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

[DI010 trade name]†

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL oral solution contains 27.45 mg zinc sulfate monohydrate equivalent to 10 mg of elemental zinc.

Excipients with potential clinical effect

Each 5 mL oral solution contains 3 mg of aspartame, 10 mg of sodium benzoate, 3.8 g of sorbitol.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution

A clear transparent, orange- flavoured solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[DI010 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 6 months: 10 mg (5 mL of syrup) once daily for 10–14 days.
Children aged 6 months–5 years: 20 mg (10 mL of syrup) once daily for 10–14 days.

It is recommended that doses are given between meals and the dose repeated if the child vomits within 30 minutes.

For missed doses, the missing dose can be taken as soon as possible, unless the next dose is due within 6 hours.

Method of administration

Oral use.

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).

4.4 Special warnings and precautions for use

Accumulation of zinc may occur in cases of renal failure.

Excipients

[DI010 trade name] contains 3 mg aspartame in each 5 mL. Aspartame is a source of 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.

[DI010 trade name] contains 10 mg sodium benzoate in each 5 mL which may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

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

[DI010 trade name] contains 3.8 g sorbitol in each 5 mL. Sorbitol is a source of fructose. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

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 [DI010 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).

Breast-feeding

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

Not applicable

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 [DI010 trade name]

Pharmacokinetic data are not available for [DI010 trade name]. No bioequivalence study has been performed. [DI010 trade name] meets the criteria for a biowaiver in accordance with the WHO guidance and criteria for zinc formulations.

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

Sodium benzoate

Sorbitol solution

Citric acid anhydrous

Sodium citrate

Aspartame

Sodium saccharin

Orange trusil flavour

Purified water

This medicine is essentially 'sodium-free'. It contains less than 1 mmol sodium (23 mg) per 5 mL.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

In-use period:

Discard the product 28 days after initial opening

6.4 Special precautions for storage

Store below 30°C. Protect from light.

Discard the product 28 days after initial opening.

6.5 Nature and contents of container

Round, amber type III glass bottle containing 60 mL of solution. The bottle is fitted with a plastic (LDPE) U-plug and closed with an aluminium cap. The product is supplied with a plastic (HDPE) graduated measuring spoon. Each bottle is packed in a carton.

6.6 Special precautions for disposal and other handling

Not applicable

7. SUPPLIER

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8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

DI010

9. DATE OF PREQUALIFICATION

12 July 2023

10. DATE OF REVISION OF THE TEXT

June 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