

1. NAME OF THE MEDICINAL PRODUCT

Avroprin 300mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Aspirin BP 300mg

3. PHARMACEUTICAL FORM

Tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Anti-inflammatory indications:

Symptomatic relief of sprains, strains, rheumatic pain, sciatica, lumbago, muscular aches, fibrositis, joint swelling and stiffness.

Analgesic and antipyretic indications:

Mild to moderate pain including headache, migraine, neuralgia, toothache, sore throat, period pains, aches and pains, symptomatic relief of influenza and feverish colds.

4.2 Posology and method of administration

Adults & children over 12 years: 1 to 3 tablets every four hours as needed, or as directed by a doctor.

Do not exceed 4 doses (12 tablets) in 24 hours.

Not for use in children below 12 years of age.

Elderly: A lower dose is recommended.

The tablets to be taken orally with water.

4.3 Contraindications

Aspirin is contraindicated in patients with;

- active peptic ulceration or a history of peptic ulceration.
- Haemophilia, haemorrhagic disease or a history of bleeding disorders.
- Gout or a history of gout.
- Hypersensitivity to aspirin (e.g. asthma, rhinitis, angioedema or urticaria), other NSAIDs or other tablet excipients
- During the third trimester of pregnancy

4.4 Special warnings and precautions for use

There is a possible association between aspirin and Reye's syndrome when given to children. Reye's syndrome is a very rare disease, which affects the brain and liver and can be fatal. For this reason aspirin should not be given to children under 12 years unless specifically indicated (e.g. for Kawasaki's disease).

Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take aspirin.

Patients should be warned:

- not to exceed the stated dose.
- not to take aspirin if they have ever suffered from stomach ulcers.

- to keep medicines out of the reach of children.

Caution is required if administered to patients suffering from, or with a previous history of bronchial asthma.

May produce haemolysis in some glucose-6-phosphate dehydrogenase deficient individuals

4.5 Interaction with other medicinal products and other forms of interaction

Aspirin should not be used in combination with other NSAIDs as this may increase the risk of side-effects.

Aspirin should be used with caution in combination with:

- ACE Inhibitors and Angio-II Receptor Antagonists: due to risk of renal impairment and the hypotensive effect is antagonized
- Antacids: excretion of Aspirin is increased by alkaline urine due to some antacids.
- Anti-depressants, SSRI's: increased risk of bleeding
- Anticoagulants: the risk of bleeding is increased with Aspirin due to the antiplatelet effect.
- Corticosteroids: increased risk of gastrointestinal bleeding.
- Anti-epileptic drug (eg phenytoin, sodium valproate): will be enhanced by Aspirin.
- Diuretics: effect will be antagonized by aspirin.
- Gout treatments such as probenacid, sulphinpyrazone: will be antagonized by aspirin.
- Methotrexate: excretion can be reduced with increased risk of toxicity.
- Metoclopramide: may enhance the effect of aspirin.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use

4.6 Pregnancy and lactation

Low doses (up to 100 mg/day):

Clinical studies indicate that doses up to 100 mg/day for restricted obstetrical use, which require specialised monitoring, appear safe.

Doses of 100- 500 mg/day:

There is insufficient clinical experience regarding the use of doses above 100 mg/day up to 500 mg/day. Therefore, the recommendations below for doses of 500 mg/d and above apply also for this dose range.

Doses of 500 mg/day and above:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, acetyl salicylic acid should not be given unless clearly necessary. If acetylsalicylic acid is used by a woman attempting to conceive, or

during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligohydroamniosis; the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour. Consequently, acetylsalicylic acid at doses of 100 mg/day and higher is contraindicated during the third trimester of pregnancy.

Lactation:

Aspirin should not be taken when breast feeding as it impairs platelet function and increases the risk of haemorrhage to the baby, i.e. intracranial haemorrhage.

4.7 Effects on ability to drive and use machines

None Stated

4.8 Undesirable effects

Adverse effects of aspirin treatment which have been reported include:

Blood and lymphatic system disorders:

Anaemia may occur following chronic gastrointestinal blood loss or acute haemorrhage. Aspirin prolongs bleeding time, and bleeding disorders, such as epistaxis, purpura and intracranial haemorrhage have occasionally been reported.

