

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. TRADE NAME OF THE MEDICINAL PRODUCT

Asyran

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Asyran 150mg:

Each tablet contains ranitidine hydrochloride equivalent to ranitidine 150mg

Asyran 300mg:

Each tablet contains ranitidine hydrochloride equivalent to ranitidine 300mg

For excipients, see 6.1.

### 3. PHARMACEUTICAL FORM

Asyran 150 mg:

Yellow, 10 mm round convex, film coated tablets and have the Delta logo on one side.

Asyran 300 mg:

Yellow, elliptical film coated tablets. The tablets are scored on one side and have the Delta logo on the other side. Diameter 17 mm x 8,2 mm.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

- Duodenal ulcer and gastric ulcer.
- Management and symptomatic relief of oesophageal reflux disease.
- Zollinger-Ellison syndrome.
- Prophylaxis of recurrent gastric or duodenal ulcer.
- Prophylaxis of gastric or duodenal ulceration due to stress in seriously ill patients.
- Prophylaxis of recurrent gastric or duodenal haemorrhage.

#### 4.2 Posology and method of administration

*Dosage for adults:*

The usual dosage is 150mg twice daily, taken in the morning and evening.

*Duodenal ulcer and gastric ulcer:* 300 mg at bedtime or 150 mg twice daily. The treatment should last for at least 4 weeks, even if the symptoms disappear earlier.

*Prophylaxis of duodenal and gastric ulcer:* 150 mg at bedtime.

*Oesophageal reflux disease:* 150 mg twice daily for 8 weeks.

*Zollinger-Ellison syndrome:* Initially 150 mg three times daily or in accordance with more detailed instructions from the doctor. Doses exceeding 900 mg daily are not recommended.

**Dosage for children:**

The drug is not recommended for children.

**Renal Failure:**

In case of impaired renal function, lower doses should be used.

The following dosages are recommended in accordance with creatinine clearance (ml/minute) or plasma concentration of ranitidine.

<b>Creatinine clearance (ml/minute)</b>	<b>Creatinine plasma concentration* (mg/100 ml)</b>	<b>Ranitidine dose/day (oral)</b>
<b>up to 30</b>	above 2.6	150 mg ranitidine
<b>above 30</b>	below 2.6	300 mg ranitidine

\*The plasma concentration of creatinine should only be used as guidance as different values do not necessarily represent the same type of dysfunction in all patients with renal impairment. This applies particularly to elderly patients where renal function is over estimated due to creatinine plasma concentration.

The following formula can be used for estimating the creatinine clearance from measured plasma concentration of creatinine (mg/100 ml), age (years) and body weight (kg). For women it is necessary to multiply the outcome by the coefficient 0.85.

$$\text{Creatinine clearance (ml/minute)} = \frac{(140 - \text{age}) \times \text{Body weight} \times 1.23}{\text{Creatinine plasma concentration}}$$

Patients on haemodialysis should receive reduced doses of ranitidine after dialysis, as ranitidine is not excreted.

**4.3 Contra-indications**

- Hypersensitivity to ranitidine or to any of the excipients.
- Children (below 16 years of age) should not take the drug because of lacking clinical data.
- It is not recommended to give ranitidine to pregnant or lactating women, unless it is considered essential.

**4.4 Special warnings and special precautions for use**

As ranitidine is excreted via the kidneys, patients with severe renal impairment should receive reduced doses. Caution should be exercised in the elderly as their renal function could be impaired (*see section 4.2*).

Before commencement of treatment for peptic ulcer with ranitidine, a biopsy should be taken in order to exclude malignant disease. The treatment may mask the symptoms of malignant disease and therefore delay the correct diagnosis.

Prolonged use of higher than recommended doses should be avoided.

#### **4.5 Interaction with other medicaments and other forms of interaction**

Antacids may reduce the gastric and duodenal absorption of H<sub>2</sub> receptor antagonists. Preferably ranitidine should be taken at least two hours after antacids.

