# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Isoniazid 50 mg Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains 50 mg of Isoniazid

Excipient with known effect
Each tablet contains 1.5 mg of hydrogenated castor oil.
For the full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Tablets

White to off white, round (approx. 6.30 mm), biconvex tablets embossed with ‘50’ on one side and plain on the other side.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Isoniazid is indicated for the treatment of all forms of pulmonary and extra-pulmonary tuberculosis.

### 4.2 Posology and method of administration

Official guidance should always be consulted when selecting the dose regimens to be used for adults and children (according to age and body weight), the duration of therapy and the total content of the combination treatment regimen.

**Posology**

*Adults*
The dose of isoniazid for the treatment of tuberculosis is commonly 4 to 5 mg per kilogram body-weight daily given by mouth in single or divided doses up to a maximum of 300 mg daily. Up to 10 mg per kilogram body-weight daily may be given particularly during the first 1 to 2 weeks of treatment of tuberculous meningitis.

A dose of 15 mg per kilogram has been given two or three times weekly in intermittent treatment regimens.

*Elderly*
No dosage reduction is necessary in the elderly, but caution should be exercised due to the possible decrease in renal and hepatic function.

*Paediatric population*
The usual daily dose for children aged three months and above is from 10 up to 15 mg per kilogram body-weight daily in single or divided doses.

Isoniazid should not be used in children aged 0 to 3 months because of the lack of specific data.

Method of Administration
Isoniazid 50 mg tablets should be taken preferably on an empty stomach, i.e. at least 30 minutes before a meal or 2 hours after a meal. Tablets must be swallowed whole and not chewed.

## 4.3 Contraindications

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

Previous experience of severe adverse reaction to Isoniazid including drug induced liver disease (See section 4.4).

## 4.4 Special warnings and precautions for use

All patients should have baseline liver function tests performed and repeated at regular intervals during treatment. If serum AST rises to more than three times normal, or there is any increase in bilirubin, treatment should be withdrawn. Special precautions are required in patients with impaired liver function. Any deterioration in liver function in these patients is an indication for stopping treatment.

Isoniazid should not be given to patients who have experienced severe adverse reactions including drug-induced liver disease. Care should be taken in giving isoniazid to patients suffering from convulsive disorders, diabetes mellitus, chronic alcoholism, or impaired liver or kidney function or to patients taking other potentially hepatoxic agents. If symptoms of hepatitis such as malaise, fatigue, anorexia and nausea develop isoniazid should be discontinued immediately.

Isoniazid should be used with caution in patients with a history of psychosis.

Advanced age, female gender, slow acetylators, malnutrition, HIV infection, pre-existing liver disease and extra-pulmonary tuberculosis were identified as risk factors for isoniazid-induced hepatotoxicity.

Patients who are at risk of neuropathy or pyridoxine deficiency, including those who are diabetic, alcoholics, malnourished, uraemic, pregnant or infected with HIV, should be given pyridoxine.

**Hydrogenated castor oil**
This product contains hydrogenated castor oil which may cause stomach upset and diarrhoea.

Severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP), which

can be life-threatening or fatal, have been reported in association with isoniazid treatment.

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions.

If signs and symptoms suggestive of these reactions appear, isoniazid should be withdrawn immediately and an alternative treatment considered.

If the patient has developed a serious reaction such as SJS, TEN, DRESS or AGEP with the use of isoniazid, treatment with isoniazid must not be restarted in this patient at any time.

## 4.5 Interaction with other medicinal products and other forms of interaction

When isoniazid is given to patients who inactivate it slowly or to patients receiving paraminosalicyclic acid concurrently, tissue concentrations may be enhanced, and adverse effects are more likely to appear. There may be an increased risk of liver damage in patients receiving rifampicin and isoniazid but liver enzymes are raised only transiently.

Isoniazid can inhibit the hepatic metabolism of a number of drugs, in some cases leading to increased toxicity. These include the antiepileptics carbamazepine, primidone and phenytoin, the benzodiazepines diazepam and triazolam, chlorzoxazone and disulfiram.

