WHO-PQ RECOMMENDED SUMMARY OF PRODUCT CHARACTERISTICS

This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.[*]

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

[*]https://extranet.who.int/prequal/sites/default/files/document_files/75%20SRA%20clarification_Feb2017_newtempl.pdf

1. NAME OF THE MEDICINAL PRODUCT

[DI011 trade name]†

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dispersible tablet contains 54.9 mg zinc sulfate monohydrate equivalent to 20 mg of zinc.

Excipients with potential clinical effect

Each dispersible tablet also contains 46.43 mg of aspartame. For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersible tablets

[DI011 trade name] is white to off-white, round, uncoated, dispersible tablet. They are flat on the top and bottom with a bevelled edge. The tablets have 'C70' debossed (stamped into) one side and a break line on the other side. The break line can be used to divide [DI011 trade name] into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[DI011 trade name] is indicated for the treatment of acute watery or persistent diarrhoea in children up to 10 years of age.

4.2 Posology and method of administration

Posology

Children aged less than 10 years: 5 mg once daily for 10 – 14 days.

Missed dose and vomiting after a dose

The child should be given a missed dose as soon as possible, unless the next dose is due within 6 hours. If the child vomits within 30 minutes of taking [DI011 trade name], the dose should be repeated.

Method of administration

Oral use.

[DI011 trade name] should be given between meals.

The tablets should be dispersed in drinking water before administration of the dose (see section 6.6). Each tablet should be dispersed in a minimum of 10 mL water; the maximum volume of water recommended for dispersion of a dose is 50 mL.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Copper deficiency (see section 4.5).

† Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

4.4 Special warnings and precautions for use

Accumulation of zinc may occur in cases of renal failure.

Excipients

[DI011 trade name] contains aspartame. Aspartame is hydrolysed in the gastrointestinal tract when orally ingested. One of the major hydrolysis products is phenylalanine. It may be harmful if the patient has phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

Neither non-clinical nor clinical data are available to assess aspartame use in infants below 12 weeks of age.

It is important to consider the contribution of excipients from all the medicines that the patient is taking.

4.5 Interaction with other medicinal products and other forms of interaction

Antibacterials:

When taken together, zinc may reduce the absorption of tetracyclines (but not doxycycline) and quinolone antibacterials. In addition, zinc may also interfere with the absorption of cephalexin or ceftibuten. An interval of at least 3 hours should be allowed between administration of zinc and any of these medicines.

Medicines that reduce the absorption of zinc such as pencillamine should not be taken together with [DI011 trade name]. An interval of at least 3 hours should be allowed between administation of zinc and medicines such as penicillamine.

Copper:
Zinc may inhibit the absorption of copper (see section 4.3).

Calcium salts:
The absorption of zinc may be reduced by calcium salts.

Iron:
The absorption of zinc may be reduced by oral iron, also the absorption of oral iron may be reduced by zinc.

Trientine:
The absorption of zinc may be reduced by trientine, also the absorption of trientine may be reduced by zinc.

4.6 Fertility, pregnancy and breastfeeding

Pregnancy
There are limited data on the use of zinc sulfate in pregnant women.
Animal studies do not indicate reproductive toxicity at the human therapeutic dose (see section 5.3).

Breastfeeding
Zinc is present in breast milk.

Fertility
No data on the effect of zinc on fertility are available.

4.7 Effects on ability to drive and use machines

[DI011 trade name] is unlikely to affect the ability to drive or operate machinery.

However, patients should be advised to consider if their clinical status, including any undesirable effects of the medicine, allows them to perform skilled tasks safely.

4.8 Undesirable effects

Gastrointestinal disorders
In clinical trials in children, administration of zinc tablets was associated with vomiting or regurgitation. In one study, vomiting within 30 minutes after administration occurred in 19.3%, 15.6%, and 13.7% of the patients in the 20-mg, 10-mg, and 5-mg groups, respectively; the risk was significantly lower in the 10-mg group than in the 20-mg group (relative risk, 0.81; 97.5% CI, 0.67 to 0.96) and in the 5-mg group than in the 20-mg group (relative risk, 0.71; 97.5% CI, 0.59 to 0.86). Lower doses were also associated with less vomiting beyond 30 minutes after administration.

Copper malabsorption
Zinc may interfere with the absorption of copper, leading to reduced copper levels, and potentially copper deficiency. The risk of copper deficiency may be greater with long-term treatment and/or with higher doses of zinc.

