

## **Direct Healthcare Professional Communication**

02/SEP/2019

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

Dear Healthcare Professional,

The marketing authorisation 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 Medicines and Healthcare Products Regulatory Agency (MHRA) and the European Medicines Agency (EMA), 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 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.

It is easiest and quickest to report adverse drug reactions online via the Yellow Card website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary), by emailing [yellowcard@mhra.gov.uk](mailto:yellowcard@mhra.gov.uk), at the back of the British National Formulary (BNF), by telephoning the Commission on Human Medicines (CHM) free phone line: 0800 731 6789, or by downloading and printing a form from the Yellow Card section of the MHRA website.

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: 01635 206 360, or by email at [vigilanceuk@baxter.com](mailto:vigilanceuk@baxter.com)

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

B Braun Medical Ltd, on tel: 0114 225 9155, or by e-mail at [productcomplaints.bbmun@bbraun.com](mailto:productcomplaints.bbmun@bbraun.com)

### ***Company contact point of the Marketing Authorisation Holders***

<b>Company</b>	<b>Medical Information contact details</b>
Baxter Healthcare Ltd	Telephone: 01635 206130 Email: <a href="mailto:medinfo_uki@baxter.com">medinfo_uki@baxter.com</a>
Fresenius Kabi	Email: <a href="mailto:medical.information-uk@fresenius-kabi.com">medical.information-uk@fresenius-kabi.com</a> Telephone: 01928 533 575
B Braun Medical Ltd	Email: <a href="mailto:medinfo.bbmun@bbraun.com">medinfo.bbmun@bbraun.com</a> Telephone: 0800 298 0299

### ***Literature references***

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