Isoniazid is an inhibitor of monoamine oxidase (MAO) and diamine oxidase (DAO), therefore can reduce tyramine and histamine metabolism, causing symptoms such as headache, sweating, palpitations, flushing, and hypotension.
Patients should be advised against ingesting foods rich in tyramine and/or histamine during treatment with isoniazid, such as cured meat, some cheeses (e.g. matured cheeses), wine, beer and some fish (e.g. tuna, mackerel, salmon).

Isoniazid has been reported to cause substantial elevations of serum concentrations of carbamazepine and symptoms of carbamazepine toxicity at isoniazid doses of 200 mg daily or more. The concurrent use is not recommended unless the effects can be closely monitored and suitable downward dosage adjustments made (a reduction between one-half or one-third was reported effective).

Concomitant benzodiazepine (diazepam) and isoniazid therapy has been reported to result in an increased risk of benzodiazepine toxicity (sedation, respiratory depression).

Isoniazid may reduce the therapeutic effects of levodopa.

Concomitant administration of isoniazid with itraconazole may result in significant decreases in itraconazole serum concentrations and therapeutic failure. Coadministration is not recommended.

Isoniazid may decrease ketoconazole serum levels. Concurrent use should be well monitored and dosage increases made if necessary.

Because the clearance of isoniazid was found doubled when zalcitabine was given in HIV-positive patients, concurrent use of isoniazid and zalcitabine should be monitored to ensure isoniazid effectiveness.

There may be an increased risk of distal sensory neuropathy when isoniazid is used in patients taking stavudine (d4T).

## 4.6 Fertility, pregnancy and lactation

Pregnancy

Isoniazid crosses the placenta. Therefore, isoniazid should only be used in pregnant women or in women of child-bearing potential if the potential benefit justifies the potential risk to the foetus. It is considered that untreated tuberculosis represents a far greater hazard to a pregnant woman and her foetus than does treatment of the disease. Pyridoxine supplementation is recommended.

Breast-feeding
Isoniazid passes into breast milk. When administered to nursing mothers, breast-fed infants should be monitored for possible signs of isoniazid toxicity.

Administration of pyridoxine to the breast-feeding mother and infant may be considered.

## 4.7 Effects on ability to drive and use machines

No specific statement, but unlikely to affect the ability to drive or use machinery.

## 4.8 Undesirable effects

Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:

Very common: ≥1/10
Common: ≥1/100 to <1/10
Uncommon: ≥1/1,000 to <1/100
Rare: ≥1/10,000 to <1/1,000
Very rare: <1/10,000
Frequency not known: cannot be estimated from the available data

| System organ class | Frequency | Adverse reactions |
|---|---|---|
| **Blood & lymphatic system disorders** | Not known | Haemolytic anaemia<br>Aplastic anaemia<br>Agranulocytosis |
| **Metabolism & nutrition disorders** | Not known | Hypoglycaemia<br>Acidosis<br>Nicotinic acid deficiency<br>Nicotinic acid deficiency may be related to an isoniazid-induced pyridoxine deficiency which affects the conversion of tryptophan to nicotinic acid. |
| **Psychiatric disorders** | Not known | Psychotic disorder<br>Elevated mood<br>Although isoniazid usually has a mood elevating effect, mental disturbances, ranging from minor personality changes to major mental derangement have been reported; these are usually reversed on withdrawal of the drug. |
| **Nervous system disorders** | Not known | Peripheral neuropathy<br>Seizure<br>Optic neuritis<br>Hyperreflexia may be troublesome |

