25 July 2013
EMA/CHMP/455080/2013
Committee for Medicinal Products for Human Use (CHMP)

Summary of positive opinion[1] for Defitelio

International nonproprietary name (INN): defibrotide

On 25 July 2013, the Committee for Medicinal Products for Human Use (CHMP), following a re-examination procedure, adopted a final positive opinion, recommending to grant a marketing authorisation for the medicinal product Defitelio 80 mg/mL concentrate for solution for infusion intended for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell transplantation (HSCT) therapy. Defitelio was designated as an orphan medicinal product on 29 July 2004. The applicant for this medicinal product is Gentium SpA.

The active substance of Defitelio is defibrotide, a drug for the treatment of severe veno-occlusive disease (VOD) in patients undergoing haematopoietic (blood) stem-cell (B01AX01). The mechanism of action of defibrotide has not been fully elucidated.

The benefits with Defitelio are its effects of defibrotide which increase the breakdown of clots in the blood. In addition there is experimental evidence that Defibrotide may protect the cells lining blood vessels. The most common side effects are haemorrhage (including but not limited to gastrointestinal haemorrhage, pulmonary haemorrhage and epistaxis), hypotension and coagulopathy.

A pharmacovigilance plan for Defitelio, as for all medicinal products, will be implemented as part of the marketing authorisation.

The approved indication is: "*Defitelio is indicated for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell transplantation (HSCT) therapy".* It is indicated in adults and in adolescents, children and infants aged 1 month to 18 years." The recommended dose is 6.25 mg/kg body weight every 6 hours (25 mg/kg/day). There is limited efficacy and safety data on doses above this level and consequently it is not recommended to increase the dose above 25 mg/kg/day.

Defitelio should be administered for a minimum of 21 days and continued until the symptoms and signs of severe VOD resolve.

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued within 67 days from adoption of the opinion.

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It is proposed that Defitelio be prescribed by physicians experienced in the diagnosis and treatment of complications of HSCT.

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and will be available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers that there is a favourable benefit-to-risk balance for Defitelio and therefore recommends the granting of the marketing authorisation under exceptional circumstances[2].

[2] Marketing authorisation under exceptional circumstances refers to the fact that in exceptional circumstances an authorisation may be granted subject to certain specific obligations, to be reviewed annually.