SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Aspirin 300mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Aspirin 300mg

Excipient with known effect
Lactose 0.018g
For the full list of **e**xcipients**,** 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 relief of mild to moderate pain, including headache, 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 and stiffness.

4.2 Posology and method of administration

Posology

Adults and children over 16 years of age:

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.

If you do not get better talk to your doctor.

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

Gastro-intestinal irritation may be reduced by taking aspirin with or immediately after food.

Method of administration

Oral

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. In patients with a history of hypersensitivity to aspirin (or any of the excipients) or any other NSAIDs and in patients in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or other NSAIDs.
- Children under 16 years unless specifically indicated (e.g. for Kawasaki's disease)
- Active peptic ulceration or a history of peptic ulceration.
- Haemophilia other coagulopathies, or concurrent anticoagulant therapy
- Gout
- Doses > 100mg/day during the third trimester of pregnancy.

4.4 Special warnings and precautions for use

Caution should be exercised in patients with asthma, allergic disease, , impairment of hepatic or renal function (avoid if severe), impaired cardiac function, uncontrolled hypertension and dehydration, dyspepsia and in patients with nasal polyps or a history of nasal polyps.

Aspirin should be used with caution in patients with infections, since symptoms such as fever and inflammation may be masked.

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.

Caution should be taken in patients with glucose-6-phosphate dehydrogenase deficiency as haemolytic anaemia may occur.

Aspirin may interfere with insulin and gluacagon in diabetes.

Aspirin prolongs bleeding time, mainly by inhibiting platelet aggregation and therefore it should be discontinued several days before scheduled surgical procedures.

Renal, hepatic and haematological status should be monitored during prolonged and high dose aspirin therapy.

Patients with rare problems of galactose intolerance, the Lapp lactase deficiency or glucose –galactose malabsorption should not take this medicine.

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

There is some evidence that drugs which inhibit cyclo-oxygenase / prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

Keep all medicines out of the sight and reach of children.

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 other forms of interaction

Alcohol: Some of the effects of aspirin on the gastrointestinal tract are enhanced by alcohol.

Anaesthetics: Aspirin may potentiate the effects of thiopental anaesthesia.

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

Anti-coagulants: Aspirin may enhance the effects of anti-coagulants (e.g. increased risk of bleeding with concomitant heparin; increased risk of major bleeding [cerebral/intracranial haemorrhage] with concomitant streptokinase); concurrent use is contraindicated (see Section 4.3).
Anti-epileptics: May enhance the effects of phenytoin and sodium valproate. Increased risk of bleeding when aspirin and sodium valproate or valproic acid used concomitantly.

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

ACE Inhibitors: Aspirin may reduce the antihypertensive effects of ACE inhibitors. Risk of renal impairment when > 300mg/day aspirin is given concomitantly with ACE inhibitors, particularly in patients with poor renal perfusion.

Angiotensin-II receptor antagonists: Concomitant administration with aspirin at doses >3g may reduce the antihypertensive effect of angiotensin-II antagonists. Risk of renal impairment with >300mg/day aspirin, particularly in patients with poor renal perfusion.

Antibacterials: The toxicity of sulphonamides may be increased.

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

Antiplatelet drugs: Possibility of increased antiplatelet effect, with abnormal bruising and prolonged bleeding time, with clopidogrel or ticlopidine.

Ascorbic acid: Absorption of ascorbic acid may be reduced.

Calcium channel blockers: Possibility of increased antiplatelet effect, with abnormal bruising and prolonged bleeding time, with calcium channel blockers such as verapamil.

Corticosteroids: The risk of gastrointestinal bleeding and ulceration is increased. Corticosteroids reduce the plasma salicylate concentration., however, salicylate toxicity may occur when corticosteroids are withdrawn in patients also taking aspirin.

Diuretics: Antagonism of the diuretic effect of spironolactone. 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.

Gold Compounds: May increase risk of aspirin-induced liver damage.

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.

Other non-steriodal anti-inflammatory drugs (NSAIDs): Concurrent administration can increase side effects, although plasma concentrations of some other NSAIDs (e.g. indometacin, fenoprofen) may be reduced.

