SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Aspirin 300mg Gastro-resistant Tablets
Postmi 300mg Gastro-resistant Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 300mg Aspirin.

Excipient(s) with known effect

Sodium Hydroxide 0.14 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro-resistant tablet.
Right round, cylindrical biconvex tablets with a glossy pink coating, printed POSTMI 300EC or Aspirin 300EC in black on one side.

4.1 Therapeutic indications

Aspirin 300mg Tablets contain an anti-pyretic, anti inflammatory and analgesic, and are gastro-resistant to reduce the gastric side-effects of aspirin in rheumatoid arthritis and in conditions requiring continued management with aspirin.

Aspirin may be used to reduce the risk of myocardial infarction in patients with unstable angina or in patients with a previous history of myocardial infarction.

4 CLINICAL PARTICULARS

4.2 Posology and method of administration

Posology

Analgesic, anti-inflammatory, anti-pyretic;
Adults (including the elderly) and children over 16 years:
3 tablets (900mg) 3-4 times daily as required, at least 4 hours apart.

Anti-thrombotic effect – to reduce the risk of myocardial infarction:
One tablet daily

Paediatric population
Aspirin should not be used in children under 16 years, unless specifically indicated (e.g. for Kawasaki's disease).

Method of administration

For oral administration.

Aspirin must not be chewed or crushed. The tablets are best taken before meals.

4.3 Contraindications

Aspirin should not be administered to patients:

- Hypersensitivity to the active substance(s), other NSAIDs or to any of the excipients listed in section 6.1;
- with active peptic ulceration or a history of peptic ulceration and/or gastric/intestinal haemorrhage e, or other kinds of bleeding such as cerebrovascular haemorrhages;
- with haemophilia and other bleeding disorders;
- for the treatment of gout;
- who are breastfeeding (see section 4.6);
- with severe hepatic impairment;
- with severe renal impairment;
- taking Methotrexate used at doses >15mg/week (see section 4.5);
- during the third trimester of pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

Aspirin should be used with caution in patients with asthma or allergic disorders.

Caution should also be exercised in patients with:
- hepatic impairment;
- renal impairment;
- dehydration;
- uncontrolled hypertension.

High doses of aspirin may precipitate acute haemolytic anaemia in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency.

Aspirin should be used with caution in the elderly because of the risk of serious side effects. 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 and perforation which may be fatal. For elderly patients, the lowest possible dose for the shortest period of time should be used.

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 it should not be given to children under 16, unless specifically indicated (e.g. for Kawasaki's disease).

Aspirin prolongs bleeding time, mainly by inhibiting platelet aggregation. 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.

Aspirin may also precipitate bronchospasm or induce attacks of asthma in susceptible subjects. 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.

Serious skin reactions, including Steven-Johnsons syndrome, have rarely been reported in association with the use of acetylsalicylic acid (see section 4.8). Aspirin should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Aspirin may interfere with insulin and glucagon in diabetes.

Salicylates should not be used in patients with a history of coagulation abnormalities as they may also induce gastro-intestinal haemorrhage, occasionally major (see section 4.3).

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

Patients with hypertension should be carefully monitored.

This medicine contains 0.14 mg sodium i.e. less than 1 mmol (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of aspirin with mifepristone should be avoided, because of a theoretical risk that prostaglandin synthetase inhibitors may decrease the efficacy of mifepristone. The manufacturer of mifepristone recommends that aspirin should be avoided until eight to twelve days after mifepristone has been discontinued.

Concomitant use of aspirin with NSAIDs may increase the risk of ulcerations and gastrointestinal bleeding due to synergistic effects. 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.

Metamizole may reduce the effect of acetylsalicylic acid on platelet aggregation, when taken concomitantly. Therefore, this combination should be used with caution in patients taking low dose aspirin for cardioprotection.

Aspirin may decrease the plasma concentration of some other NSAIDs, for example, fenbufen, diclofenac sodium, indometacin, and piroxicam.

The antiplatelet effect of aspirin may be reduced by ibuprofen.

Carbonic anhydrase inhibitors: Reduced excretion of acetazolamide; salicylate intoxication has occurred in patients on high dose salicylate regimes and carbonic anhydrase inhibitors. Concurrent administration of carbonic anhydrase inhibitors such as acetazolamide and salicylates may result in severe acidosis and increased central nervous system toxicity.

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

The rate of absorption of aspirin is increased by metoclopramide.

The excretion of aspirin may be increased by alkaline urine, which can occur with some antacids. Antacids and adsorbents: The excretion of aspirin is increased in alkaline urine; kaolin possibly reduces absorption. Patients should be advised against ingesting antacids simultaneously to avoid premature drug release e.g. aluminium hydroxide and magnesium carbonate.