Nervous system disorders:

Mental confusion.

Dizziness

Ear and labyrinth disorders:

hearing disturbances (such as tinnitus), vertigo

Respiratory, thoracic and mediastinal disorders;

Aspirin may precipitate bronchospasm and induce asthma in susceptible patients. Dyspnoea also have been reported.

Gastrointestinal disorders:

gastric irritation, dyspepsia, nausea, vomiting, gastrointestinal erosions, ulcerations, gastritis.

In some cases of intensive use may induce gastrointestinal haemorrhage, occasionally major, which may manifest as melaena or haematemesis.

General disorders and administration site conditions:

Hypersensitivity reactions include skin rashes, urticaria and angioedema

4.9 Overdose

Salicylate poisoning is usually associated with plasma concentrations >350mg/L (2.5mmol/L). Most adult deaths occur in patients whose concentrations exceed 700mg/L (5.1 mmol/L). Single doses less than 100mg/kg are unlikely to cause serious poisoning.

Symptoms: Common features include vomiting, dehydration, tinnitus, vertigo, deafness, sweating, warm extremities with bounding pulses, increased respiratory rate and hyperventilation. Some degree of acid-base disturbance is present in most cases.

A mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) is usual in adults and children over the age of four years. In children aged four years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common. Acidosis may increase salicylate transfer across the blood brain barrier.

Uncommon features include haematemesis, hyperpyrexia, hypoglycaemia, hypokalaemia, thrombocytopenia, increased INR/PTR, intravascular coagulation, renal failure, and non-cardiac pulmonary oedema.

Central nervous system features including confusion, disorientation, coma and convulsions are less common in adults than in children.

Management: Give activated charcoal if an adult presents within one hour of ingestion of more than 250mg/kg. The plasma salicylate concentration should be measured, although the severity of poisoning cannot be determined from this alone and the clinical and biochemical features must be taken into account. Elimination is increased by urinary alkalinisation, which is achieved by the administration of 1.26% sodium bicarbonate. The urine pH should be monitored. Correct metabolic acidosis with intravenous 8.4% sodium bicarbonate (first check serum potassium). Forced diuresis should not be used since it does not enhance salicylate excretion and may cause pulmonary oedema.

Haemodialysis is the treatment of choice for severe poisoning and should be considered in patients with plasma salicylate concentrations >700mg/L (5.1mmol/L), or lower concentrations associated with severe clinical or metabolic features. Patients under ten years or over 70 have an increased risk of salicylate toxicity and may require dialysis at an earlier stage

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Aspirin has analgesic, anti-inflammatory and antipyretic actions due to inhibition of the biosynthesis of prostaglandins

5.2 Pharmacokinetic properties

Absorption of non-ionised aspirin occurs in the stomach. Acetylsalicylates and Salicylates are also readily absorbed from the intestine. Hydrolysis to salicylic acid occurs rapidly in the intestine and in the circulation.

Salicylates are extensively bound to plasma proteins; aspirin to a lesser degree. Aspirin and salicylates are rapidly distributed to all body tissues; they appear in milk and cross the placenta. The rate of excretion of aspirin varies as the pH rises, being greatest at 7.5 and above. Aspirin is also excreted as salicylic acid and as glucuronide conjugate, and as salicylic acid and gentisic acid.

5.3 Preclinical safety data

No data of relevance in addition to that already stated

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone K.30
Maize Starch
Stearic Acid
Talc
Avicel PH 101
Isopropyl Alcohol

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30°C.

Keep container tightly closed and protected from light and moisture.

6.5 Nature and contents of container

Opaque plastic containers (securitainers) composed of either high density polypropylene or high density polyethylene with a tamper-evident closure composed of high density polyethylene with a packing inclusion of a silica desiccant pack.

Pack size: x500's and x1000's

6.6 Special precautions for disposal and other handling

Not applicable

7 APPLICANT/MANUFACTURER

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