs, including darbepoetin alfa, epoetin alfa, epoetin beta, 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 (ADRs) with HuEPOs to the MHRA through the Yellow Card Scheme.

It is easiest and quickest to report ADRs online via the Yellow Cards website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form from the Yellow Card section of the MHRA website

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name. r-HuEPOs are biological medicines, healthcare professionals should report adverse reactions by brand name and batch number.

Companies contact points

Alternatively, suspected adverse reaction may also be reported to the marketing authorisation holders using the details provided below. If you have further questions or require additional information, please contact:

Company	Product name	Email	Phone	Fax
Amgen Ltd	Aranesp	gbinfoline@amgen.com	+44 (0)1223 436 441	+44 (0)1223 426 314
Hospira UK Limited, now a Pfizer company	Retacrit (epoetin zeta)	medical.information@pfizer.com	+44 (0) 1304 616161	N/A
Janssen-Cilag Ltd	EPREX	Additional Information: e-mail: medinfo@its.jnj.com Suspected adverse reactions: e-mail: dsafety@its.jnj.com	Additional Information: Tel: 0800 731 8450 or 01494 567 444 Suspected adverse reactions: Tel: 01494 567447	Additional Information: Fax: 01494 567 445 Suspected adverse reactions: Fax: 01494 567799

Roche Products Ltd	Mircera	Additional Information: e-mail: medinfo.uk@roche.com Suspected adverse reactions: e-mail: welwyn.uk_dsc@roche.com	Additional Information: Tel: +44 (0)800 328 1629 Suspected adverse reactions: Tel: +44 (0)1707 367554	N/A
Roche Products Ltd	NeoRecormon	Additional Information: e-mail: medinfo.uk@roche.com Suspected adverse reactions: e-mail: welwyn.uk_dsc@roche.com	Additional Information: Tel: +44 (0)800 328 1629 Suspected adverse reactions: Tel: +44 (0)1707 367554	N/A
Members of the Sandoz group including Sandoz Limited	Binocrit (not marketed) and Epoetin alfa HEXAL (not marketed)	Additional Information: e-mail: uk.patientsafety@novartis.com Suspected Adverse reactions: *https://psi.novartis.com*	+44 (0)1276 698020	N/A

Yours faithfully,

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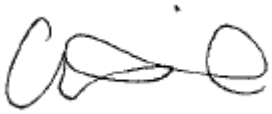

Dr Christopher Goode
Medical Director
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