Concommitant use of anticoagulants e.g. coumarins, phenindione, heparins; antidepressants e.g. clopidogrel, iloprost and sibutramine with aspirin may lead to an increased risk of bleeding.

Aspirin enhances the effects of antiepileptics e.g. phenytoin and valproate.

There is a risk of renal impairment when aspirin (in doses over 300mg daily) is given with ACE inhibitors or angiotensin-II receptor antagonists and the hypotensive effect of these drugs is antagonised e.g. captopril, enalapril maleate, valsartan, losartan.

Diuretics: Antagonism of the diuretic effect of spironolactone. Generally, there is a risk of acute renal failure due to the decreased glomerular filtration via decreased renal prostaglandin synthesis. Hydrating the patient and monitoring renal function at the start of the treatment is recommended.

Co-administration of aspirin with zafirlukast may result in increased plasma concentration of zafirlukast.

Aspirin may reduce the effectiveness of spironolactone and inhibit the action of uricosurics e.g. probenecid and sulfinpyrazone when administered concurrently with these drugs.

The toxicity of methotrexate and carbonic anhydrase inhibitors may be increased when administered concurrently with aspirin. The activity of methotrexate may be markedly enhanced and its toxicity increased. The combined drugs, methotrexate and acetylsalicylic acid, enhance haematological toxicity of methotrexate due to decreased renal clearance of methotrexate by acetylsalicylic acid. Therefore doses higher than 15 mg/week are contraindicated. If doses lower than 15 mg/week are used, weekly blood count checks should be done during the first week of the combination. Enhanced monitoring should take place in the presence of even mildly impaired renal function and in elderly patients.

Short term (≤ 4 days) co-administration of aspirin with cilostazol suggested a 23-25% increase in inhibition of ADP-induced *ex vivo* platelet aggregation when compared to aspirin alone. Therefore it is recommended that the daily dose of aspirin should not exceed 80mg.

Alcohol: Some of the effects of aspirin on the gastrointestinal tract are enhanced by alcohol. Concomitant administration of alcohol and acetylsalicylic acid increases the risk of gastrointestinal bleeding.

Hypoglycaemic agents: Aspirin may enhance the effects of insulin and oral hypoglycaemic agents including insulin, sulphonylurea oral hypoglycaemics (e.g. glipizide).

The bleeding risk associated with aspirin might be further increased by the concurrent use of a SSRI (Selective Serotonin Reuptake Inhibitor) such as citalopram or fluoxetine or a SNRI (Serotonin–norepinephrine reuptake inhibitor) such as venlafaxine.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

Although clinical and epidemiological evidence suggests the safety of aspirin for use in pregnancy, caution should be exercised when administered to pregnant patients.

Aspirin has the ability to alter platelet function and, therefore, there may be a risk of haemorrhage in infants whose mothers have consumed aspirin during pregnancy. The onset of labour may be delayed and the duration increased, with an increase in maternal blood loss. Therefore, analgesic doses should be avoided during the last trimester of pregnancy.

High doses of aspirin may result in closure of foetal ductus arteriosus in utero and possibly persistent pulmonary hypertension in the new-born. Kenicterus may be a consequence of jaundice in neonates.

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/day 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, acetylsalicylic 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 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. Administration of aspirin at doses greater than 300 mg/day, shortly before birth, can lead to intra-cranial haemorrhage, particularly in premature babies.

Breast-feeding
The intake of aspirin by breast-feeding patients is contraindicated as there is a risk of Reye's syndrome. Regular use of high doses could impair platelet function and produce hypoprothrombinaemia in the infant if neonatal vitamin K stores are low.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Aspirin has minor influence on the ability to drive or use machines, as it may make you feel dizzy.

4.8 Undesirable effects

The information below lists reported adverse reactions, ranked using the following frequency classification:

Common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); not known (cannot be estimated from the available data).

