Questions and answers on the outcome of extension of indication application for Exjade (deferasirox)

On 25 April 2013, the Committee for Medicinal Products for Human Use (CHMP) finalised its assessment of an application to modify the use of Exjade from second- to first-line treatment in patients aged six years and older with beta thalassemia major who receive infrequent blood transfusions. The CHMP did not consider the data submitted to be sufficient to recommend this change in the use of Exjade. However, the Committee concluded that new data relating to kidney function in patients treated with Exjade should be included in the product information.

What is Exjade?

Exjade is a medicine that contains the active substance deferasirox. It is available as dispersible tablets (125, 250 or 500 mg) that are mixed with a liquid to make a drinkable suspension. Exjade is used to treat chronic iron overload (an excess of iron in the body) in patients with certain blood conditions.

It is used as first-line treatment in patients aged six years and older with beta thalassaemia major (an inherited blood disorder where there is not enough haemoglobin in the blood) who receive frequent blood transfusions.

Exjade can also be used as second-line treatment, when deferoxamine (another medicine used to treat iron overload) cannot be used or is inadequate, in the following groups of patients:

- children aged two to five years with beta thalassaemia major who receive frequent blood transfusions;
- patients aged two years and older with beta thalassaemia major who receive infrequent blood transfusions;
- patients aged two years and older who suffer from different types of anaemia (low levels of haemoglobin in the blood) who receive blood transfusions;
• patients aged ten years and older with non-transfusion-dependent thalassaemia syndromes. Non-transfusion-dependent thalassaemia syndromes are blood disorders similar to beta thalassaemia major but which do not require blood transfusions. In these patients iron overload is caused by excess absorption of iron from the gut.

Because the number of patients with chronic iron overload is low, the disease is considered ‘rare’, and Exjade was designated an ‘orphan medicine’ (a medicine used in rare diseases) on 13 March 2002.

The medicine can only be obtained with a prescription.

**What was Exjade expected to be used for?**

Exjade was expected to be used as first-line instead of second-line treatment in patients aged six years and older with beta thalassaemia major who receive infrequent blood transfusions. This means that there would be no requirement to ensure that deferoxamine cannot be used or is inadequate before treating the patient with Exjade.

**What did the company present to support its application?**

The company presented an analysis of combined data from six separate studies involving patients with beta thalassaemia major, comparing the effects of Exjade in patients aged six years and older receiving infrequent blood transfusions with those receiving frequent blood transfusions. It also submitted a re-analysis of the results of the main study that originally supported the use of Exjade in patients receiving infrequent blood transfusions, in which Exjade was compared with deferoxamine. The analyses considered the medicine’s effect on levels of iron in the liver, blood levels of ferritin (a protein that stores iron) and the amount of iron excreted by the patients.

**What were the conclusions of the CHMP?**

The CHMP concluded that there were important weaknesses in the analyses submitted. The Committee considered that the analysis of combined data from six separate studies was undermined by important differences in the way the studies were designed and carried out, including how patients were selected and the treatments they received, which made the analysis unreliable. Similarly, there were methodological weaknesses in the re-analysis of data from the main study comparing Exjade with deferoxamine, including the small sub-group of patients analysed and the way patients were allotted to sub-groups to compare results. The CHMP did not consider that this approach could provide a reliable comparison of the two medicines’ benefits. Therefore, the CHMP concluded that the submitted analyses did not provide enough evidence to show that Exjade is at least as effective as deferoxamine in treating patients aged six years and older with beta thalassaemia major receiving infrequent blood transfusions, and decided that the benefits of Exjade as first-line treatment for these patients had not been demonstrated.

At the same time, the newly submitted data provided more information on the clearance of creatinine from the blood (a marker of kidney function) seen in patients during treatment with Exjade. Therefore, the CHMP recommended including the relevant data in the product information for Exjade.