| | | |
|---|---|---|
| | | with doses of 10 mg per kg bodyweight. |
| **Musculoskeletal and connective tissue disorders** | Not known | Systemic lupus erythematosus<br>Lupus-like syndrome |
| **General disorders and administration site conditions** | Not known | Pyrexia |
| **Ear & labyrinth disorders** | Not known | Deafness<br>Tinnitus<br>Vertigo<br>These have been reported in patients with end stage renal impairment.<br>Vertigo may be troublesome with doses of 10 mg per kg bodyweight. |
| **Respiratory, thoracic & mediastinal disorders** | Not known | Interstitial lung disease |
| **Gastrointestinal disorders** | Not known | Nausea<br>Vomiting,<br>Constipation<br>Dry mouth<br>Pancreatitis acute<br>Other gastrointestinal effects |
| **Hepatobiliary disorders** | Not known | Acute hepatic failure<br>Liver injury<br>Jaundice<br>The risk of these undesirable effects increases with age, especially over the age of 35; it may be serious and sometimes fatal with the development of necrosis. |
| | Uncommon | Hepatitis |
| **Skin and subcutaneous tissue disorders** | Not known | Erythema multiforme<br>Stevens-Johnson syndrome<br>Acute generalised exanthematous pustulosis |
| | Rare | Toxic epidermal necrolysis (TEN)<br>Drug reaction with eosinophilia and systemic symptoms (DRESS) |
| **Renal & urinary disorders** | Not known | Dysuria |
| **Reproductive system & breast disorders** | Not known | Gynaecomastia |
| **Vascular disorders** | Not known | Vasculitis |
| **Investigations** | Not known | Hepatic enzyme increased |

Withdrawal symptoms, which may occur on the cessation of the treatment include headache, insomnia, excessive dreaming, irritability and nervousness.

**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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme website www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

### 4.9 Overdose

The most commonly reported adverse events associated with isoniazid overdose are nausea, vomiting and central nervous system toxicity such as vertigo, seizures and coma.

Treatment of overdosage consists of gastric lavage following intubation and the control of convulsions by anti-convulsants given intravenously as well as the intravenous injection of large doses of pyridoxine. Any acidosis is corrected with sodium bicarbonate. Forced diuresis may be tried and haemodialysis or peritoneal dialysis has been used.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimycobacterials, ATC code: J04AC01

Isoniazid has no significant antibacterial action against any micro-organisms except the mycobacteria; against mycobacterium tuberculosis it is bacteriostatic in extremely low concentrations.

Isoniazid is used mainly in the treatment of pulmonary tuberculosis but it appears to be effective also in the treatment of extrapulmonary lesions, including meningitis and genito-urinary disease.

### 5.2 Pharmacokinetic properties

Absorption
Readily and completely absorbed after oral administration.

Distribution
Readily diffuses into all tissues and fluids including the cerebrospinal fluid. Isoniazid is retained in the skin and in infected tissue; it crosses the placenta and is secreted in the milk of lactating mothers.

Protein binding
Isoniazid does not appear to be bound in the blood.

Half-life
Plasma elimination half-life, in rapid acetylators is about 1.2 hours and in slow acetylators about 3.5 hours.

Metabolic reactions
Acetylation, hydrolysis and glycine conjugation, hydrazone formation, and n-methylation; acetylation is polymorphic and two groups of acetylators have been identified, rapid and slow acetylators. The rate of hydrolysis is more rapid in the rapid acetylators than in the slow ones. The metabolites formed include acetyl isoniazid, isonicotinic acid, isonicotinuric acid, isonicotinoyl-hydrazones of pyruvic and glutaric acids, and n-methylisoniazid.

Excretion

Over 90% of a dose is excreted in the urine in 24 hours, most being excreted in the first 12 hours, 4-32 % is unchanged, but no more than 10 % of a dose is excreted in the faeces.

### 5.3 Preclinical safety data

Not applicable since isoniazid tablets have been used in clinical practice for many years and its effects in man are well known.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Maize starch
Microcrystalline cellulose
Starch, pregelatinized partially
Crospovidone
Colloidal anhydrous silica
Talc
Hydrogenated castor oil
Purified water

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

36 months

### 6.4 Special precautions for storage

This product does not require any special temperature storage conditions.

### 6.5 Nature and contents of container

Alu-PVC-PVDC blister pack.

Pack sizes: 28, 56 and 100 tablets.
Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

No special precautions are required.

## 7 MARKETING AUTHORISATION HOLDER

DAWA Limited

5 Sandridge Close,

Harrow, Middlesex,

HA1 1XD, UK

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 30684/0162

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/02/2023

## 10 DATE OF REVISION OF THE TEXT

10/10/2025