

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Aspirin 300 mg Tablets BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains aspirin 300 mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablets

White, biconvex tablets; breakline on one side and debossed <A> on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of mild to moderate pain, including headaches, migraine, neuralgia, toothache, sore throat, period pains, aches and pains.

For the symptomatic relief of influenza, feverishness, feverish colds

For the symptomatic relief of sprains, strains, rheumatic pain, sciatica, lumbago, fibrositis, muscular aches and pains, joint swelling & stiffness.

4.2 Posology and method of administration

For Oral use

If symptoms persist for more than 3 days, consult your doctor.

Adults & children over 16 years of age:

Analgesic, antipyretic and anti-inflammatory actions: One to three tablets.

Dose should not be repeated more frequently than 4 hour intervals and not more than 4 times in any 24 hour period.

In acute rheumatic disorders the dose is in the range of 4-8g, taken in divided doses.

Elderly:

Analgesic, antipyretic and anti-inflammatory actions: As for adults. The elderly are more likely to experience gastric side-effects and tinnitus.

Children: Do not give to children under 16 years, unless specifically indicated (e.g. for Kawasaki's Disease). See Section 4.4

4.3 Contraindications

- i) Children under 16 years unless specifically indicated (e.g. for Kawasaki's disease).
- ii) Active peptic ulceration or a history of peptic ulceration
- iii) Haemophilia, other coagulopathies or concurrent anticoagulant therapy.
- iv) Hypersensitivity to aspirin, any other NSAIDs, or any of the excipients (See section 6.1)
- v) Gout

4.4 Special warnings and precautions for use:

If symptoms persists for more than 3 days consult your doctor.

Caution should be exercised in patients with impairment of hepatic function, allergic disease and in patients with asthma (as they may precipitate bronchospasm or induce attacks of asthma in susceptible subjects)

Patients with hypertension should be carefully monitored.

The elderly may be more susceptible to the toxic effects of salicylates. Continuous, prolonged use of aspirin should be avoided in the elderly because of the risk of gastrointestinal bleeding. Salicylates should be used with caution in patients with a history of coagulation abnormalities. They may also induce gastro-intestinal haemorrhage, occasionally major.

Aspirin should not be taken by patients with a stomach ulcer or history of stomach ulcers (see section 4.3)

Caution should be used in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency as haemolytic anaemia may occur.

Aspirin may interfere with insulin and glucagon in diabetes.

Aspirin prolongs bleeding time, mainly by inhibiting platelet aggregation and therefore it should be discontinued several days before scheduled surgical procedures. Haematological and haemorrhagic effects can occur, and may be severe. Patients should report any unusual bleeding symptoms to their physician.

This medicine contains Lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Aspirin should be used with caution in patients with impaired renal function (avoid if severe), or in patients who are dehydrated.

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 aged under 16 years unless specifically indicated (e.g. for Kawasaki's disease).

4.5 Interaction with other medicinal products and ether forms of interaction

Anticoagulants: Aspirin may potentiate the effect of heparin and increase the risk of bleeding with oral anticoagulants, antiplatelet agents and fibrinolytics: concurrent use is contraindicated (See section 4.3)

Other non-steroidal anti-inflammatory drugs (NSAIDs): Concurrent administration can increase side effects. Increased risk of serious gastrointestinal haemorrhage.

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 regarding 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 (see section 5.1)

Alcohol: Some of the effects of aspirin on the gastrointestinal tract are enhanced by alcohol. (See Section 4.4)

Antacids and adsorbents: The excretion of aspirin is increased in alkaline urine; kaolin possibly reduces absorption.

Antiemetics: Metoclopramide enhances the effects of aspirin by increasing the rate of absorption.

Corticosteroids: The risk of gastrointestinal bleeding and ulceration is increased. Corticosteroids reduce the plasma salicylate concentration. Salicylate toxicity may occur following withdrawal of the corticosteroids.

Carbonic anhydrase inhibitors: Reduced excretion of acetazolamide with an increased risk of toxicity. Salicylate intoxication has occurred in patients on high dose salicylate regimens and carbonic anhydrase inhibitors.

Antimetabolites: The activity of methotrexate may be markedly enhanced and its toxicity increased.

ACE inhibitors: Aspirin may reduce the antihypertensive effect of ACE inhibitors.

Antiepileptics: May enhance the effects of phenytoin and sodium valproate.

Antibacterials: Inhibits the uricosuric effect of probenecid and may increase the toxicity of sulfonamides.

Diuretics: Antagonism of the diuretic effect of spironolactone.

Hypoglycaemic agents: Aspirin may enhance the effects of insulin and oral hypoglycaemic agents.

