SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Zincfant® 20mg*

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 54.9 mg zinc sulfate monohydrate equivalent to 20 mg of zinc.
Each tablet contains 46.435 mg of aspartame. For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Round, ivory-white uncoated, dispersible tablets, flat on one side and with a score on the other side. The tablet can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

Zincfant® 20mg Tablet is indicated for the treatment of acute and persistent diarrhoea in infants and children up to 5 years of age.

This product is intended for use in children. Nonetheless, safety information is provided with respect to adult health issues such as liver disease, pregnancy and lactation, to allow full access to all relevant information.

4.2 Posology and method of administration

For acute and persistent diarrhoea

For children less than 6 months of age: ½ tablet once daily for 10-14 days.
For children 6 months of age to 5 years of age: 1 tablet once daily for 10-14 days.

The tablet (or half tablet) should be dispersed completely in 1 teaspoon (5 ml) of clean water or breast milk and the entire amount administered orally to the infant or child.

It is recommended that doses be administered between meals and a repeat dose be given if vomiting occurs within 30 minutes.

For missed doses, the missing dose can be taken as soon as possible, unless there is less than 6 hours until the next dose.

4.3 Contraindications

Not applicable

* Trade names are not prequalified by WHO. This is under local drug regulatory authority's responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

4.4 Special warnings and precautions for use

Drugs which may inhibit zinc absorption, such as penicillamine, sodium valproate and ethambutol, should not be coadministred with Zincfant® 20mg Tablets, unless the risks of discontinuation of the drug are judged to outweigh the benefit of zinc in treatment of the child's diarrhoea.

Excipients
Zincfant® 20mg Tablets contain aspartame, a source of phenylalanine. This should be considered when prescribing the product to patients with phenylketonuria.

4.5 Interactions with other medicinal products and other forms of interaction

Antibiotics
When taken together, zinc may reduce the absorption of tetracyclines (but not doxycycline), and quinolone antibiotics. In addition, zinc may also interfere with the absorption of cephalexin or ceftibuten. An interval of at least three hours should be allowed between administration of zinc and any of these medicines.

4.6 Pregnancy and lactation

Pregnancy
The safety of Zincfant® 20mg Tablet in pregnancy has not been established.

Lactation
Zinc crosses the placenta and is present in breast milk. The safety of Zincfant® 20mg Tablet in lactation has not been established.

4.7 Effects on ability to drive and use of machines

There is no evidence regarding the effect of zinc on the ability to drive or use machines, however Zincfant® 20mg Tablet is not expected to have any effect on the ability to drive and use machines.

4.8 Undesirable effects

In clinical trials in children, administration of Zincfant® 20mg Tablets was associated with vomiting or regurgitation. In one study vomiting attributed to the tablet was reported very commonly (≥ 10%), i.e. in 14% and regurgitation was reported commonly (≥ 1% to <10%), i.e. in 5.2% of the children, respectively. In most cases vomiting or regurgitation occurred shortly after administration of the first dose (within 10 minutes) and was not recurrent. Zinc salts may also cause abdominal pain and dyspepsia (frequency unknown).

4.9 Overdose

Symptoms
High doses of zinc cause emesis. In addition, zinc sulfate is corrosive at high doses, and may cause irritation and corrosion of the gastrointestinal tract, including ulceration of the stomach and possible perforation. Overdosage with zinc has also been associated with acute renal tubular necrosis and interstitial nephritis. Prolonged high dose zinc supplementation may result in copper deficiency.

Treatment
In cases of acute zinc overdose, treatment is primarily supportive, however induced emesis, gastric lavage, or activated charcoal may be useful in cases of substantial ingestions of zinc tablets. Chelating agents such as calcium disodium EDTA may be useful.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other mineral supplements, ATC code: A12CB01

Zinc sulfate is a zinc salt used for the treatment of acute and persistent diarrhoea in children.

Zinc is an essential trace element which is present in a wide range of foods. It is found in all tissues.

Normal growth and tissue repair depend upon adequate zinc levels. Zinc acts as an integral part of several enzymes important to protein and carbohydrate metabolism. . Severe zinc deficiency is associated with growth retardation, primary hypogonadism, skin disease, disturbances of taste and smell, and impaired immunity, with increased susceptibility to infection.

Zinc supplementation has been shown to reduce the duration and severity of diarrhea in populations of children with a high incidence of zinc deficiency, and also to reduce the frequency of recurrences in the subsequent 2-3 months. The beneficial effects of zinc are likely associated with reconstitution of the immune response, however direct inhibitory effects of zinc on enteric pathogens have also been reported.

5.2 Pharmacokinetic properties

Absorption
Zinc is incompletely absorbed from the small bowel, with between 10 and 40% of an ingested dose absorbed. Numerous dietary components can interfere with zinc absorption, particularly phytates and fibre, which bind to zinc, resulting in poorly absorbed zinc complexes.
The absorption of zinc from ZinCfant® tablets was examined in 10 healthy, zinc replete, adult male volunteers (baseline mean plasma zinc level ±SD of 15.1 ±3.5 mmol/L). Absorption of zinc from 1½ ZinCfant® tablets (i.e. a 30 mg dose) was rapid, with a maximal increase in mean plasma zinc level (±SD) of 11.6 (±6.0) mmol/L observed within approximately 2 hours of administration.

Distribution
Approximately 60% of circulating zinc is bound to albumin and roughly 30% is bound to macroglobulin. The majority of zinc is stored in the liver and kidney, chiefly intracellularly,and bound to metalloproteins.

Elimination
In adults, it has been estimated that approximately 0.5 to 1.0 mg/day is secreted in the biliary tract and excreted in the stool, while 0.5 to 0.8 mg/day is excreted in the urine.

5.3 Preclinical safety data

Non-clinical data have not revealed significant hazards for humans, based on standard studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and reproductive toxicity. Effects in non-clinical studies were observed only at exposures sufficiently in excess of the maximum human exposure to be of little clinical relevance.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Aspartame
colloidal anhydrous silica
ethyl vanillin
magnesium stearate
maize starch
microcrystalline cellulose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C, protect from moisture.

6.5 Nature and contents of container

White PVC/PVDC-aluminium foil blister with green ink printing.
Each blister strip contains 10 tablets, and 10 of such strips are packed in a packet.

6.6 Special precautions for disposal

No special requirements.

7. SUPPLIER

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8. WHO REFERENCE NUMBER (PREQUALIFICATION PROGRAMME)

DI002

9. DATE OF FIRST PREQUALIFICATION

December 2012

10. DATE OF REVISION OF THE TEXT

February 2013

Reference list:

General

Dietary Supplement Fact Sheet: Zinc. National Institutes of Health (US): http://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/

Posology

The Treatment of Diarrhoea. A manual for physicians and other senior health workers, WHO 2005:

http://whqlibdoc.who.int/publications/2005/9241593180.pdf

Clinical Management of Acute Diarrhoea. WHO/UNICEF Joint Statement, 2004:

http://whqlibdoc.who.int/hq/2004/WHO_FCH_CAH_04.7.pdf

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Overdose

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Clinical Environmental Health and Toxic Exposures. 2nd edition. Sullivan JB, Krieger GR (eds.). 1999. p 904.

Pharmacokinetics

Krebs NF. Overview of Zinc Absorption and Excretion in the Human Gastrointestinal Tract. *J Nutr.* 2000;130: 1374S-1377S