SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Aspirin 75mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITIONS:

Each tablet contains Acetylsalicylic acid (Aspirin) 75.0 mg.
Excipients with known effect
Also contains 50.2 mg lactose monohydrate.
For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM:

Tablet
White to off white, circular flat beveled edge, uncoated tablet, scored on one side and plain on other side.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

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 administration :

For the management of cardiovascular or cerebrovascular disease:

The advice of a doctor should be sought before commencing therapy for the first time. The usual dosage, for long term use, is 75-150 mg once daily. In some Circumstances a higher dose may be appropriate, especially in the short term, and up to 300 mg 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.

These tablets should be taken orally with a drink of water.

Children under 16 years: Aspirin 75mg tablets are not indicated for use in children and young people less than 16 years of age (see 'Special Warnings and Precautions for Use').
Children 16 years or over: As for adults and the elderly.

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 or non-steroidal anti-inflammatory drugs. Not to be given to children under 16 years unless specifically indicated (eg. For Kawasaki's disease)
- Active, or history of recurrent peptic ulcer and/or gastric/intestinal haemorrhage, or other kinds of bleeding such as cerebrovascular haemorrhages;
- Haemorrhagic diathesis; coagulation disorders such as haemophilia and thrombocytopenia;
- Patients who are suffering from gout;
- Severe hepatic impairment;
- Severe renal impairment;
- Doses >100 mg/day during the third trimester of pregnancy (see section 4.6);
- Methotrexate used at doses >15mg/week (see section 4.5).

4.4 Special warnings and precautions for use:

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

Aspirin 75mg tablets 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.

Aspirin may induce gastro-intestinal haemorrhage, occasionally major. 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 75mg tablets 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 75mg tablets 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 75mg tablets taken at over dosage (see section 4.5).
Aspirin should be avoided in late pregnancy and generally during breast feeding (see section 4.6).

Aspirin 75mg tablet contain 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 interactions:

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 75mg tablets is Contraindicated (see section 4.3).

Not recommended combinations

Uricosuric agents, e.g. probenecid

Inhibits the effect of uricosurics (probenecide and sulfinpyrazone). Salicylates reverse the effect of probenecid. The combination should be avoided.

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. sulphonylureas

Salicylics may increase the hypoglycaemic effect of sulphonylureas.

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.

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 NSAIDs
Aspirin may also potentiate the effects and side effects of other non-steroidal anti-inflammatory drugs. Increased risk of ulcerations and gastrointestinal bleeding due to synergistic effects.

Ibuprofen
Experimental data suggest that 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 (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

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

Metamizole

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 cardio protection.

4.6 Fertility, pregnancy and lactation

Pregnancy

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:

*T*here 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 oligohydroamniosis; 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. Since adverse effects for the infant have not been reported up to now, short-term use of the recommended dose does not require suspending breastfeeding. In cases of long-term use and/or administration of higher doses, breastfeeding should be discontinued.

4.7 Effects on ability to drive and use machines

Aspirin tablets has no or negligible influence on the ability to drive and use machines.

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 (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data)

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

disorders	
Gastrointestinal disorders	*Common:* Dyspepsia. *Rare:* Severe gastrointestinal haemorrhage, nausea, vomiting. *Not known:* Gastric or duodenal ulcers and perforation, diarrhoea.
Hepatobiliary disorders	*Not known:* Hepatic insufficiency
Skin and subcutaneous tissue disorders	*Uncommon:* Urticaria. *Rare:* Steven-Johnsons syndrome, Lyells syndrome, purpura, erythema nodosum, erythema multiforme.
Renal and urinary tract disorders	*Not known:* Impaired renal function, salt and water retention.

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 Overdoses:

Although considerable inter-individual variations are involved, it can be considered that the toxic dose is about 200mg/kg in adults and 100mg/kg in children. The lethal dose of acetylsalicylic acid is 25-30 grams. 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.

Overdose may be harmful for elderly patients and particularly for small children (therapeutic overdose or frequent accidental intoxications my be fatal)

Common features of salicylate poisoning include abdominal pain, vomiting, dehydration, tinnitus, headache, vertigo, deafness, and 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 4 years. In children aged 4 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 of salicylate poisoning include haematemesis, hyperpyrexia,
hypoglycaemia, hypokalaemia, thrombocytopenia, increased INR/PTR, intravascular coagulation, renal failure and non-cardiac pulmonary oedema, hyperthermia and perspiration, resulting in dehydration: feelings of restlessness, convulsions and hallucinations.

Central nervous system features including confusion, disorientation, coma and convulsions, are less common in adults than in children.

If a toxic dose has been ingested, hospital admission is required. In the event of moderate intoxication, inducing the patient to vomit should be attempted.
If this fails, gastric lavage may be attempted during the first hour after ingestion of a substantial amount of the medicine.

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 10 years or over 70 have increased risk of salicylate toxicity and may require dialysis at an earlier stage.
Other symptoms to be treated symptomatically.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antithrombotic agents: platelet aggregation inhibitors excl. heparin, ATC code: B01AC06

Aspirin inhibits platelet aggregation.
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 hours before or within 30 minutes after immediate release aspirin (81mg) a decreased effect of aspirin 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 occassional ibuprofen use.

5.2 Pharmacokinetic properties

Non ionised acetylsalicylic acid is absorbed from the stomach.
There is also absorption of acetylsalicylates from the intestines.
Aspirin appears rapidly in all body tissues. It does cross the placenta and appears in breast milk and it is moderately bound to plasma proteins.
Excretion is as salicylic acid and as compounds in the urine and increases as the pH rises.

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:

Lactose monohydrate
Maize starch
Purified talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months
HDPE container: 200 tablets
Unopened: 36 months

After opening: 90 days

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Alu- PVC/ PVDC blister containing 28 tablets

HDPE container with child resistant polypropylene cap and polyurethane foam cushion. Pack size: 200 tablets

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

RUDIPHARM LIMITED
Unit 6, Salbrook Road Industrial Estate
Salbrook Road, Redhill
Surrey, RH1 5GJ
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 49565/0092

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/12/2021

10 DATE OF REVISION OF THE TEXT

13/08/2024