Ranitidine treatment increases the plasma concentration of fluorouracil.

#### **4.6 Pregnancy and lactation**

*Pregnancy:* Ranitidine is contra-indicated during pregnancy. The safety of ranitidine during pregnancy has not been established and its use should be avoided unless the benefit is considered to be greater than the risk.

*Lactation:* Ranitidine is excreted into breast milk and may affect the breast-fed child. It is not recommended to give ranitidine to pregnant or lactating women, unless it is considered essential.

#### **4.7 Effects on ability to drive and use machines**

No known effects on the ability to drive or use machines.

#### **4.8 Undesirable effects**

- Fatigue, diarrhoea or constipation.
- Headache, sometimes severe and dizziness may occur. Rare cases of reversible mental confusion and hallucinations, particularly in seriously ill and elderly patients. Blurred vision, probably due to change in posture.
- Hypersensitivity (anaphylactic shock, fever, rash, angioneurotic oedema, bronchospasm) may occur rarely.
- Leucopenia and thrombocytopenia have occurred but they usually resolve when the treatment is stopped.
- Rare cases of agranulocytosis and pancytopenia, sometimes with bone marrow hypoplasia or aplasia.
- Reversible changes of liver function with or without jaundice.
- Gynaecomastia has been reported very rarely.
- Bradycardia is seen rarely. AV-block and even asystole. Arthralgia and chest pain have been reported rarely.

#### **4.9 Overdose**

There is very limited experience regarding the toxic effects of ranitidine.

Symptoms include bradycardia, dyspnoea and myoclonus.

Treatment consists of gastric lavage and charcoal. Atropine can be used for bradycardia. Otherwise, symptomatic therapy should be administered.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: H<sub>2</sub> receptor antagonist for the treatment of peptic ulcer  
ATC code: A02B A02

Ranitidine is a specific rapid acting H<sub>2</sub> receptor antagonist which blocks histamine receptors in hydrochloric acid producing cells in the gastric mucosa. This block causes reduced secretion of gastric acid, reducing both the volume and the acid and pepsin content of the secretion. The duration of action is relatively long as ranitidine 150 mg causes potent reduction of gastric acid for 12 hours.

### **5.2 Pharmacokinetic properties**

The bioavailability after oral administration is approximately 50%. Peak plasma concentration ranges from 300 to 550 ng/ml and is usually reached within two to three hours of administration of the 150 mg dose. Excretion is primarily via the kidneys by tubular secretion as the free drug and in minor amounts as metabolites. The elimination half-life of ranitidine is approximately two to three hours. About 60-70% is excreted in the urine and 25% in the faeces.

### **5.3 Preclinical safety data**

Ranitidine is well tolerated in all animal species. No indications of risk in clinical use.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Microcrystalline cellulose *Ph. Eur.*

Hypromellose *Ph. Eur.*

Macrogol *Ph. Eur.*

Magnesium stearate *Ph. Eur.*

Riboflavin *Ph. Eur.*

Titanium dioxide (E171) *Ph. Eur.*

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

3 years.

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

Do not store above 25°C.

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

Asyran 150 mg: Cartons of 10, 30, 60 and 120 tablets, in aluminium foil blisters.

Asyran 300 mg: Cartons of 30, 60 and 100 tablets, in aluminium foil blisters.

**6.6 Instructions for use/handling**

No special requirements.

**7. MARKETING AUTHORISATION HOLDER**

Delta Ltd.  
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IS-220 Hafnarfjörður  
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**8. MARKETING AUTHORISATION NUMBER**

Asyran 150 mg: 853664 (IS)  
Asyran 300 mg: 860240 (IS)

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

Asyran 150 mg: 23<sup>rd</sup> April 2002  
Asyran 300 mg: 23<sup>rd</sup> April 2002

**10. DATE OF (PARTIAL) REVISION OF THE TEXT**

Asyran 150 mg: 23<sup>rd</sup> April 2002  
Asyran 300 mg: 23<sup>rd</sup> April 2002