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

[TB383 trade name]†

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg pyridoxine hydrochloride

3. PHARMACEUTICAL FORM

Uncoated tablets

White, circular, flat face, bevelled edged, uncoated tablet having a scoreline on one side and plain surface on the other side.

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[TB383 trade name] is indicated for the treatment of isoniazid-induced peripheral neuropathy.

Pyridoxine is also indicated for preventing isoniazid toxicity in all children receiving high-dose isoniazid regimens for the treatment of drug-resistant tuberculosis.

Pyridoxine can be used for preventing isoniazid-induced peripheral neuropathy in patients at risk of the condition but other formulations of pyridoxine (e.g. tablets containing 10 mg) are more suitable.

In children, to prevent isoniazid toxicity:

- pyridoxine is indicated for all children aged from 4 years treated for drug-resistant tuberculosis with high-dose isoniazid regimens;
- pyridoxine can be given to children aged from 4 years treated with isoniazid regimens for severe forms of tuberculosis such as tuberculous meningitis and osteoarticular tuberculosis.

Other formulations of pyridoxine (e.g. tablets containing 10 mg) are more suitable for preventing isoniazid toxicity in children aged under 4 years.

4.2 Posology and method of administration

Posology

The recommended doses of pyridoxine for the different indications are shown below.

Treatment of isoniazid-induced neuropathy

Adult: 50 mg 1–2 times daily, increased up to 200 mg daily in divided doses

Adolescent over 12 years: 25–50 mg 2–3 times daily

Child under 12 years: 50 mg 1–2 times daily

Prevention of isoniazid toxicity in children

Child over 4 years: 25–30 mg once daily

Child under 4 years: 10–12.5 mg once daily

For some children, other formulations of pyridoxine (e.g. tablets containing 10 mg) may be required.

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

Prevention of isoniazid-induced peripheral neuropathy in patients at risk

Adult and adolescent: 10 mg once daily

Neonate and child under 12 years: 5–10 mg once daily

[TB383 trade name] is not suitable for this indication and other formulations of pyridoxine (e.g. tablets containing 10 mg) are required.

Administration

The recommended dose should be administered orally. Patients requiring half tablet of [TB383 trade name] may break the tablet along the scoreline.
[TB383 trade name] is unaffected by food and may be taken with food or between meals.
For instructions on preparing an extemporaneous formulation for children, see section 6.6.

Missed dose and vomiting after a dose

If the patient misses a dose, the patient should take it as soon as possible. If it is almost time for the next dose, then the patient should not take the missed dose and take the next dose at the usual time.

If the patient vomits within 1 hour of taking [TB383 trade name], the patient should take an extra dose. If vomiting occurs more than an hour after taking the dose, the patient does not need to take an extra dose and can take the next dose as usual when it is due.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Excessive doses of pyridoxine over prolonged periods can cause peripheral neuritis, with symptoms similar to isoniazid toxicity.

4.5 Interaction with other medicinal products and other forms of interaction

Pyridoxine can reduce the effect of levodopa (used for treating Parkinson's disease) unless a dopa decarboxylase inhibitor is also given. High doses of pyridoxine can also reduce the effects of the epilepsy medicines phenobarbital, phenytoin and primidone.

Combined hormonal contraceptives, cycloserine, hydralazine and penicillamine may increase the metabolism of pyridoxine.

4.6 Fertility, pregnancy and breastfeeding

Pregnancy and breastfeeding

Data from women taking pyridoxine during pregnancy indicate no adverse effects of pyridoxine in therapeutic doses on pregnancy or the health of the fetus or of the newborn baby

Breastfeeding

The therapeutic use of pyridoxine is compatible with breast-feeding.

4.7 Effects on ability to drive and use machines

Pyridoxine is not expected to have an effect on the ability to drive and use machines.

4.8 Undesirable effects

Side effects are not expected to occur with recommended doses of pyridoxine. Large doses taken for a prolonged period can cause severe peripheral neuropathy.

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

Single doses of pyridoxine doses of 2–3 g may cause headache but no treatment is necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pyridoxine is one of the vitamin B_6 compounds. It is converted to the co-enzyme pyridoxal phosphate, which is involved in many metabolic processes in the body.

