Direct Healthcare Professional Communication

23rd September 2019

Parenteral nutrition products: light protection required to reduce the risk of serious adverse effects in premature neonates

Dear Healthcare professional,

The marketing authorization holders of parenteral nutrition products containing amino acids and/or lipids, indicated for use in neonates and in children below 2 years, in agreement with the Health Products Regulatory Authority (HPRA) and the European Medicines Agency, would like to inform you of the following new safety information:

Summary

- **During administration to neonates and children below 2 years of age, parenteral nutrition products containing amino acids and/or lipids, should be protected from light (containers and administration sets).**
- **Use of light-exposed parenteral nutrition products containing amino acids and/or lipids, particularly in admixtures with vitamins and/or trace elements, may lead to severe adverse effects in premature neonates. This is because exposure of such solutions to light causes formation of peroxides and other degradation products.**
- **Premature neonates are considered at high risk of oxidative stress related to multiple risk factors including oxygen therapy, phototherapy, weak immune system and inflammatory response with reduced oxidant defence.**

Affected Product Details

Company	Product Name	License Number
Baxter Healthcare Ltd	Numeta G13%E Preterm Emulsion for infusion	PA2299/030/003
	Numeta G16%E Emulsion for infusion	PA2299/030/001
	Primene 10%	PA 2299/018/001
	Clinimix	PA 2299/020/001
Fresenius Kabi	SMOFlipid 200 mg/ml emulsion for infusion	PA 2059/062/001 PA 2059/062/002
	Vaminolact solution for infusion	PA 2059/065/001 PA 2059/065/002
	Intralipid 10% emulsion for infusion	PA 2059/041/004
	Intralipid 20% emulsion for infusion, Glass bottle	PA 2059/041/001
	Intralipid 20% emulsion for infusion	PA 2059/041/005

Background on the safety concern

Parenteral nutrition (PN) is indicated for use in pre-term and term neonates when oral or enteral nutrition is not possible, insufficient or contraindicated.

Laboratory and clinical studies have shown that exposure of PN products to light causes the formation of peroxides and other degradation products that are quantifiable in experimental PN solutions, in animals, and in neonates. PN containing vitamins and/or lipids may be most susceptible. Ambient and environmental light and especially phototherapy contribute to generation of peroxides.

Data in support of this effect from light exposure include studies showing that the formation of PN photodegradation products can be slowed down or prevented by the application of various light protection measures. A meta-analysis of four randomised controlled trials suggests a reduced mortality at 36 weeks´ gestational age when light protection is in place (Chessex et al, 2017).

The clinical relevance of light protection of PN products is especially notable in premature infants with high nutritional requirements and slow intravenous infusion rates. Several conditions related to prematurity with insufficient anti-oxidative capacity are thought to be risk factors for the underlying pathological mechanism related to generation of peroxides. Very premature neonates are considered at high risk of oxidative stress related to multiple risk factors including oxygen therapy, weak immune system and inflammatory response with reduced oxidant defence and exposure to high energy light

(phototherapy). While data on harm primarily concerns premature neonates, light protection should be provided for such products also in neonates and in children below 2 years as a precautionary measure.

Light protection of PN products is recommended in paediatric PN guidelines by the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), including coverage of both the container and administration sets.

The product information (Summary of Product Characteristics, Package Leaflet and Labelling) for the concerned products is being updated accordingly.

Call for reporting

Healthcare professionals should report suspected adverse drug reactions (ADRs) in neonates and children below 2 years of age treated with PN products in accordance with the national spontaneous reporting system:

HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2;
Tel: +353 1 6764971;
Fax: +353 1 6762517.
Website: www.hpra.ie;
Email: medsafety@hpra.ie.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset dates, treatment dates, product brand name and batch numbers.

Suspected adverse reactions should also be reported to:

Baxter Healthcare Ltd, on tel: +44 (0) 1635 206 360, or by email at vigilanceuk@baxter.com

Fresenius Kabi, on tel: +44 (0) 1928 533 575, or by email at Pharmacovigilance.GB@Fresenius-kabi.com.

Company contact point of the Marketing Authorisation Holders

Company	**Medical Information contact details**
Baxter Healthcare Ltd	Telephone: +44 (0)1635 206130 Email: medinfo_uki@baxter.com
Fresenius Kabi	Email: Pharmacovigilance.GB@Fresenius-kabi.com Telephone: +44 (0) 1928 533 575

Signed for Baxter Healthcare and on behalf of Fresenius Kabi

Gerard Spicer

Country QA Manager UK and Ireland

Literature references

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