Medicines Safety Update

Australian Government
Department of Health
Therapeutic Goods Administration

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In this issue

Epoetin alfa (Eprex) and increased risk of pure red cell aplasia with subcutaneous administration

The Product Information for epoetin alfa has been updated to provide further information regarding an increased risk of pure red cell aplasia with subcutaneous administration, particularly in patients who have chronic renal disease.

Epoetin alfa (marketed in Australia under the brand name Eprex) is a recombinant product that stimulates erythropoiesis and reduces the need for blood transfusions. Among its indications is the treatment of patients with symptomatic or transfusion-requiring anaemia associated with chronic renal failure.

It has been identified that there is an increased risk of pure red cell aplasia with subcutaneous use of epoetin alfa, particularly in patients with chronic renal disease.

The Product Information (PI) had previously stated that pure red cell aplasia was identified post-market as a potential rare adverse event, which could occur after months to years of treatment. However, there was no mention of an association between the development of pure red cell aplasia and either chronic renal disease or the route of administration.

The PI has been updated to advise health professionals that most cases of pure red cell aplasia associated with epoetin alfa occurred in patients with chronic renal failure receiving subcutaneous administration. The subcutaneous route should only be used when intravenous access is not readily available.

Adverse events

From January 2001 to 20 August 2014, the TGA has received 41 reports of pure red cell aplasia associated with epoetin alfa, including 34 cases where it was the sole suspected drug. Of those cases, three resulted in death.

Reports received did not contain sufficient detail to identify how many of those cases involved subcutaneous administration in chronic renal disease patients.

Information for health professionals

When administering epoetin alfa to patients with chronic renal disease, the intravenous route is preferable.

Where intravenous access is not readily available, epoetin alfa can still be administered subcutaneously, but you should be mindful of the increased risk of pure red cell aplasia in these situations.

If pure red cell aplasia is diagnosed, epoetin alfa must be immediately discontinued and testing for erythropoietin antibodies should be considered. If erythropoietin antibodies are detected, patients should not be switched to another erythropoiesis-stimulating agent.

Please report any suspected adverse event associated with epoetin alfa, particularly cases of suspected pure red cell aplasia, to the TGA.

Medicines Safety Update is the medicines safety bulletin of the Therapeutic Goods Administration (TGA)

TGA Health Safety Regulation

MEDICINES SAFETY UPDATE

Pregabalin and suicidality

Health professionals are reminded of the risk of suicidality associated with the use of pregabalin for any indication, including off-label use.

Pregabalin is an analogue of the neurotransmitter, gamma-aminobutyric acid. It is indicated for the treatment of neuropathic pain in adults and as adjunctive therapy in adults with partial seizures, with or without secondary generalisation.

The Product Information (PI) for pregabalin includes a precaution that antiepileptic drugs, including this drug, increase the risk of suicidal thoughts or behaviour.

This increased risk applies to patients taking these drugs for any indication, including off-label uses.

Clinical trials

Clinical trial data documented in the PI for pregabalin identify an increased risk of suicidal thoughts or behaviour with antiepileptic drugs as early as one week after starting treatment.

Pooled analyses of 199 placebo-controlled clinical trials (mono- and adjuvant therapy) of 11 different antiepileptic drugs showed that patients randomised to one of these drugs had approximately twice the risk (adjusted relative risk 1.8; 95% confidence interval 1.2–2.7) of suicidal thoughts or behaviour, compared with patients randomised to placebo treatment.

In these trials, which had a median treatment duration of 12 weeks, the estimated incidence rate of suicidal behaviour or ideation among 27 863 antiepileptic drug-treated patients was 0.43% compared with 0.24% among 16 029 placebo-treated patients. This represented an increase of approximately one case for every 530 patients treated.

It should be noted that epilepsy and some other illnesses for which pregabalin may be prescribed are themselves associated with an increased risk of suicidal thoughts or behaviour.

