

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1 NAME OF THE MEDICINAL PRODUCT

Isoniazid Tablets BP 50mg

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Isoniazid BP 50mg

Excipient with known effect

Lactose monohydrate – 30mg/tablet

For the full list of excipients, see section 6.1

### 3 PHARMACEUTICAL FORM

White to off white biconvex uncoated tablets embossed 50 151 on one face and EVANS on the obverse.

### 4 CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

Isoniazid is indicated in 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 5mg per kilogram body-weight daily given by mouth in single or divided doses up to a maximum of 300mg daily. Up to 10mg per kilogram body-weight daily may be given particularly during the first 1 to 2 weeks of treatment of tuberculous meningitis. A dose of 15mg 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 15mg 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 tablets should be taken preferably on an empty stomach, i.e. at least 30 minutes before a meal or 2 hours after a meal.

### **4.3 Contraindications**

Patients who are known to be hypersensitive to isoniazid or drug-induced liver disease.

### **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 If serum AST rises to more than three times normal, or there is any increase in bilirubin, treatment should be withdrawn.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 experience 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 hepatotoxic 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, alcoholic, malnourished, uraemic, pregnant, or infected with HIV, should be given pyridoxine.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 paraminosalicylic 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 200mg 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. Co administration 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).

There may be a potential interaction between isoniazid and foods containing histamine or tyramine.

#### **4.6 Fertility, pregnancy and lactation**

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.

Isoniazid passes into breast milk. When administered to nursing mother, 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 effect 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:  $\geq 1/10$

Common:  $\geq 1/100$  to  $< 1/10$

Uncommon:  $\geq 1/1,000$  to  $< 1/100$

Rare:  $\geq 1/10,000$  to  $< 1/1,000$

Very rare:  $< 1/10,000$

Frequency not known: cannot be estimated from the available data

The frequency of the reactions described below cannot be determined from the data available.

##### Blood and lymphatic system disorders

*Frequency not known:* Agranulocytosis, Aplastic anaemia, Haemolytic anaemia

##### Ear and labyrinth disorders

*Frequency not known:* Deafness, Tinnitus, Vertigo

These have been reported in patients with end stage renal impairment

Vertigo may be troublesome with doses of 10mg per kg body weight

##### Gastrointestinal disorders

*Frequency not known:* Constipation, Dry mouth Nausea, Pancreatitis acute, Vomiting and other gastrointestinal effects

##### General disorders and administration site conditions

*Frequency not known:* Pyrexia

### Hepatobiliary disorders

*Frequency uncommon:* Hepatitis

*Frequency not known:* Acute hepatic failure, Liver injury, Jaundice

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.

### Investigations

*Frequency not known:* Hepatic enzyme increased

### Metabolism and nutrition disorders

*Frequency not known:* Acidosis, Hypoglycaemia, Nicotinic acid deficiency

Nicotinic acid deficiency may be related to an isoniazid-induced pyridoxine deficiency which affects the conversion of tryptophan to nicotinic acid.

### Musculoskeletal and connective tissue disorders

*Frequency not known:* Systemic lupus erythematosus, lupus-like syndrome

### Nervous system disorders

*Frequency not known:* Neuropathy peripheral, Optic neuritis, Seizure

Hyperreflexia may be troublesome with doses of 10mg per kg body weight

### Psychiatric disorders

*Frequency not known:* Elevated mood, Psychotic disorder

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

### Renal and urinary disorders

*Frequency not known:* Dysuria

### Reproductive system and breast disorders

*Frequency not known:* Gynaecomastia

### Respiratory, thoracic and mediastinal disorders

*Frequency not known:* Interstitial lung disease

### Skin and subcutaneous tissue disorders

*Frequency rare:* Toxic epidermal necrolysis, eosinophilia systemic symptoms,

*Frequency not known:* Erythema multiforme, Stevens-Johnson syndrome, acute generalised exanthematous pustulosis

### Vascular disorders

*Frequency not known:* Vasculitis

### Miscellaneous

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 Yellow Card Scheme on the MHRA website ([www.mhra.gov.uk/yellowcard](http://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**

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 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**

Lactose 170 Mesh  
Maize Starch  
Microcrystalline Cellulose  
Alginic Acid  
Magnesium Stearate  
Purified Water

### **6.2 Incompatibilities**

None

### **6.3 Shelf life**

36 months

### **6.4 Special precautions for storage**

Store below 25°C

### **6.5 Nature and contents of container**

Polyethylene bottle with child-resistant closure container fitted with a tamper-evident closure containing 7, 14, 21, 28, 30, 50, 56, 60, 84, 90, 100, 112, 120 or 250 tablets. Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal**

No special precautions are required

**7      MARKETING AUTHORISATION HOLDER**

RPH Pharmaceuticals AB,  
Box 603,  
101 32 Stockholm,  
Sweden

**8      MARKETING AUTHORISATION NUMBER(S)**

PL 36301/0017

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

24/01/1991

**10     DATE OF REVISION OF THE TEXT**

21/08/2025