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Direct Healthcare Professional Communication (DHPC)

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

Dear Healthcare professional,

Baxter Healthcare Limited, Baxter Holding B.V., Central Procurement and Supplies Unit, Fresenius Kabi Italia S.r.l., in agreement with the European Medicines Agency and Malta Medicines Authority, 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.**

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 randomized 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 pediatric 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.

Literature references

Chessex P, Laborie S, Nasef N, Masse B, Lavoie JC. Shielding Parenteral Nutrition From Light Improves Survival Rate in Premature Infants. JPEN J Parenter Enteral Nutr. 2017;41(3):378-383.

Puntis J, Hojsak I, Ksiazyk J, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Organisational aspects. Clin Nutr. 2018;37(6 Pt B):2392-2400.

Lapillonne A, Fidler Mis N, Goulet O, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids. Clin Nutr. 2018;37(6 Pt B):2324-2336.

Hill S, Ksiazyk J, Prell C, Tabbers M, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Home parenteral nutrition. Clin Nutr. 2018;37(6 Pt B):2401-2408.

Hartman C, Shamir R, Simchowitz V, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Complications. Clin Nutr. 2018;37(6 Pt B):2418-2429.

Domellöf M, Szitanyi P, Simchowitz V, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Iron and trace minerals. Clinical Nutrition. 2018;37(6):2354-2359.

Bronsky J, Campoy C, Braegger C, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Vitamins. Clin Nutr. 2018;37(6 Pt B):2366-2378.

Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are reminded to continue to report suspected adverse reactions associated with parenteral nutrition products in accordance with the national spontaneous reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Post-licensing directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta or sent by email to postlicensing.medicinesauthority@gov.mt

Company contact point

Should you have any questions or require additional information, please call Medical Information at:

Company	Product Name	Email	Phone
Baxter Healthcare Limited	ClinOleic 20% Numeta G16%E Emulsion for infusion	safety@drugsalesltd.com	+356 21419070/1/2
Baxter Holding B.V.	Numeta G13%E Preterm Emulsion for Infusion G13E		
Central Procurement and Supplies Unit	SMOFlipid Emulsion for Infusion 200mg/ml	richard.despott@gov.mt	+356 23439150
Fresenius Kabi Italia S.r.l.	Intralipid 20% Lipid Emulsion for intravenous infusion Vamin 18 Electrolyte-Free Solution for Infusion	paola.ragazzo@fresenius-kabi.com	T: +39 045 6649402 M: +39 3489710480

Yours faithfully,

Post-Licensing Directorate

Medicines Authority

Disclaimer

This Direct Healthcare Professional Communication has been submitted to you on behalf of Baxter Healthcare Limited, Baxter Holding B.V., Central Procurement and Supplies Unit, Fresenius Kabi Italia S.r.l.