Clinical Study Report: 7032-001

Title:	A Multicenter, Non-interventional, Uncontrolled, Open-label, Observational Study in Children (up to Age 24 Months) to Evaluate Serum Mg Levels Associated with the Intake of Numeta G 16% E
Study Number:	7032-001
Version identifier of the final study report	2017 OCT 31
Date of last version of the final study report	2017 OCT 31
EU PAS register number:	ENCEPP/SDPP/7113
Active substance	Alanine, arginine, aspartic acid, cysteine, glucose, glutamic acid, glycine, histidine, isoleucine, leucine, lysine monohydrate, methionine, ornithine hydrochloride, phenylalanine, proline, serine, taurine, threonine, tryptophan, tyrosine, valine, calcium chloride, magnesium acetate, potassium acetate, sodium chloride, sodium glycerophosphate, refined soybean oil, refined olive oil
Medicinal product	Numeta G 16% E
Product reference	SE/H/0918/02/DC
Procedure number:	SE/H/918
Marketing Authorization Holder (MAH)	Baxter Healthcare Corporation initiated, managed, and financed this study
Joint PASS	No
Research question and objectives	The primary objective of this study was to generate descriptive data for serum magnesium (Mg) levels in full-term, new born infants and children up to 24 months of age following dosing with Numeta G 16% E. The secondary objectives of this study were to observe the following parameters in subjects who receive parenteral nutrition (PN) with Numeta G 16% E: Actual infused Numeta G 16% E intake (mL/kg/day) Actual nutritional intake (total calories from oral, enteral, and parenteral sources other than Numeta) Adverse events (AEs) and serious adverse events (SAEs), including clinically significant (CS) abnormal laboratory results and CS abnormal vital signs
Countries of study	Belgium, France, Sweden

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1. ABSTRACT

Title: A Multicenter, Non-interventional, Uncontrolled, Open-label, Observational Study in Children (up to Age 24 Months) to Evaluate Serum Magnesium (Mg) Levels Associated with the Intake of Numeta G 16% E.

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Keywords:

Neonates, hypermagnesemia, parenteral nutrition, pediatric, Numeta

Rationale and background:

This non-interventional, observational study was undertaken to generate data to assess the impact of Numeta G 16% E on serum magnesium (Mg) levels in full-term, new born infants and children up to 24 months of age who require >70% parenteral nutrition (PN) at study entry and who are expected to require at least 50% PN for 5 days.

Research question and objectives:

The objective of this study was to generate descriptive data for serum Mg levels in full-term, new born infants and children up to 24 months of age following dosing with Numeta G 16% E.

Study design: This was a multicenter, non-interventional, uncontrolled, open-label, observational, safety study conducted in 11 study centers in 3 European countries (Belgium, France, and Sweden). Baseline serum Mg was obtained, as Standard of Care, prior to initiating Numeta G 16% E infusions. Subsequent Mg levels were obtained during routine/Standard of Care for serum electrolyte blood draws. In the event a serum Mg level was found to be outside the reference range for the study site, the Mg level could have been repeated at the discretion of the Investigator.

Setting: Target enrollment for this study was 100 children (full-term, new born infants and children up to age 24 months) who required >70% PN at study entry and who were

expected to require at least 50% PN for 5 days. Efforts were made to enrol an adequate distribution of infants in the age groups of 0 to 1 month and >1 month to 12 months as well as at least 20 subjects age >12 months to 2 years.

Subjects and study size, including dropouts

A total of 104 subjects were enrolled. There were a total of 15 subjects who were discontinued or dropped out once the study had started and there were 2 subjects who had screen failures. In total, 102 subjects were analyzed; 81 subjects in the 0 – 1 year bracket, and 21 patients in the 1 – 2 years bracket. Eleven sites participated in this study throughout Belgium, France, and Sweden. Only study centers that routinely collect Mg blood levels as Standard of Care participated in this study.

Variables and data sources:

The key safety variables collected for analysis included:

- Serum Mg levels during the study
- Numeta dosing information (actual)
- Nutritional intake (actual)
- Adverse Event (AE) assessment
- Reason for end of study participation

Data was collected from the medical records of the enrolled subjects and from observation of the subjects during the study.

Results:

The treatment with Numeta G 16% E was well tolerated across all subject age groups in the study including neonates and children up to 2 years of age. Throughout the study there were a total of 92 reported AEs in 49 subjects (48.0%). Thirty subjects (30; 29.4%) experienced AEs classified as mild, 11 subjects (10.8%) experienced moderate AEs, and 8 (7.8%) experienced severe AEs. Seven (7; 6.9%) subjects reported 9 Serious Adverse Events (SAEs), none of which were related to Numeta G 16% E. Three subjects (3; 2.9%) experienced mild SAEs, 2 subjects (2.0%) experienced moderate SAEs, and 2 subjects (2.0%) experienced severe SAEs. There were 16 AEs in 12 subjects (11.8%) which were reported as being related to Numeta G 16% E. None of these study product-related AEs were serious. Of the 12 subjects who reported product-related AEs, 10 subjects (9.8%)

experienced mild AEs, 2 subjects (2.0%) experienced moderate AEs, and no subjects (0.0%) experienced severe product-related AEs. Among the 16 study product-related AEs there were 4 reports of hypermagnesaemia occurring in 4 patients with 3 of these cases being mild and 1 being moderate in severity. The age of the subjects who experienced hypermagnesemia ranged from [redacted] days to [redacted] days, and the average age was 12 days. Serum Mg levels in these hypermagnesaemia cases ranged from 0.99 mmol/L to 1.27 mmol/L.

Discussion:

In this study involving 102 neonates and infants on Numeta G 16% E there were 4 case reports of hypermagnesemia occurring in 4 subjects; 3 of these events were mild and 1 was moderate in severity. Average age of these 4 infants was 12 days. In conclusion, the safety data in this study suggest that Numeta G 16% E provided a safe and well tolerated treatment PN regimen for neonates and children up to 2 years of age.