

September 2017

## 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 Health Products Regulatory Authority (HPRA), 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, epoetin alfa, epoetin beta, epoetin theta, epoetin zeta and methoxy polyethylene glycol-epoetin beta**.

#### 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 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 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

Suspected adverse reactions should be reported to the HPRA using a Yellow Card obtained either from the HPRA, or electronically via the website at [www.hpra.ie](http://www.hpra.ie). Adverse reactions can also be reported to the HPRA by calling (01) 676 4971.

### Companies contact points

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

Company	Product name	Email	Phone	Fax
Amgen Ltd	Aranesp	<a href="mailto:gbinfo@amgen.com">gbinfo@amgen.com</a>	+44 (0)1223 436 441	+44 (0)1223 426 314
Pfizer Healthcare Ireland	Retacrit (epoetin zeta)	<a href="mailto:eumedinfo@pfizer.com">eumedinfo@pfizer.com</a>	1800 633 363	N/A
Janssen-Cilag Ltd	EPREX	Additional Information: e-mail: <a href="mailto:medinfo@its.jnj.com">medinfo@its.jnj.com</a> Suspected adverse reactions: e-mail: <a href="mailto:dsafety@its.jnj.com">dsafety@its.jnj.com</a>	Additional Information: Tel: 1 800 709 122 Suspected adverse reactions: Tel: +44 (0)1494 567447	Additional Information: Fax: +44 (0)1494 567 445 Suspected adverse reactions: Fax: +44 (0)1494 567799
Roche Products (Ireland) Ltd	Mircera	<a href="mailto:ireland.drug_surveillance_centre@roche.com">ireland.drug_surveillance_centre@roche.com</a>	+353 1 4690700	+353 1 4690793
Roche Products (Ireland) Ltd	NeoRecormon	<a href="mailto:ireland.drug_surveillance_centre@roche.com">ireland.drug_surveillance_centre@roche.com</a>	+353 1 4690700	+353 1 4690793
Ratiopharm GmbH/Teva	Eporatio	<a href="mailto:medinfo@tevauk.com">medinfo@tevauk.com</a>	+44 (0)20 7540 7117	+44 (0)20 7540 7349

Yours faithfully,

A handwritten signature in black ink, appearing to be 'AP' with a long horizontal stroke extending to the right.

Dr Anthony Patrikios  
Executive Medical Director, UK & Ireland  
MBBCh MRCGP FFPM MBA

A handwritten signature in black ink, clearly legible as 'Emma Lynch'.

Emma Lynch,  
Pfizer Essential Health Medical Director, Ireland

A handwritten signature in black ink, appearing to be 'B. Seoighe'.

Dr Brid Seoighe  
Head of Medical Affairs  
Janssen Ireland

A handwritten signature in blue ink, clearly legible as 'Michal Starnawski'.

Michal Starnawski, M.D., Ph.D.  
Medical Director  
Roche Products (Ireland) Ltd

A handwritten signature in black ink, clearly legible as 'E. Walters'.

Dr. Ewan Walters,  
TEVA Senior Director Medical Affairs UK & Ireland