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Summary of the risk management plan (RMP) for Praxbind (idarucizumab)

This is a summary of the risk management plan (RMP) for Praxbind, which details the measures to be taken in order to ensure that Praxbind is used as safely as possible. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Praxbind, which can be found on Praxbind's EPAR page.

Overview of disease epidemiology

Praxbind (idarucizumab) is a medicine used to neutralise the effects of dabigatran (the active substance of Pradaxa) which is a medicine that prevents blood clots. Praxbind is used in emergency situations when the anticlotting effect of dabigatran needs to be stopped rapidly, before emergency surgery or in life-threatening bleeding.

In observational studies, it was found that Pradaxa when used for prevention of stroke in patients with atrial fibrillation (abnormal heart beat), major bleeding events were reported in 2.1 to 4.3 cases per 100 patient-years.

In the main study (RE-LY) on the effects of Pradaxa in patients with atrial fibrillation, life-threatening bleeding events occurred in 1.3 cases per 100 patient-years for Pradaxa 110 mg given twice daily and in 1.5 cases per 100 patient-years for Pradaxa 150 mg twice daily. In this study, Pradaxa had to be interrupted for emergency surgery or procedures in 1.5 cases per 100 patient-years in those taking Pradaxa 110 mg twice daily and in 1.8 cases per 100 patient-years in those taking Pradaxa 150 mg twice daily.

Summary of treatment benefits

The active substance in Praxbind, idarucizumab, is a monoclonal antibody (a type of protein) fragment that attaches firmly to dabigatran in Pradaxa and stops Pradaxa's anticlotting effect.

Praxbind has been investigated in three main studies involving 141 healthy adults who previously received dabigatran. In the studies, volunteers received either Praxbind or placebo (a dummy treatment) after receiving Pradaxa for 3.5 days. Results showed that Praxbind was able to completely neutralise Pradaxa's anticlotting effect within 5 minutes of use. The interim analysis of another trial showed similar results in 123 patients who had uncontrolled bleeding or required emergency surgery while using Pradaxa. Most patients in the study were taking Pradaxa to prevent stroke due to an abnormal heart beat (atrial fibrillation).

Unknowns relating to treatment benefits

Praxbind was not investigated in children (aged younger than 18 years), and in pregnant or breastfeeding women. Experience with re-treatment with Praxbind is limited.

Summary of safety concerns

Important identified risks

None identified.

Important potential risks

Risk	What is known
Production by the body's natural defences of antibodies against the active substance of Praxbind, idarucizumab (immunogenicity)	Like related medicines, the active substance in Praxbind, idarucizumab, may cause the immune system (the body's natural defence system) to produce antibodies (a protein that recognises Praxbind as 'foreign'). These antibodies could decrease the efficacy of Praxbind and they may increase the chance of side effects. Data on such antibodies were available for 47 patients from the clinical phase III trial. No adverse events that could have been caused by antibodies were observed in any of the patients.
Allergic reactions (hypersensitivity)	Idarucizumab is a monoclonal antibody fragment. Allergic reactions may occur with this type of medicine. So far, no allergic reactions have occurred in association with the use of Praxbind. No such adverse events were reported in the main clinical study.
Blood clotting events (thrombotic events)	Praxbind will be used emergency situations, in adults who are being treated with dabigatran to prevent blood clots. As Praxbind reverses dabigatran's anticlotting effect, use of Praxbind may once again make the patient prone to blood clotting.

Missing information

Risk	What is known
Children (paediatric patients)	Praxbind has not been studied in patients younger than 18 years.
Pregnancy and breastfeeding	Praxbind has not been studied in pregnant or breastfeeding women. Reproductive and developmental toxicity studies have not been performed, given the nature and the intended clinical use of the medicine. Praxbind may be used during pregnancy, if the clinical benefit outweighs the potential risks. It is unknown if Praxbind passes into the breast milk.
Re-exposure to Praxbind	Only limited information is available for patients who were given Praxbind again after they had developed anti-idarucizumab antibodies (re-exposure). The available data suggested that patients tolerated re-exposure to Praxbind well. Data on re-exposure in patients is available for 2 patients, both having received Praxbind twice. In both patients, the clotting times normalised and the bleeding stopped after the second 5-g dose, indicating the Praxbind was effective when used again.

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also

describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as 'routine risk minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Praxbind can be found on Praxbind's EPAR page.

This medicine has no additional risk minimisation measures.

Planned post-authorisation development plan

List of studies in post-authorisation development plan

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
Trial 1321.3 - A Phase III case series clinical study of the reversal of the anticoagulant effects of dabigatran by intravenous administration of 5.0 g idarucizumab in patients treated with dabigatran etexilate who have uncontrolled bleeding or require emergency surgery or procedures	To evaluate the reversal of the anticoagulant effects of dabigatran by intravenous administration of 5.0 g Praxbind in patients treated with dabigatran who have uncontrolled bleeding or require emergency surgery or procedures	Immunogenicity, hypersensitivity, thrombotic events	Started	Final report Q1 2017

Studies which are a condition of the marketing authorisation

The above study is not a condition of the marketing authorisation.

Summary of changes to the risk management plan over time

Not applicable.

This summary was last updated in 10-2015