

ASPIRIN TABLETS

COMPOSITION

Aspirin 300mg Tablets: Each tablet contains: 300mg Aspirin BP

Aspirin 500mg Tablets: Each tablet contains: 500mg Aspirin BP

Pharmaceutical form

White uncoated tablets.

CLINICAL PARTICULARS

Therapeutic indications

Aspirin has analgesic, antipyretic and anti-inflammatory actions. It is indicated for:

- 1) The relief of headache, toothache, migraine, neuralgia, sore throat, dysmenorrhoea.
- 2) The symptomatic relief of influenza, feverishness, rheumatic pains, sciatica, lumbago, fibrositis, muscular aches and pains.
- 3) It also has an antithrombotic action, mediated through inhibition of platelet activation, which has been shown to be useful in secondary prophylaxis following myocardial infarction, and in patients with unstable angina and cerebral transient ischaemic attacks.

Posology and method of administration

Posology

Adults including elderly: 1-2 tablets (300-600mg) every 3-4 hours as required, to a maximum of 12 tablets (3.6g) daily in divided doses.

Children: Do not give to children aged under 16 years, unless specifically indicated (e.g. for Kawasaki's disease).

Antithrombotic action: For its antithrombotic effect following myocardial infarction, transient ischaemic attack, or in patients with unstable angina, the recommended dose is 300mg daily.

Method of Administration

For oral administration.

Contraindications

Aspirin should not be taken by patients with the following conditions:

- Known hypersensitivity to aspirin, other ingredients in the product, other salicylates or non-steroidal anti-inflammatory drugs (a patient may have developed anaphylaxis, angioedema, asthma, rhinitis or urticaria induced by aspirin or other NSAIDs).
- Nasal polyps associated with asthma (high risk of severe sensitivity reactions).
- Active peptic ulceration or a past history of ulceration or dyspepsia.
- Haemophilia or other haemorrhagic disorder (including thrombocytopenia) as there is an increased risk of bleeding.
- Concurrent anticoagulant therapy should be avoided.
- Severe hepatic impairment
- Severe renal impairment
- Severe cardiac failure
- Third trimester of pregnancy.
- Children under 16 years old, unless specifically indicated (e.g. Kawasaki's disease).

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 aged under 16 years, unless on the advice of a doctor e.g. Kawasaki's Syndrome

Aspirin should be used with caution in patients with:

- Acetylsalicylic acid may promote bronchospasm and asthma attacks or other hypersensitivity reactions. Risk factors are existing asthma, hay fever, nasal polyps or chronic respiratory diseases. The same applies for patients who also show allergic reaction to other substances (e.g. with skin reactions, itching or urticaria).

Pregnancy and lactation

Pregnancy

Regular or high dose use of salicylates late in pregnancy may result in:

- kernicterus in jaundiced neonates. 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 oligo-hydroamniosis; 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

Low quantities of salicylates and of their metabolites are excreted into the breast milk. Adverse effects for the infant have not been reported up to now. However, aspirin should be avoided during lactation because of the possible risk of Reye's syndrome. In cases of long-term use and/or administration of higher doses, breastfeeding should be discontinued.

Regular use of high doses of aspirin could impair platelet function and produce hypoprothrombinaemia in the infant neonatal vitamin K stores are low.

Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed with Acetylsalicylic acid. Based on the pharmacodynamic properties and the side effects of acetylsalicylic acid, no influence on the reactivity and the ability to drive or use machines is expected.

Children

Aspirin may be associated with the development of Reye's Syndrome (encephalopathy and hepatic failure) in children presenting with an acute febrile illness.

Overdose

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/PTT, intravascular coagulation, renal failure and non-cardiac pulmonary oedema.

Other symptoms may include: headache, nausea, or abdominal pain.

Central nervous system features including confusion, restlessness, hallucinations, disorientation, coma, cardiovascular collapse, respiratory arrest and convulsions are less common in adults than in children.

Management

If a toxic dose has been ingested, hospital admission is required

Give activated charcoal if an adult presents within one hour of ingestion of more than 250 mg/kg.

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 > 700 mg/L (5.1 mmol/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. Other symptoms to be treated symptomatically.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

ATC code: N02BA01

Aspirin is an anti-inflammatory analgesic and antipyretic.

Aspirin is analgesic, anti-inflammatory, antipyretic and an inhibitor of platelet aggregation. It prolongs the bleeding time. It inhibits fatty acid cyclo-oxygenase by acetylation of the active site of the enzyme, and most of

- Dehydration
- Glucose-6-phosphate dehydrogenase deficiency (aspirin rarely causes haemolytic anaemia)
- Gout (serum urate may be increased)

There is an increased risk of haemorrhage particularly during or after operative procedures (even in cases of minor procedures, e.g. tooth extraction). Use with caution before surgery, including tooth extraction. Temporary discontinuation of treatment may be necessary.

Elderly patients are particularly susceptible to the adverse effects of NSAIDs, including acetylsalicylic acid especially gastrointestinal bleeding and perforation which may be fatal. Where prolonged therapy is required, patients should be reviewed regularly.

Before commencing long-term aspirin therapy for the management of cardiovascular or cerebrovascular disease patients should consult their doctor who can advise on the relative benefits versus the risks for the individual patient.

