

SUMMARY OF PRODUCT CHARACTERISTICS**1. NAME OF THE MEDICINAL PRODUCT**

Dispersible Aspirin 75 mg Tablets

APPROVED*By Geeta at 5:01 pm, Sep 28, 2016***2.****QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains aspirin 75 mg as the active ingredient.

Excipients with known effect: Also contains lactose monohydrate 27.5 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Dispersible Tablets

White, flat tablets, debossed <F> on one side.

4. CLINICAL PARTICULARS**4.1 Therapeutic indications**

For the secondary prevention of thrombotic cerebrovascular or cardiovascular disease and following by –pass surgery.

4.2 Posology and method of administrationPosology

The advice of a doctor should be sought before commencing therapy for the first time. The usual dosage, for long term use, is 75-150mg once daily. In some circumstances a higher dose may be appropriate, especially in the short term, and up to 300mg a day may be used on the advice of a doctor. In general, acetylsalicylic acids should be used with caution in elderly patients who are more prone to adverse events. The usual adult dose is recommended in the absence of severe renal or hepatic insufficiency (see sections 4.3 and 4.4). Treatment should be reviewed at regular intervals.

Children:

Do not give to children aged under 16 years, unless specifically indicated e.g. for Kawasaki's disease (see section 4.4).

Method of administration

Oral administration, after dissolution in water.

4.3 Contraindications

- Hypersensitivity to salicylic acid compounds or prostaglandin synthetase inhibitors (e.g. certain asthma patients who may suffer an attack or faint and certain patients who may suffer from bronchospasm, rhinitis and urticaria) and to any of the excipients listed in section 6.1
- Children under 16 years unless specifically indicated (e.g. for Kawasaki's disease)
- Active peptic ulceration or a history of peptic ulceration or dyspepsia and/or gastric/intestinal haemorrhage, or other kinds of bleeding such as cerebrovascular haemorrhages.
- Haemorrhagic diathesis; coagulation disorders such as haemophilia and thrombocytopenia or concurrent anticoagulant therapy
- Patients who are suffering from Gout
- Severe hepatic impairment
- Severe renal impairment
- Doses >100mg/day during the third trimester of pregnancy (see section 4.6); Methotrexate used at doses >15mg/week (see section 4.5)
- Nasal polyps associated with asthma (high risk of severe sensitivity reactions)

4.4 Special warnings and precautions for use

Aspirin 75 mg is not suitable for use as an anti inflammatory/analgesic/antipyretic.

Recommended for use in adults and adolescents from 16 years of age. This medicinal product is not recommended for use in adolescents/children under 16 years unless the expected benefits outweigh the risks. Acetylsalicylic acid may be a contributory factor in the causation of Reye's Syndrome in some children.

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 75 mg is not recommended during menorrhagia where it may increase menstrual bleeding.

Aspirin 75 mg 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.

Acetylsalicylic acid should be used with caution in patients with moderately impaired renal or hepatic function (contraindicated if severe), or in patients who are dehydrated since the use of NSAIDs may result in deterioration of renal function. Liver function tests should be performed regularly in patients presenting slight or moderate hepatic insufficiency.

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).

Serious skin reactions, including Steven-Johnsons syndrome, have rarely been reported in association with the use of acetylsalicylic acid (see section 4.8). Aspirin 75 mg should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Elderly patients are particularly susceptible to the adverse effects of NSAIDs, including acetylsalicylic acid especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2). Where prolonged therapy is required, patients should be reviewed regularly.

Concomitant treatment with Aspirin 75 mg and other drugs that alter haemostasis (i.e. anticoagulants such as warfarin, thrombolytic and antiplatelet agents, anti-inflammatory drugs and selective serotonin reuptake inhibitors) is not recommended, unless strictly indicated, because they may enhance the risk of haemorrhage (see section 4.5). If the combination cannot be avoided, close observation for signs of bleeding is recommended.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration, such as oral corticosteroids, selective serotonin-reuptake inhibitors and deferasirox (see section 4.5).

Acetylsalicylic acid in low doses reduces uric acid excretion. Due to this fact, patients who tend to have reduced uric acid excretion may experience gout attacks (see section 4.5).

The risk of hypoglycaemic effect with sulfonylureas and insulins may be potentiated with Aspirin 75 mg taken at over dosage (see section 4.5).

Aspirin should be avoided in late pregnancy and generally during breast feeding (see section 4.6).

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

4.5 Interaction with other medicinal products and other forms of interaction

Combinations requiring precautions for use or to be taken into account

Anticoagulants: e.g. coumarin, heparin, warfarin and phenindione

Increased risk of bleeding due to inhibited thrombocyte function, injury of the duodenal mucosa and displacement of oral anticoagulants from their plasma protein binding sites. The bleeding time should be monitored (see section 4.4).

