6 September 2013
EMA/531101/2013

PRAC recommends suspension and reformulation for Numeta G13%E and risk minimisation measures for Numeta G16%E

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended suspending the marketing authorisation of the intravenous (into a vein) nutrition preparation Numeta G13%E because of a risk of hypermagnesaemia (high blood levels of magnesium). Numeta G13%E, which is given to premature babies to provide nutritional support, will remain suspended until a re-formulated preparation is made available.

For another intravenous nutrition preparation, Numeta G16%E, used in full-term newborns and children up to 2 years, the PRAC considered the benefit-risk balance to remain positive, provided that healthcare professionals monitor their patients' blood magnesium levels before giving the preparation and at appropriate intervals thereafter in accordance with routine clinical practice and the clinical needs of the individual patient. In patients whose blood magnesium levels are elevated or signs of hypermagnesaemia are identified Numeta G16%E should be stopped or the infusion rate reduced.

Numeta intravenous preparations are given to provide nutritional support in children who cannot be fed by mouth or with a feeding tube. They contain nutrients such as glucose (sugar), lipids (fats), aminoacids and other important substances including magnesium.

Hypermagnesaemia is a serious condition and symptoms may include weakness, nausea and vomiting, breathing difficulties and hypotension (low blood pressure).

The PRAC review was started following several reports of hypermagnesaemia (without clinical symptoms) in preterm infants. As a precautionary measure, the manufacturer decided to voluntarily recall Numeta G13%E in the EU. The PRAC has now assessed the available data on the risk of hypermagnesaemia with Numeta G13%E and Numeta G16%E preparations from clinical studies, post-marketing reports and the published literature and considered available treatment guidelines. Stakeholders were also invited to submit any relevant information to support the assessment, and the Agency's Paediatric Committee (PDCO) was consulted for advice.

Having considered available guidelines and relevant literature and considering the magnesium content of Numeta, the PRAC concluded that the administration of Numeta G13%E could lead to a higher risk of hypermagnesaemia. In addition, the PRAC noted that this risk is further increased in premature newborns because their kidneys are immature and less able to clear the body of magnesium. The PRAC

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7129
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

also noted the difficulty in identifying symptoms of hypermagnesaemia in premature newborns, which means that hypermagnesaemia may not be detected until it causes serious complications. While Numeta G13%E is suspended healthcare professionals should use alternative nutrition solutions which may include authorised standardised or individually prepared solutions.

For Numeta G16%E, the PRAC concluded that although the magnesium content may result in a magnesium intake that is slightly higher than suggested in some guidelines, the proposed measures, including updating the product information and a further study, are sufficient to ensure the safe use of this product. The product information should be revised accordingly and healthcare professionals should be informed in writing of the potential risk of hypermagnesaemia, which is increased in patients with impaired kidney function and those whose mothers were receiving supplemental magnesium before delivery, and of the measures to be taken to minimise this risk. In addition, the PRAC recommended a study be carried out to further evaluate blood magnesium levels observed in term newborn infants and children up to two years of age following use of Numeta G16%E.

The PRAC recommendation will be considered by the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) at its meeting of 16-18 September 2013.

More about the medicine

Numeta G13%E and Numeta G16%E (glucose, lipids, aminoacids and electrolytes) are parenteral nutrition solutions. Parenteral nutrition is the providing of nutrients and fluids through a vein in patients who cannot be fed by mouth or by enteral nutrition (the use of a feeding tube passed directly into the gut). Parenteral nutrition is necessary in premature neonates and in some full-term babies in order to prevent complications such as growth retardation and breathing complications and to promote the normal development of the brain.

Numeta G13%E and Numeta G16%E have been authorised since 2011 via national procedures in the following Member States: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Spain, Sweden, United Kingdom.

More about the procedure

The review of Numeta G13%E and Numeta G16%E was initiated on 13 June 2013 at the request of Sweden, under Article 107i of Directive 2001/83/EC, also known as the urgent Union procedure.

The review was conducted by the Pharmacovigilance Risk Assessment Committee (PRAC). As the review only covers nationally authorised medicines, the PRAC recommendation will now be forwarded to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position. The CMDh is a medicines regulatory body representing the EU Member States.

If the CMDh position is agreed by consensus, the agreement will be directly implemented by the Member States where the medicines are authorised. Should the CMDh position be adopted by majority vote, the CMDh position will be sent to the European Commission, for the adoption of an EU-wide legally binding decision.