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DATA SHEET

Sodium DL-3-Hydroxybutyrate Powder, 50g

Product Code
H03 and H03-ROW.

Active Ingredient
Sodium DL-3-hydroxybutyrate.

Description of Product
Sodium DL-3-hydroxybutyrate is a racemic mixture therefore contains equal amounts of both left and right-handed enantiomers. The product is supplied as a pure hygroscopic white to off-white crystalline powder.

Presentation
The product is supplied in a labeled white polypropylene container with a low density polyethene (LDPE) tamper evident closure containing 50g of free-flowing powder.

Storage
Store below 25°C in a dry place.

Shelf Life
23 months.

Excipients of Known Effect
This product is supplied as a pure powder containing no additional excipients.

Free-From Information
This product is supplied as a pure powder containing no additional excipients.

Therapeutic Indication
Multiple acyl-CoA dehydrogenase deficiency (MADD).[1]

Sodium DL-3-hydroxybutyrate is a naturally occurring ketone in the body. It is used as an energy source for the brain and muscles. Patients that have multiple acyl-CoA dehydrogenase deficiency (MADD) cannot produce DL-3-hydroxybutyrate.

MADD is a genetic defect of the electron transfer flavoprotein (ETF) chain causing dysfunction of dehydrogenases linked to flavin adenine dinucleotide (FAD), including those of fatty acid β oxidation.

The clinical presentation varies widely. Neonates with a severe deficiency sometimes die in infancy with malformations and severe metabolic decompensations. Patients who first present as infants and children have a less severe enzyme deficiency. They present with a milder metabolic decompensation and exhibit hepatic dysfunction, myopathy, and cardiomyopathy.

Since fats cannot provide a source of energy, due to the enzyme deficiency, patients lack energy and can suffer spastic quadriplegia and cardiomyopathy.

Dosage
Treatment with Sodium Hydroxybutyrate should be initiated under expert supervision.
For the management of MADD, the recommended dose is 80-900 mg/kg/day in three divided doses (4 hourly)[1] Start at the lower dose and increase to obtain measurable concentrations of physiological ketone bodies (sum of DL-3-hydroxybutyrate and acetoacetate) at all times. Higher doses to 2600 mg/kg/day have also been reported in literature in cases where patients do not respond to the maximum recommended 900 mg/kg/day.[2] This higher dose should be considered with caution, as it is associated with a sodium supplementation of 20 mmol/kg per day.[2] These high doses inevitably impair fluid and sodium homeostasis with potential secondary cardiovascular and cerebral effects.[2]

Administration
This product is a pure powder intended to be used as an ingredient for oral extemporaneous preparations. The product may be divided into individual powders which can be weighed into individual tablet bottles and dispensed to the patient. The individual powders can be mixed with water and taken orally or via a gastrostomy tube. Alternatively, the powder could be sprinkled onto cold food and consumed immediately.

Contraindications and Precautions
The high sodium intake limits the maximum dose.

Side-effects and Adverse Reactions
No side-effects were reported.[1]

Mode of Action
DL-3-hydroxybutyrate is a ketone body that can cross the blood/brain barrier and provide an alternative energy source for the brain. It also provides an energy source for the heart, kidney and muscle. This results in the return of mobility.[1]

Pharmacokinetics
Plasma concentration of Sodium DL-3-Hydroxybutyrate peaks (C_{max}) 30-60 minutes after administration via a gastrostomy tube.[1]
Free fatty acids decreased by up to 75% 1 hour after administration, returning to pretreatment concentrations after 3 hours. This suggests that the product should be administered every 3-4 hours.

Interactions with other Medications
No information available.

Pregnancy and Breastfeeding
No information available.

Legal Category
Sodium DL-3-Hydroxybutyrate Powder is an ‘Unlicensed Medicine’ within the meaning of the current legislation, governed by the Human Medicines Regulations 2012.

This publication is solely for the technical guidance of prescribers and dispensers of Sodium DL 3-Hydroxybutyrate Powder and must not be considered as a recommendation or endorsement for the clinical use of the product. The information provided in this publication may not be exhaustive or reflective of all the information in the public domain.

Transmissible Spongiform Encephalopathies
All starting materials are certified as compliant with EMA/410/01 rev.3 (S.I. 2003/1680) for minimising the risk of BSE/TSE contamination.

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Reference:

1. Van Hove J: K et al., DL-3-hydroxybutyrate treatment of multiple acyl-CoA dehydrogenase deficiency (MADD); *The Lancet*; 2003; 361; 1433-1435 available via: https://www.ncbi.nlm.nih.gov/pubmed/12727399
2. Van Rijt WJ, Heiner-Fokkema MR, du Marchie Sarvaas GJ, et al., Favorable Outcome After Physiologic Dose of Sodium-d, l-3-Hydroxybutyrate in Severe MADD; *Pediatrics Oct 2014*, 134 (4) e1224-e1228; DOI: 10.1542/peds.2013-4254 Available via: https://www.ncbi.nlm.nih.gov/pubmed/25246622