Anti-platelet agents (e.g. clopidogrel and dipyridamole) and selective serotonin re-uptake inhibitors (SSRIs; such as sertraline or paroxetine)

Increased risk of gastrointestinal bleeding (see section 4.4).

Antidiabetics, e.g. sulfonylureas

Salicylics may increase the hypoglycaemic effect of sulfonylureas.

Digoxin and lithium

Acetylsalicylic acid impairs the renal excretion of digoxin and lithium, resulting in increased plasma concentrations. Monitoring of plasma concentrations of digoxin and lithium is recommended when initiating and terminating treatment with acetylsalicylic acid. Dose adjustment may be necessary.

Diuretics and antihypertensives

NSAIDs may decrease the antihypertensive effects of diuretics and other antihypertensive agents. As for other NSAIDs concomitant administration with ACE-inhibitors increases the risk of acute renal insufficiency.

Diuretics: 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.

Carbonic anhydrase inhibitors (acetazolamide)

May result in severe acidosis and increased central nervous system toxicity. Salicylate intoxication has occurred in patients on high dose salicylate regimens and carbonic anhydrase inhibitors.

Systemic corticosteroids

The risk of gastrointestinal ulceration and bleeding may be increased when acetylsalicylic acid and corticosteroids are co-administered (see section 4.4).

Methotrexate (used at doses <15 mg/week)

The combined drugs, methotrexate and acetylsalicylic acid, may increase haematological toxicity of methotrexate due to decreased renal clearance of methotrexate by acetylsalicylic acid. Weekly blood count checks should be done during the first weeks of the combination. Enhanced monitoring should take place in the presence of even mildly impaired renal function, as well, as in elderly.

Other non-steroidal anti-inflammatory drugs (NSAIDS)

Increased risk of ulcerations and gastrointestinal bleeding due to synergistic effects.

Ibuprofen

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)

Ciclosporin, tacrolimus

Concomitant use of NSAIDs and ciclosporin or tacrolimus may increase the nephrotoxic effect of ciclosporin and tacrolimus. The renal function should be monitored in case of concomitant use of these agents and acetylsalicylic acid.

Valproate

Acetylsalicylic acid has been reported to decrease the binding of valproate to serum albumin, thereby increasing its free plasma concentrations at steady state.

Phenytoin (an antiepileptic)

Salicylate diminishes the binding of phenytoin to plasma albumin. This may lead to decreased total phenytoin levels in plasma, but increased free phenytoin fraction. The unbound concentration, and thereby the therapeutic effect, does not appear to be significantly altered.

Alcohol:

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

Antacids and adsorbents:

Antacids will reduce the effect of aspirin. Principle incompatibilities are iron salts, carbonates and alkali hydroxides.

Antiemetics:

Metoclopramide and domperidone enhances the effects of aspirin by increasing the rate of absorption.

Antibacterials:

The toxicity of sulfonamides may be increased.

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.

Ototoxic medicine (e.g vancomycin)

potential for ototoxicity increased. Hearing loss may occur and may progress to deafness even after discontinuation of the medication. Effects may be reversible but are usually permanent.

Not recommended combinations

Uricosuric agents, e.g. probenecid

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

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 Aspirin Tablets BP 75 mg is contraindicated (see section 4.3).

4.6 Fertility, Pregnancy and Lactation

Pregnancy

Controlled trials in humans using aspirin have not shown evidence of teratogenic effects. However, studies in animals have shown that salicylates can cause birth defects including fissure of the spine and skull, facial clefts and malformations of the CNS, viscera and skeleton. Ingestion of aspirin during the last two weeks of pregnancy may increase the risk of fetal or neonatal haemorrhage. Regular or high dose use of salicylates late in pregnancy may result in constriction or premature closing of the fetal ductus arteriosus, increased risk of still birth or neonatal death, decreased birth weight, prolonged gestation and labour, complicated deliveries and increased risk of maternal or fetal haemorrhage and possibly persistent pulmonary hypertension of newborn or kernicterus in jaundiced neonates. Pregnant women should be advised not to take aspirin in the last three months of pregnancy unless under medical supervision.

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.

Lactation

Aspirin should be avoided while breastfeeding – due to the possible risk of Reye’s syndrome in the infant. Regular use of high doses could impair platelet function and produce hypoprothrombinaemia in the infant if neonatal Vitamin K stores are low.