Adverse events

From April 2005 to 20 August 2014, the TGA has received two reports of suicide in which pregabalin was being taken and was the sole suspected drug. In the same time period, there were also two cases of attempted suicide, seven cases of suicidal behaviour, and 57 cases of suicidal thoughts reported to the TGA. In all but one case of attempted suicide and three cases of suicidal thoughts, pregabalin was the sole suspected drug.

Information for health professionals

Patients being treated with pregabalin, including those prescribed it off-label, should be monitored for the emergence or worsening of depression, suicidal thoughts or behaviours and/or any unusual changes in mood or behaviour.

Advise patients and caregivers of the risk of suicidality and educate them regarding the associated symptoms and the need to contact you if they experience any.

If symptoms of suicidal thoughts or behaviour are identified, consider whether they are related to treatment with pregabalin or could be related to the illness being treated. The risks of treatment with pregabalin should be weighed against the risks of the untreated illness.

Online reporting form for consumers

Health professionals are encouraged to advise consumers of a new web-based service that makes it easier for them to report adverse events involving medicines and vaccines.

While consumers are still able to report adverse events to their health professional, who can then report on their behalf, the online form is designed to help improve the number and quality of reports the TGA receives directly from consumers.

Each year the TGA receives more than 17 000 reports of suspected adverse events involving medicines and vaccines. In 2013, about 3% of these reports came directly from consumers, compared with 55% coming via sponsors, 17% from state and territory health departments (predominantly vaccines), 10% from hospitals and hospital pharmacists, and the remainder from community pharmacists and general practitioners.

The form can be accessed at www.tga.gov.au. Click on ‘Report a problem’ and follow the links.

MEDICINES SAFETY UPDATE

Topiramate and visual field defects

The sponsor of topiramate, in consultation with the TGA, has issued a Dear Healthcare Professional letter advising that a precaution for visual field defects has been added to the Product Information.

Topiramate is a sulfamate substituted monosaccharide. It is indicated in adults and children aged two years and over:

- as monotherapy in patients with newly diagnosed epilepsy
- for conversion to monotherapy in patients with epilepsy
- as add-on therapy in partial onset seizures (with or without secondary generalised seizures), primary generalised tonic-clonic seizures or drop attacks associated with Lennox-Gastaut syndrome.

Topiramate is also indicated for the prophylaxis of migraine headache in adults.

New information

A precaution regarding visual field defects has been added to the Product Information (PI) for topiramate.

Visual field defects have been reported in patients being treated with topiramate independent of elevated intraocular pressure.

In clinical trials, most of these adverse events were reversible after topiramate was discontinued. However, some cases were not.

In a large proportion of postmarket reports, reversibility was unknown. In cases where an outcome was reported, most were reversible.

The TGA recommends that you advise patients and caregivers of this issue and educate them regarding the signs and symptoms of visual field defects. Instruct them to seek immediate medical attention if any problems are suspected.

If a patient receiving topiramate experiences visual problems, consider discontinuing treatment with this drug.

What to report? You don't need to be certain, just suspicious!

The TGA encourages the reporting of all **suspected** adverse reactions to medicines, including vaccines, over-the-counter medicines, and herbal, traditional or alternative remedies. We particularly request reports of:

- all suspected reactions to new medicines
- all suspected medicines interactions
- suspected reactions causing death, admission to hospital or prolongation of hospitalisation, increased investigations or treatment, or birth defects.

Reports may be submitted:

- **using the 'blue card'** available from the TGA website and with the October issue of *Australian Prescriber*
- **online** at www.tga.gov.au
- **by fax** to (02) 6232 8392
- **by email** to ADR.Reports@tga.gov.au

For more information about reporting, visit www.tga.gov.au or contact the TGA's Office of Product Review on 1800 044 114.

For the latest safety information from the TGA, subscribe to the TGA Safety Information email list via the TGA website

For correspondence or further information about Medicines Safety Update, contact the TGA's Office of Product Review at ADR.Reports@tga.gov.au or 1800 044 114

Medicines Safety Update is written by staff from the Office of Product Review