Leukotriene antagonists: The plasma concentration of zafirlukast is increased.

Mifepristone: The manufacturer of Mifepristone recommends that aspirin should be avoided until eight to twelve days after Mifepristone has been discontinued.

Uricosurics: Effect of probenecid and sulfinpyrazone reduced.

4.6 **Pregnancy and lactation**

Pregnancy: Although clinical and epidemiological evidence suggests the safety of aspirin in pregnancy, caution should be exercised when considering use in pregnant patients.

Aspirin has the ability to alter platelet function and there may be a risk of haemorrhage in infants whose mothers have consumed aspirin during pregnancy. Aspirin may prolong gestation, delay the onset of or prolong labour and may contribute to maternal and neonatal bleeding; decreased birth weight and increased rate of stillbirth have been reported with high blood salicylates levels. With high doses there may be premature closure of the ductus arteriosus and possible persistent pulmonary hypertension in the newborn. Analgesic doses of aspirin should be avoided during the last trimester of pregnancy. Maternal use of aspirin prior to birth may increase the risk of intracranial haemorrhage in premature or low birth weight infants. Regular use of high doses could impair platelet function and produce hypoprothrombinaemia in the infant if neonatal Vitamin K stores are low.

Lactation: As aspirin is excreted in human milk, Aspirin should not be taken by patients who are breast-feeding, as there is a risk of Reye's syndrome in the infant. High maternal doses may impair platelet function in the infant.

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

Aspirin does not usually affect the ability to drive or operate machinery.

4.8 **Undesirable effects**

Side effects are generally mild and infrequent.

Blood disorders: Aspirin increases bleeding time, decreases platelet adhesiveness and, in large doses, may cause hypoprothrombinaemia. It may also cause other blood disorders including thrombocytopenia. Haemolytic anaemia can occur in patients with glucose 6-phosphate dehydrogenase deficiency (G6PD). Fatalities have occurred.

Immune System: Aspirin may precipitate bronchospasm, induce asthma attacks, rhinitis, angioedema, or other hypersensitivity reaction in susceptible individuals.

Skin and Subcutaneous tissue disorder: Symptoms include skin rashes, urticaria, and rarely anaphylaxis. Skin reactions may occur in susceptible patients.

Gastro-intestinal: There is a relatively high incidence of gastro-intestinal irritation with a slight asymptomatic blood loss. Nausea, vomiting, dyspepsia, gastritis, gastrointestinal erosions and ulceration have been reported. Anaemia may occur following chronic gastrointestinal blood loss or acute haemorrhage.

Renal and Urinary disorders: Urate kidney stones

Ear & Labyrinth disorder: tinnitus.

Investigations: Aspirin may interfere with thyroid function test.

4.9 Overdose

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

a) 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.

b) Treatment

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 increased risk of salicylate toxicity and may require dialysis at an earlier stage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

N02B A01- (Nervous system- analgesics/ antipyretics)

Aspirin is an analgesic and antipyretic with anti-inflammatory properties. Aspirin inhibits prostaglandin synthetase.

It also has antithrombotic action, which is mediated through inhibition of platelet activation.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release aspirin dosing (81mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding 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.

5.2 Pharmacokinetic properties

Absorption

Aspirin is rapidly absorbed after oral administration, with some hydrolysis to salicylate before absorption. Absorption is delayed by the presence of food and is impaired in patients suffering migraine attacks. Absorption is more rapid in patients with achlorhydria and also following administration of polysorbates and antacids.

Blood concentration

Peak plasma concentrations of approximately 45mcg/ml are attained 1 to 2 hours after an oral dose of 640mg, but stabilise at approximately 270mcg/ml after oral doses of 3g daily. After an oral dose of about 2g, peak plasma concentrations of approximately 15mcg/ml of aspirin are attained in about one hour and peak plasma concentrations of approximately 130mcg/ml of salicylate are attained in 2 to 4 hours.

6.4 Special precautions for storage

Do not store above 25°C.

Blister packs: store in the original package.

Polypropylene / polyethylene containers: keep the bottle tightly closed.

6.5 Nature and contents of container

Blister Packs:

20, 24, 28, 30 or 32 as Pharmacy.

Blister Strips consists of a 35 gsm paper/9 µ soft tempered aluminium foil lid and 250 µ PVC film base in cartons.

Polypropylene / Polyethylene Containers:

25 tablets as Pharmacy

6.6 Instructions for use, handling and disposal

None

7. MARKETING AUTHRISATION HOLDER

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8. MARKETING AUTHORISATION NUMER(S)

PL 17907/0153

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16/01/2006

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