Thyroid function tests: aspirin may interfere with thyroid function tests.

Uricosurics: Effect of probenecid and sulfinpyrazone reduced. Uricosuric effects of aspirin reduced by phenylbutazone.

Vasodilators: Daily aspirin should not exceed 80mg/day when given with cilostazol.

4.6 Fertility, Pregnancy and lactation

Pregnancy

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 salicyclic acid should not be given unless clearly necessary. If acetylsalicyclic 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 oligo-hydroaminiosis; 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.
- inhibiton of uterine contractions resulting in delayed or prolonged labour.

Consequently, acetylsalicyclic acid at doses of 100mg/day and higher is contraindicated during the third trimester of pregnancy.

Breastfeeding

Aspirin should be avoided during breast feeding – possible risk of Reye's syndrome.

4.7 Effects on ability to drive and use machines

Aspirin does not usually affect the ability to drive and use machines.

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, aplastic anaemia, agranulocytosis and

pancytopenia. Haemolytic anaemia can occur in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Immune system: Aspirin may precipitate bronchospasm and induce dyspnoea**,** asthma attacks, rhinitis, angioedema **,** urticaria, rash, or other hypersensitivity in susceptible individuals.

Gastro-intestinal: There is a relatively high incidence of irritation with nausea, vomiting, diarrhoea and dyspepsia. Slight blood loss, which is often asymptomatic, may occur in some patients; it is not usually of clinical significance but may result in iron-deficiency anaemia during long-term therapy. Haematemesis and/or melaena may occur. It may induce gastrointestinal ulceration and haemorrhage, occasionally major.

Hepatobiliary: Increased aminotransferase levels, usually reversible on withdrawal; dose-dependent focal hepatic necrosis.

Renal and urinary disorders: Haematuria may occur.

Skin: Skin reactions, including Stevens-Johnson syndrome or toxic epidermal necrolysis, may occur in susceptible patients.

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 the Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

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 (5.1mmol/L). Single doses less than 100mg/kg are unlikely to cause serious poisoning.

Symptoms

Common features include nausea, vomiting, dehydration, headache, tinnitus, vertigo, dizziness, deafness, sweating, warm extremities with bounding pulses, restlessness, 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. Cardiovascular collapse and respiratory failure may also occur.

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 or haemoperfusion are effective methods of removing salicylate from plasma, however, haemodyalisis is the treatment of choice for severe poisoning and should be considered in patients with plasma-salicylate concentrations mg/litre (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

Pharmacotherapeutic group:

Other analgesics and antipyretics, Salicylic acid and derivatives, ATC code: N02B A01

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

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.

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.

Distribution
Aspirin is found in the saliva, milk, plasma and synovial fluid at concentrations less than blood and crosses the placenta.
Salicylate - extensive protein binding.
Aspirin - protein binding to a small extent.

Biotransformation
In the blood, rapid hydrolysis to salicylic acid; glucuronic acid/glycine conjugation to form glucuronides and salicyluronic acid; oxidation of a small proportion.

Elimination
Excreted in the urine mainly as salicyluronic acid. Salicylate reabsorbed by renal tubules in acid urine, and alkaline diuresis will increase the rate of excretion; 85% of dose excreted as free salicylate.

Plasma / Aspirin	Approximately 17 minutes
Plasma / Salicylate	Low doses 2-4 hours High doses up to 19 hours

5.3 Preclinical safety data
There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Starch

Lactose

Purified talc

6.2 Incompatibilities

Aspirin is pharmaceutically incompatible with iron salts and alkalis.

6.3 Shelf life

3 years from the date of manufacture.

6.4 Special precautions for storage

Store in a cool dry place below 25°C.

6.5 Nature and contents of container

Blister packs:

8, 10, 12, 16, 20, 24, 28, 30, 32, 48, 50, 96 or 100

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

Polypropylene/polyethylene Containers:

25, 50, 100, 250, 500, 1000 and 5,000.

Not all pack sizes may be marketed

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Medipoint UK Ltd

30 Hatfeild Mead
Morden
Surrey
SM4 5PE
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 57630/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19 June 1980 / 27 September 1996

10 DATE OF REVISION OF THE TEXT

21/04/2023