# 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/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

# 1. NAME OF THE MEDICINAL PRODUCT
[DI013 trade name]†

# 2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each dispersible tablet contains 54.9 mg zinc sulfate monohydrate equivalent to 20 mg of zinc.

Each dispersible tablet also contains 46.43 mg of aspartame and 4.5 mg vanilla flavour (contains 3.42 mg glucose).
For the full list of excipients, see section 6.1.

# 3. PHARMACEUTICAL FORM
Dispersible tablets.

White to off-white coloured, round-shaped, flat, dispersible tablet; one face is plain and the other face has a break line. The tablet may have brown specks.

The tablet can be divided into two equal doses.

# 4. CLINICAL PARTICULARS

## 4.1 Therapeutic indications
[DI013 trade name] is indicated for the treatment of acute and persistent diarrhoea in infants and children aged up to 5 years.

## 4.2 Posology and method of administration
**Posology**

Children aged less than 6 months: 10 mg (½ tablet) once daily for 10–14 days.

Children aged 6 months–5 years: 20 mg (1 tablet) 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**
The tablet (or half-tablet) should be dispersed completely in 1 teaspoon (5 mL) clean water or breast milk and the entire amount administered orally.

## 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).

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† 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*

This medicine contains 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.

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 [DI013 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*

This medicine is not intended for adults.

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

[DI013 trade name] is not expected to have any effect on the ability to drive and use machines.

### 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 attributed to the tablet was reported in 14% and regurgitation in 5.2% of the children. In most cases, vomiting or regurgitation occurred within 10 minutes of the first dose and was not recurrent.

*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 (≥ 1/10), common (1/100 to 1/10), uncommon (1/1000 to 1/100), rare (1/10 000 to 1/1000), and very rare (< 1/10 000).

| | |
|---|---|
| **Gastrointestinal disorders** | |
| Very common | vomiting |
| Common | regurgitation |
| Frequency not known | abdominal pain, dyspepsia, nausea, gastric irritation and gastritis |
| **Nervous system disorders** | |
| Frequency not known | headache |
| **General disorders** | |
| Frequency not known | irritability, lethargy |

***Reporting of suspected adverse reactions***

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care providers are asked to report any suspected adverse reactions to the marketing authorisation holder, or, if available, via the national reporting system.

### 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

*Pharmacokinetics of zinc sulfate*

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|---|---|
| **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.<br>85% of total body zinc is found in skeletal muscle and bone.<br>The highest concentrations occur in hair, eyes, male reproductive organs and bone. Lower levels are present in liver, kidney and muscle.<br>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
Maize starch
Aspartame
Colloidal silicon dioxide
Vanilla flavour
Magnesium stearate

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

36 months

### 6.4 Special precautions for storage

Do not store above 30°C. Protect from moisture and light. Store tablets in blisters in the provided carton.

### 6.5 Nature and contents of container

White, opaque PVC/PVdC-aluminium blister. Each blister strip contains 10 tablets, such 10 blisters are packed in a paper board carton along with the patient information leaflet.

### 6.6 Special precautions for disposal and other handling

No special precautions for disposal.

## 7. SUPPLIER

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## 8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

DI013

## 9. DATE OF PREQUALIFICATION

02 November 2021

## 10. DATE OF REVISION OF THE TEXT

January 2022
Section 6.3 updated in January 2023

***References***

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*Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/pqweb/medicines*