LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

NOTIFICATION OF A REFERRAL UNDER ARTICLE 107i OF DIRECTIVE 2001/83/EC
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 107i of Directive 2001/83/EC to the PRAC made by Sweden – Medical Products Agency/MPA:

Product Name, Strength and Pharmaceutical Form	Numeta G13E (300 ml) Solutions for parenteral nutrition/combination ATC Code: B05 BA10
Marketing Authorisation Holder (MAH) in the referring member state	Baxter Medical AB

Background

Parenteral nutrition is the use of intravenous macronutrients, micronutrients and fluids to provide nutritional support in patients who cannot be fed by oral or enteral nutrition. Nutritional support in the preterm neonate is imperative in order to prevent morbidity, prevent growth retardation, promote positive nitrogen balance, reduce the incidence of respiratory distress syndrome and to promote neurocognitive development.

Numeta G13E (glucose, lipids, amino-acids and electrolytes) is an industrially manufactured, heat sterilized parenteral nutrition solution(300 ml container) which was specifically designed for preterm neonates, for whom oral or enteral nutrition is not possible, insufficient or contraindicated. It has a fixed content (per cc) of macronutrients and micronutrients including electrolytes.

Numeta G13E is licensed through EU Decentralized Procedure in Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Norway, Poland, Portugal, Spain, Sweden, United Kingdom, with Sweden being the Reference Member State. It is also registered nationally in Malta. It was first authorised in 2011.

On 10 June 2013, Sweden, Reference Member State for Numeta G13E, was informed by the MAH that, on the basis of safety concerns, Numeta G13E batches have been put on hold at the warehouse level. Further, the MAH also outlined a decision to enact a recall of the product from the market to prevent any potential harm to preterm neonates.

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Safety

The MAH has received spontaneous case reports of hypermagnesemia in preterm neonates who have been receiving Numeta G13E. Additionally, cases of hypermagnesemia were reported from a small investigator-initiated clinical trial. Adverse events were not reported in association with the hypermagnesemia cases. Clinical symptoms of hypermagnesemia can include generalized weakness, respiratory failure, hypotension, arrhythmias and altered mental status. Many of these symptoms can be present in preterm infants because of their early birth status and immature organ function. Therefore, it may be difficult to discern effects of hypermagnesemia from common clinical symptoms seen in the preterm infant.

The MAH suspects that the levels of magnesium in Numeta G13E can result in hypermagnesemia in the preterm neonate. On this basis, the MAH has decided to recall and reformulate Numeta G13E to reduce the levels of magnesium in the product.

Conclusions

Based on the information provided by the MAH, it is suggested that the levels of magnesium in Numeta G13E may in certain cases result in hypermagnesemia in preterm neonates. Given the uncertainty regarding the appropriateness of the levels of magnesium in Numeta G13E, and the clinical consequences of this, there is a need to undertake an in depth assessment of the benefit/risk balance for Numeta as currently formulated.

There is currently also uncertainty regarding the availability of adequate alternatives across the European Union Member States. Thus, there is urgency to undertake this review, to agree whether the benefit/risk balance remains positive, and if there is need for additional risk minimisation measures.

In view of the above, Sweden requests the PRAC to give a recommendation under the urgent union procedure, Article 107i of Directive 2001/83/EC, for Numeta G13E (300 ml).

Signed [redacted]

Date

2013-06-13

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Director General

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