The adverse reactions considered related to zinc sulfate are listed below by body system, organ class and absolute frequency. Frequencies are defined as very common (at least 1 in 10), common (1 in 100 to 1 in 10) uncommon (1 in 1000 to 1 in 100), rare (1 in 10 000 to 1 in 1000), very rare (less than 1 in 10 000) or not known (frequency cannot be estimated from available data).

Nervous system disorders

Frequency not known	headache

Gastrointestinal disorders

Very common	vomiting
Common	regurgitation
Frequency not known	abdominal pain, dyspepsia, nausea, gastric irritation and gastritis

General disorders

Frequency not known	irritability, lethargy

Reporting of suspected adverse reactions

Health care providers are asked to report adverse reactions that may be linked to a medicine, to the marketing authorisation holder, or, if available, to the national reporting system. Reports of suspected adverse reactions to a medicine are important for the monitoring of the medicine's benefits and risks.

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. Overdose 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
For acute zinc overdose, treatment is primarily supportive, but giving milk or alkali carbonates and activated charcoal may be useful in cases of substantial ingestions of zinc tablets. Chelating agents such as sodium calcium edetate may be useful.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other mineral supplements, ATC code: A12CB01.

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

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

Normal growth and tissue repair depend on adequate zinc levels. Zinc is an integral part of several enzymes important for 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 diarrhoea in populations of children with a high incidence of zinc deficiency, and also to reduce the frequency of recurrence in the subsequent 2–3 months. The benefits of zinc are possibly associated with reconstitution of the immune response. Direct inhibitory effects of zinc on enteric pathogens have also been reported.

5.2 Pharmacokinetic properties

Absorption of [DI011 trade name]

Pharmacokinetic data are not available for [DI011 trade name]. No bioequivalence study has been performed. [DI011 trade name] meets the criteria for a biowaiver in accordance with the WHO guidance and criteria for zinc sulfate tablets.

Pharmacokinetics of zinc sulfate

Absorption	
Oral bioavailability	10-40%
Food effect	Numerous dietary components can interfere with zinc absorption, particularly phytates and fibre, which bind to zinc, resulting in poorly absorbed zinc complexes.
Distribution	
Volume of distribution (mean)	NA*
Plasma protein binding	80% of serum zinc bound to albumin and the remainder to alpha2-macroglobulin and amino acids.
Tissue distribution	Zinc is distributed throughout the body. 85% of total body zinc is found in skeletal muscle and bone. The highest concentrations occur in hair, eyes, male reproductive organs and bone. Lower levels are present in liver, kidney and muscle. In blood, zinc is mainly localized within erythrocytes.
Metabolism	
	Not applicable
Elimination	
General note	Primarily excreted via the gastrointestinal tract and eliminated in the faeces. A smaller amount of zinc is excreted via the kidneys in the urine.
Elimination half life	NA*
Mean systemic clearance (Cl/F)	NA*
% of dose excreted in urine	NA*
% of dose excreted in faeces	NA*

*Information not available

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

Microcrystalline cellulose

Crospovidone

Aspartame

Sucralose

Orange flavour

Colloidal silicon dioxide

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

PVdC/PVC-Alu blister
48 months

Alu-Alu blister
48 months

6.4 Special precautions for storage

Do not store above 30ºC. Protect from moisture.

6.5 Nature and contents of container

Blister
[DI011 trade name] is provided in PVdC/PVC-Alu blister cards, each containing 10 tablets. Such 1, 3 or 10 blisters are packed in a carton along with the patient information leaflet.

Strip
[DI011 trade name] is provided in Alu-Alu blister, each containing 10 tablets. Such 1, 3 or 10 blisters are packed in a carton along with the patient information leaflet.

6.6 Special precautions for disposal and other handling

Preparation and administration - extemporaneous formulation

You will need:

- 1 tablet of [DI011 trade name]
- drinking water/breast milk
- a 10-mL oral syringe
- a container such as a bowl or a cup

1. Use the oral syringe to measure 10 mL drinking water or break milk into the container
2. Add 1 tablet of [DI011 trade name] and stir gently until the tablet disperse completely
3. Use the oral syringe to give the 2.5 mL of the mixture
4. Throw away any mixture remaining in the container

Repeat these steps every time you need to give the medicine

7. SUPPLIER

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8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

DI011

9. DATE OF PREQUALIFICATION

25 May 2020

10. DATE OF REVISION OF THE TEXT

July 2025

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Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products