Side effects are generally mild and infrequent:

System Organ Class	Frequency	Undesirable Effects
Blood and lymphatic system disorders	Common	Increased bleeding tendencies
	Rare	Thrombocytopenia, granulocytosis, aplastic anaemia, anaemia following chronic GI blood loss or acute haemorrhage.
	Not known	Bleeding time prolonged**, epistaxis, gingival bleeding, platelet adhesiveness decreased, hypoprothrombinaemia when large doses are used, haematuria, purpura, ecchymoses, haemoptysis,

		haematemesis, malaena*, gastrointestinal bleeding haematoma, cerebral haemorrhage, haemolytic anaemia (in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency).
Immune system disorders	Rare	Hypersensitivity reactions, allergic respiratory disease exacerbated by aspirin, angio-oedema, allergic oedema, anaphylactic reaction including shock.
Metabolism and nutrition disorders	Not known	Hyperuricaemia
Nervous system disorders	Rare	Intracranial haemorrhage
	Not known	Headache, vertigo
Ear and Labyrinth disorders	Not known	Reduced hearing ability; tinnitus
Vascular disorders	Rare	Haemorrhagic vasculitis
Respiratory, thoracic and mediastinal disorders	Uncommon	Rhinitis, dyspnoea
	Rare	Bronchospasm, asthma attacks
Gastrointestinal disorders	Common	Dyspepsia
	Rare	Gastrointestinal haemorrhage, nausea, vomiting
	Not known	Gastric or duodenal ulcers and perforation, diarrhoea or gastritis
Hepatobiliary disorders	Not known	Hepatic insufficiency
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	Rare	Steven-Johnsons syndrome, Lyells syndrome, purpura, erythema nodosum, erythema multiforme or skin rash.
Renal and urinary tract disorders	Not known	Impaired renal function, salt and water retention.

* Existing (haematemesis, melaena) or occult gastrointestinal bleeding, which may lead to iron deficiency anaemia (more common at higher doses).

** Symptoms may persist for a period of 4–8 days after acetylsalicylic acid discontinuation. As a result there may be an increased risk of bleeding during surgical procedures.

Paediatric population

Association with Reye's syndrome in children can lead to hearing disturbances (such as tinnitus), vertigo or mental confusion see Section 4.4.

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 Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Salicylate poisoning is usually associated with plasma concentrations>350 mg/L (2.5 mmol/L). Most adult deaths occur in patients whose concentrations exceed 700 mg/L (5.1 mmol/L). Single doses less than 100 mg/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, thrombocytopaenia, 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 250 mg/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>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.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Blood and blood forming organs – antithrombotic agents, ATC code: B01AC

Mechanism of action

Aspirin has analgesic, anti-inflammatory, anti-pyretic and uricosuric actions.

It is used for the relief of the less severe types of pain such as headache, neuritis, acute and chronic rheumatoid arthritis, myalgias and toothache.

Gastro-resistant tablets may be used with the intention of minimising gastric irritation. In the treatment of minor febrile conditions, such as colds or influenza, aspirin is of value for the reduction of temperature and relief of the headache and the joint and muscle pains.
As an anti-pyretic, aspirin, like many related drugs, acts on the heat-regulating centres in the brain to bring about a dissipation of body heat through cutaneous vasodilatation. The usual dose of aspirin as an analgesic and anti-pyretic is 0.3 to 1g which may be repeated according to clinical needs, up to a maximum of 4g daily.

Pharmacodynamic effects

Aspirin is used in the treatment of acute and chronic rheumatic states. Maximum suppression of rheumatic symptoms occurs with plasma concentrations of about 300 µg/ml, but these concentrations are frequently associated with mild toxic effects such as nausea and tinnitus; adequate control of rheumatic symptoms may often be achieved with lower concentrations. In chronic rheumatic disease, 300 to 900mg is administered every 4 hours over long periods. In acute rheumatism, 4 to 8g daily in divided doses is sometimes recommended, but doses of 150mg/kg body-weight daily have been given initially.

5.2 Pharmacokinetic properties

Absorption

Absorption of non-ionised aspirin occurs in the stomach. 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.

Acetylsalicylates and salicylates are also readily absorbed from the intestine. Hydrolysis to salicylic acid occurs rapidly in the intestine and in the circulation.

Distribution

Aspirin and salicylates are rapidly distributed to all body tissues.

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

The rate of excretion of aspirin varies as the pH rises, being greatest at pH 7.5 and above. Aspirin is also excreted as salicylic acid and as glucuronide conjugate, and as salicyluric and gentisic acid. 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.

5.3 Preclinical safety data

None stated

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose, Methacrylic Acid Copolymer, Talc, Maize Starch, Silica, Triethyl Citrate, Zinc Stearate, Sodium Hydroxide, Polyethylene Glycol 6000, propylene glycol, Shellac, Titanium Dioxide (E171) and Iron Oxide (E172).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Polypropylene and polyethylene containers (Tracer packs): pack sizes 25, 28, 30, 50, 84, 100.

Polypropylene containers (Securitainers): pack size 1000.

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

Focus Pharmaceuticals Limited

Dashwood House,
69 Old Broad Street,
London, EC2M 1QS,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 20046/0033

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/07/2004 / 12/02/2009

10 DATE OF REVISION OF THE TEXT

07/11/2023