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 grouped on the basis of System Organ Class. Within each system organ class the frequencies are defined as: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) and not known (cannot be estimated from the available data)

<p>Blood and lymphatic system disorders</p>	<p><i>Common:</i></p> <p>Increased bleeding tendencies.</p> <p><i>Rare:</i></p> <p>Thrombocytopenia, granulocytosis, aplastic anaemia.</p> <p><i>Not known:</i></p> <p>Cases of bleeding with prolonged bleeding time such as epistaxis, gingival bleeding, hypoprothrombinaemia. 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.</p> <p>Existing (haematemesis, melaena) or occult gastrointestinal bleeding, which may lead to iron deficiency anaemia (more common at higher doses).</p>
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Immune system disorders	<p><i>Rare:</i></p> <p>Hypersensitivity reactions (bronchospasm, asthma, rhinitis, urticaria), angio-oedema, allergic oedema, anaphylactic reactions including shock.</p>
Metabolism and digestive system disorders	<p><i>Not known:</i></p> <p>Hyperuricemia.</p>
Nervous system disorders	<p><i>Rare:</i></p> <p>Intracranial haemorrhage</p> <p><i>Not known:</i></p> <p>Headache, vertigo.</p>
Ear and labyrinth disorders	<p><i>Not known:</i></p> <p>Reduced hearing ability; tinnitus.</p>
Vascular disorders	<p><i>Rare:</i></p> <p>Hemorrhagic vasculitis.</p>
Respiratory, thoracic and mediastinal disorders	<p><i>Uncommon:</i></p> <p>Rhinitis, dyspnoea.</p> <p><i>Rare:</i></p> <p>Bronchospasm, asthma attacks.</p>
Reproductive system and mammary disorders	<p><i>Rare:</i> Menorrhagia</p>
Gastrointestinal disorders	<p><i>Common:</i></p> <p>Dyspepsia.</p> <p><i>Rare:</i></p> <p>Severe gastrointestinal haemorrhage, nausea, vomiting.</p>

	<p><i>Not known:</i></p> <p>Gastric or duodenal ulcers (black tarry stools, severe stomach pain, vomiting blood) and perforation, diarrhoea.</p>
Hepatobiliary disorders	<p><i>Not known:</i></p> <p>Hepatic insufficiency</p>
Skin and subcutaneous tissue disorders	<p><i>Uncommon:</i></p> <p>Urticaria.</p> <p><i>Rare:</i></p> <p>Steven-Johnsons syndrome, Lyells syndrome, purpura, erythema nodosum, erythema multiforme.</p>
Renal and urinary tract disorders	<p><i>Not known:</i> Impaired renal function, salt and water retention.</p>

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 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, coma, fever 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.

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 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

Pharmaceotherapeutic group: Blood and blood forming organs - antithrombotic agents

ATC Code: BO1A C

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

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 (see section 5.1).

5.2 Pharmacokinetic properties

Absorption

Absorption of non-ionised aspirin occurs in the stomach and intestine. Some aspirin is hydrolysed to salicylate in the gut wall. After absorption aspirin is rapidly converted to salicylate but during the first 20 minutes aspirin is the predominant form of the drug in the plasma. 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 130 mcg/ml of salicylate are attained in 2 to 4 hours.

Distribution

Aspirin is bound to plasma proteins and is widely distributed. Aspirin is found in the saliva, milk, plasma and synovial fluid at concentrations less than blood and crosses the placenta.

Metabolism

Plasma – aspirin concentrations decline rapidly (half – life 15-20 minutes) as plasma salicylate concentrations increase. Both aspirin and salicylate have pharmacological activity; only aspirin has an anti-platelet effect.

Salicylate is mainly eliminated by hepatic metabolism- the metabolites include salicylic acid, salicyl phenolic glucuronide, salicylic acyl glucuronide, gentisic acid, and gentisuric acid.

*Excretion*Plasma / Aspirin $t_{1/2}$

Approximately 17 minutes

Plasma / Salicylate $t_{1/2}$

Low doses 2-4 hours

High doses up to 19 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.

5.3 Preclinical safety data

There is no pre-clinical data of relevance to a prescriber which is additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS**6.1 List of excipients**

Sodium Saccharin
Citric acid
Calcium Carbonate
Maize Starch
Purified Talc
Sodium Lauryl Sulfate
Lactose monohydrate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

Blister packs: store in the original package.

Polypropylene/polyethylene containers: keep the container tightly closed.

6.5 Nature and contents of container

Polypropylene/polyethylene containers:

500 & 1000 tablets

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

Or

Child resistant Aluminium/PVC blister packs: 20µm hard aluminium foil laminated to 15µm rigid PVC and 250µ PVC film base in cartons:

Blister packs: 112

6.6. Special precautions for disposal and other handling

No special requirement.

7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories Ltd,
Unit 3, Canalside,
Northbridge Road
Berkhamsted
HP4 1EG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0156

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/02/2006

10 DATE OF REVISION OF THE TEXT

27/09/2016