5.2 Pharmacokinetic properties

Absorption Pyridoxine is readily absorbed from the gastrointestinal tract after oral administration	
Distribution Pyridoxine's main active metabolite, pyridoxal 5'-phosphate, is released into the circulation and is highly protein-bound, mainly to albumin. Pyridoxine crosses the placenta and also appears in breastmilk	
Metabolism Pyridoxine is converted to the active forms of pyridoxal 5'-phosphate and pyridoxamine phosphate, which are stored in the liver. Pyridoxine is mainly metabolized to 4-pyridoxic acid, an inactive compound, formed by the action of hepatic aldehyde oxidase on free pyridoxal	
Elimination The principal metabolite, 4-pyridoxic acid, is excreted in the urine	
Elimination half life	Estimated to be 15-20 days

Pharmacokinetics of pyridoxine

As [TB383 trade name] met the WHO criteria for a BCS-based biowaiver a bioequivalence study was not conducted. Therefore, no pharmacokinetic data are available for this product. Comparability between the WHO-accepted comparator product and [TB383 trade name] regarding the qualitative and quantitative composition of the formulations have been sufficiently proven

5.3 Preclinical safety data

There are no preclinical data of relevance to the use of pyridoxine for the treatment or prevention of isoniazid-induced peripheral neuritis. Effects in non-clinical studies occurred at doses that were well in excess of the maximum doses used for therapeutic purposes.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core tablet: Microcrystalline cellulose

Colloidal anhydrous silica
Sodium starch glycolate
Anhydrous citric acid
Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

In-Use Period:

HDPE Bottle

Should be used within 90 days, once opened

6.4 Special precautions for storage

Store in a dry place below 30°C,protected from light.

6.5 Nature and contents of container

Strip

Alu/Alu strip. Each strip pack contains 10 tablets. Such 9 or 10 strip packs are packed in a carton along with a patient information leaflet.

HDPE bottle

White, round HDPE bottle with polypropylene continuous thread closure with pulp and white heat seal liner. Pack size: 1000 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements

Preparation and administration - extemporaneous formulation for children

Method of administration

1. The required number of tablets as per above dosing of {DotWP-ProductName}, should be disintegrated by adding a small amount of water (about 5 mL) in a small bowl.
2. A small amount of semi-solid food should be mixed to improve palatability
3. The mixture should be administered immediately to the child

7. SUPPLIER

Macleods Pharmaceuticals Ltd.
304, Atlanta Arcade,
Marol Church Road,
Andheri (East),
Mumbai- 400 059,
India

8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

TB383

9. DATE OF PREQUALIFICATION

13 May 2022

10. DATE OF REVISION OF THE TEXT

August 2022

Section 6 updated in May 2023

References

Summary of product characteristics: Tor Pyridoxine Tablets 10 mg https://www.medicines.org.uk/emc/product/11766/smpc#gref [Accessed September 2020]

Summary of product characteristics: Pyridoxine 50 mg Tablets (Wockhardt UK Ltd) https://www.medicines.org.uk/emc/product/1208/smpc#gref [Accessed September 2020]

WHO operational handbook on tuberculosis. Module 1: prevention - tuberculosis preventive treatment (2020) https://www.paho.org/en/documents/who-operational-handbook-tuberculosis-module-1-prevention-tuberculosis-preventive [Accessed September 2020]

WHO operational handbook on tuberculosis. Module 4: treatment – drug-resistant tuberculosis treatment (2020) https://www.who.int/publications/i/item/9789240006997 [Accessed September 2020]

WHO operational handbook on tuberculosis Module 4: Treatment – drug-susceptible tuberculosis treatment (2022) https://www.who.int/publications/i/item/9789240050761 [Accessed June 2022]

Section 4.6

Breastfeeding and Maternal Medication: Recommendations for Drugs in the Eleventh WHO Model List of Essential Drugs (2002) https://apps.who.int/iris/bitstream/handle/10665/62435/55732.pdf?sequence=1 [Accessed September 2020]

Section 5.2

DrugBank (version 5.1.7, released 2020-07-02): Pyridoxine https://go.drugbank.com/drugs/DB00165 [Accessed September 2020]

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