

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

[DI009 trade name][†]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipients with potential clinical effect

Each dispersible tablet also contains 20 mg of aspartame.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Dispersible tablets

[DI009 trade name] are white to off-white, round, biconvex (rounded on top and bottom) tablet. The tablets have a break line on one side and plain on the other side.

The tablet can be divided into two equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[DI009 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 [DI009 trade name], the dose should be repeated.

Method of administration

Oral use.

[DI009 trade name] should be given between meals.

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

[DI009 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

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

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 [DI009 trade name]. An interval of at least 3 hours should be allowed between administration 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 100), 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 [DI009 trade name]

Pharmacokinetic data are not available for [DI009 trade name]. No bioequivalence study has been performed. [DI009 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

Microcrystalline cellulose
Ethyl vanillin
Sodium saccharin
Aspartame
Orange trusil flavour
Pregelatinized starch
Colloidal silicon dioxide
Crospovidone

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

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C. Protect from moisture and light.

6.5 Nature and contents of container

Alu-Alu blister.

Each blister card contains 10 tablets. Available in cartons of 1 x 10 tablets

6.6 Special precautions for disposal and other handling

How to give [DI009 trade name]

You will need:

1 tablet of [DI009 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 [DI009 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

PharmEvo Private Limited

A-29, North Western Industrial Zone

Port Qasim, Karachi 75020

Pakistan

Tel. No.: +92-21-34720155-159 (five lines)

Fax No.: +92-21-34720161

Email: mail@pharmevo.biz

8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

DI009

9. DATE OF PREQUALIFICATION

12 July 2023

10. DATE OF REVISION OF THE TEXT

June 2025

References

General references

Dietary Supplement Fact Sheet: Zinc. National Institutes of Health (US):

<http://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/>

Posology

Guideline on Management of Pneumonia and Diarrhoea in Children up to 10 years of Age: Available at:
<https://www.who.int/publications/i/item/9789240103412>

Dhingra U et al. Lower-Dose Zinc for Childhood Diarrhea - A Randomized, Multicenter Trial. N Engl J Med 2020; 383 (13):1231-1241; available at <https://www.nejm.org/doi/full/10.1056/NEJMoa1915905>

Interactions with other medicinal products

Penttilä O. et al. Effect of zinc sulphate on the absorption of tetracycline and doxycycline in man. Eur J Clin Pharmacol 1975; 19:9:131-4

Ding Y et al. The effect of staggered administration of zinc sulfate on the pharmacokinetics of oral cephalexin. Br. J Clin Pharmacol 2012; 73:422-7.

Overdose

Barceloux DG. Zinc.. J Toxicol Clin Toxicol 199; 37:279-292.

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 T

Solvazinc® 45mg Effervescent Tablets {Galen Limited (UK)} SmPC, revised 14 December 2017. Available on Electronic Medicines Compendium [<https://www.medicines.org.uk/emc/product/4930/smpc>]

Zinc sulphate injection {American Regent, Inc. (USA)} Prescribing Information, revised July 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/209377s000lbl.pdf

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