SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Aspirin 300mg Caplets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Aspirin 300mg

3 PHARMACEUTICAL FORM

Tablet

White capsule shaped tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of mild to moderate pain, for example, migraine, toothache, neuralgia, headache, sore throat, dysmenorrhoea or period pain.

For the relief of the symptoms of minor inflammatory conditions such as rheumatic pain, aches and pains**,** sciatica, lumbago, fibrositis, muscular pains, joint swelling, sprains and strains and stiffness.

To reduce feverishness , feverish cold and aches and pains of cold and flu (not in children under 16).

4.2 Posology and method of administration

Route of administration: oral.

Adults and Children over 16 years: 1 to 3 caplets to be swallowed with water. The dose should not be taken more frequently than every 4 hours and not more than 4 times in any 24 hour period.

Maximum dose: 12 caplets (3.6g) every 24 hours in divided doses.

The elderly: A total reduction in the daily dose may be advisable.

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.

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 or any of the excipients (see 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.
v) Gout.
vi) 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 with patients with glucose-6-phosphate dehydrogenase deficiency as haemolytic anaemia may occur.
Aspirin may interfere with insulin and glucagons 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.
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 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.

Antidepressants: Increased risk of bleeding when aspirin given with selective serotonin re-uptake inhibitors (SSRIs) or venlafaxine.

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 sprionolactone. 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 zafirlukst 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-steroidal anti-inflammatory drugs (NSAIDs): Although plasma concentrations of some other NSAIDs (e.g. indometacin, fenoprofen) may be reduced, concomitant administration of aspirin with other NSAIDs can increase side effects and should therefore be avoided. The combination of low dose aspirin with other NSAIDs should only be used if absolutely necessary and patients on this combination should be closely monitored. 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).

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.

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

4.7 Effects on ability to drive and use machines

None known.

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, dyspepsia and slight asymptomatic blood loss. 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.

4.9 Overdose

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 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, hypepryrexia, hypoglycaemia, hypokalaemia, thrombocytopaenia, increased INR/PTR, intravascular coagulation, renal failure and non-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 alkalisation, 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

Aspirin is an analgesic and anti-pyretic 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.

Blood Concentration

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

Half Life

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

Distribution

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

Metabolism

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

Excretion

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

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 SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch
Microcrystalline Cellulose
Calcium Stearate

6.2 Incompatibilities

None stated except as in 'Interactions with other medicaments'.
No Data Held

6.3 Shelf life

3 years from date of manufacture.

6.4 Special precautions for storage

Store in the original container in order to protect from moisture.

Do not store above 25°C.

6.5 Nature and contents of container

Blister Pack*:*

Pack sizes: 8, 10, 12, 16, 20, 24, 28, 30 & 32, 48, 50, 96 & 100.

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

Polypropylene/polyethylene containers:

Pack sizes: 25, 50 & 100
250, 500 & 1000 as Dispensary pack

6.6 Special precautions for disposal

Return any left over tablets to the Pharmacist

7 MARKETING AUTHORISATION HOLDER

Medipoint UK Ltd
30 Hatfeild Mead
Morden
Surrey
SM4 5PE
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 57630/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/03/2009

10 DATE OF REVISION OF THE TEXT

24/04/2023