- Vaccine recipients should avoid use of salicylates for 6 weeks after varicella vaccination.
- Acetylsalicylic acid is not recommended during menorrhagia where it may increase menstrual bleeding.
- Acetylsalicylic acid is to be used with caution in cases of hypertension and when patients have a past history of gastric or duodenal ulcer or haemorrhagic episodes or are undergoing therapy with anticoagulants
- Patients should report any unusual bleeding symptoms to their physician. If gastrointestinal bleeding or ulceration occurs the treatment should be withdrawn
- Serious skin reactions, including Steven-Johnson's syndrome, have rarely been reported in association with the use of acetylsalicylic acid. Acetylsalicylic acid should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- The following warnings are on the OTC product labelling:
 - Do not take if you have a stomach ulcer
 - If symptoms persist for more than 3 days, consult your doctor
 - Medicines should not be taken in pregnancy without consulting your doctor
 - Keep this medicine out of the sight and reach of children
 - Do not give to children aged under 16 years, unless on the advice of a doctor.

Interaction with other medicinal products and other forms of interaction

The following drug interactions should be considered when prescribing aspirin:

- Analgesics - avoid concomitant administration of other salicylates or other NSAIDs (including topical formulations) as increased risk of side effects.
- Alkalizers of urine (eg antacids, citrates) - increased excretion of aspirin.
- Metoclopramide and domperidone - increased rate of absorption of aspirin.
- Mifepristone - avoid aspirin until 8-12 days after mifepristone.

Contraindicated combinations

Methotrexate (used at doses > 15 mg/week):

The combined drugs, methotrexate and acetylsalicylic acid, enhance haematological toxicity of methotrexate due to the decreased renal clearance of methotrexate by acetylsalicylic acid. Therefore, the concomitant use of methotrexate (at doses > 15 mg/week) with acetylsalicylic acid is contraindicated.

Not recommended combinations

Uricosuric agents, e.g. probenecid

Salicylates reverse the effect of probenecid. The combination should be avoided.

Alcohol

Concomitant administration of alcohol and acetylsalicylic acid increases the risk of gastrointestinal bleeding.

Ibuprofen

Ibuprofen may inhibit the effect of low dose acetylsalicylic acid 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.

its pharmacological effects are due to inhibition of the formation of cyclo-oxygenase products including thromboxanes, prostaglandins and prostacyclin. The effect on platelets is cumulative over their 8-day life span because they have no capacity to resynthesize the cyclo-oxygenase enzyme. Aspirin has an active metabolite (salicylate) which, in addition to possessing some anti-inflammatory properties in its own right, also has important effects on respiration, acid-base balance and the stomach. Salicylates stimulate respiration by a direct effect on the medulla, and at high concentrations, uncouple oxidative phosphorylation in muscle, increasing oxygen consumption and carbon dioxide production. Hyperventilation causes respiratory alkalosis which is compensated by renal excretion of bicarbonate. When large toxic doses of salicylate are ingested and carbohydrate metabolism is deranged, lactic and pyruvic acids accumulate and renal function is impaired, resulting in metabolic acidosis. Salicylates have a direct irritant effect on the gastric mucosa and further predispose to ulceration by inhibiting synthesis of vasodilator and cytoprotective prostaglandins.

Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release acetylsalicylic acid 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.

Pharmacokinetic properties

Following oral administration, absorption of non-ionised aspirin occurs in the stomach and intestine. Some aspirin is hydrolysed salicylate in the gut wall. After absorption aspirin is rapidly converted to salicylate but during the first twenty minutes following oral administration, aspirin is the predominant form of the drug in the plasma. Aspirin is bound to plasma proteins and is widely distributed. Plasma-aspirin concentrations decline rapidly (half-life 15-20 minutes) as plasma salicylate concentrations increase. Salicylates are extensively bound to plasma proteins and are rapidly distributed to all body parts. Salicylates appear in breast milk and cross the placenta. Salicylate is mainly eliminated by hepatic metabolism; the metabolites include salicylic acid, salicyl phenolic glucuronide, salicylic acyl glucuronide, gentisic acid, and gentisic acid. Following a 325mg aspirin dose, elimination is a first-order process and the serum-salicylate half-life is about two to three hours; at high aspirin doses, the half-life increases to fifteen to thirty hours. Salicylate is also excreted unchanged in the urine; the amount excreted by this route increases with increasing dose and also depends on urinary pH, about 30% of a dose being excreted in alkaline urine compared with 2% of a dose in acidic urine. Renal excretion involves glomerular filtration, active renal tubular secretion, and passive tubular reabsorption. Salicylates are removed by haemodialysis.

LEGAL CATEGORY: Pharmacy Medicine (PM).

SHELF LIFE: As per product label.

STORAGE CONDITIONS:

Store in a dry place below 30°C. Protect from light.

Keep all medications out of reach of children.

PRESENTATION:

Aspirin 300mg Tablets: Available in blister pack of 10 x 10's, 20x10's and bulk packs of 500's and 1000's.

Aspirin 500mg Tablets: Available in bulk packs of 500's and 1000's.

LAST DATE OF REVIEW: May 2017

LICENCE HOLDER: LABORATORY & ALLIED LTD.

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