SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Aspirin Tablets B.P. 300mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Aspirin Tablets contain 300mg of Aspirin B.P.

3 PHARMACEUTICAL FORM

Compressed Tablets

White, circular, normal convex tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Aspirin has Analgesic, Antipyretic and Anti-inflammatory actions. It is indicated for:

- The relief of headache, toothache, migraine, neuralgia, sore throat, dysmenorrhea.
- The symptomatic relief of cold, influenza, feverishness, rheumatic pains, sciatica, lumbago, fibrositis, muscular aches and pains.
- It also has an antithrombotic action, which is used in secondary prophylaxis for myocardial infarction and in patient with unstable angina and cerebral transient ischaemic attacks.

4.2 Posology and method of administration:

Route of administration:

For oral administration

Adults including elderly: 1 to 3 tablets daily.

Children: Do not give to children under 16 years, unless specifically indicated (e.g. for Kawasaki’s disease)
**Antithrombotic action:** For its antithrombotic effect following myocardial infarction, transient ischaemic attack, or in patients with unstable angina, the recommended dose is 300mg daily.

### 4.3 Contraindications

Aspirin should not be taken by patients with the following conditions:

- Known hypersensitivity to aspirin, other ingredients in the product, other salicylates or non-steroidal anti-inflammatory drugs (a patient may have developed anaphylaxis, angioedema (gout), asthma, rhinitis or urticaria induced by aspirin or other NSAIDs).

- Nasal polyps associated with asthma (high risk of severe sensitivity reactions).

- Active peptic ulceration or a past history of ulceration or dyspepsia.

- Haemophilia or other haemorrhagic disorder (including thrombocytopenia) as there is an increased risk of bleeding.

- Concurrent anticoagulant therapy should be avoided.

- Severe hepatic impairment

- Severe renal impairment

- Severe cardiac failure

- third trimester of pregnancy

- Breast feeding, because of possible risk of Reye’s Syndrome

- Children under 16 years old, unless specifically indicated (e.g. Kawasaki’s disease)

- Hypertension

### 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) and dehydration. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
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 on the advice of a doctor. (e.g. for Kawasaki’s disease)

Aspirin should be used with caution in patients with:

- allergic disease
- anaemia (may be exacerbated by GI blood loss)
- asthma (increased risk of bronchospastic sensitivity reactions)
- cardiac failure (conditions which predispose to fluid retention)
- dehydration
- glucose-6-phosphate dehydrogenase deficiency (aspirin rarely causes haemolytic anaemia)
- gout (serum urate may be increased)
- hepatic function impairment (avoid if severe)
- renal function impairment
- surgery. Aspirin should be discontinued several days before scheduled surgery (including dental extractions)
- systemic lupus erythematosus and other connective tissue disorders (hepatic and renal function may be impaired in these conditions)
- thyrotoxicosis (may be exacerbated by large doses of salicylates)
- long term use in elderly patients should be avoided due to a risk of gastrointestinal bleeding.

Before commencing long-term aspirin therapy for the management of cardiovascular or cerebrovascular disease patients should consult their doctor who can advise on the relative benefits versus the risks for the individual patient.

Vaccine recipients should avoid use of salicylates for 6 weeks after varicella vaccination (see section 4.5).

The following warnings are on the OTC product labelling

- Do not take if you have a stomach ulcer
- If symptoms persist for more than 3 days, consult your doctor
- Medicines should not be taken in pregnancy without consulting your doctor
- Keep this medicine out of the sight and reach of children
- Do not give to children aged under 16 years, unless on the advice of a doctor
• Do not exceed stated dose except under medical advice and supervision of a doctor.

4.5 Interaction with other medicinal products and other forms of interaction

The following drug interactions should be considered when prescribing aspirin:

• Alcohol - may enhance gastro-intestinal side effect of aspirin.

• Analgesics - avoid concomitant administration of other salicylates or other NSAIDs (including topical formulations) as increased risk of GI side effects.

• Alkalizers of urine (eg carbonic anhydrase inhibitors, antacids, citrates) - increased excretion of aspirin.

• Anticoagulants or platelet aggregation inhibitors - increased risk of bleeding.

• Antiepileptic drugs (eg phenytoin, sodium valproate) - increased effect. However, no special precautions are needed.

• Corticosteroids - increased risk of gastro-intestinal bleeding or ulceration.

• Dipyridamole - increase in peak concentration.

• Diuretics – sulphonamides such as frusemide and acetazolamide (risk of toxic effects), spironolactone (antagonized diuretic action).

• Hypoglycaemics - enhanced activity.

• Methotrexate - Delayed excretion and increased toxicity of methotrexate.

• Metoclopramide and domperidone - increased rate of absorption of aspirin. However, concurrent use need not be avoided.

• Mifepristone - avoid aspirin until 8-12 days after mifepristone.

• Ototoxic medicine (eg 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.

• Uricosurics (eg probenecid, sulphinpyrazone) - effects of uricosurics reduced.
• Laboratory investigations - aspirin may interfere with some laboratory tests such as urine 5-hydroxyindoleacetic acid determinations and copper sulphate urine sugar tests.

• ACE inhibitors – reduced hypotensive effect, increased risk of renal impairment and hypokalaemia. Monitoring of renal function may be required

• Calcium-channel blockers – reduced hypotensive effects, increased antiplatelet effect which rarely results in prolonged bleeding time.

• SSRIs – increased risk of gastrointestinal bleeding

• Varicella vaccine - Vaccine recipients should avoid use of salicylates for 6 weeks after vaccination with varicella vaccine as Reye's syndrome has been reported following use of salicylates during wild-type varicella infection (see section 4.4).

• Ginkgo Biloba – possible increase in risk of bleeding.

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).

4.6 Fertility, pregnancy and lactation

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiology studies suggest an increased risk of miscarriage and of cardiac malformation 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%.

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, pre and post implantation loss and embryo-fetal lethality. During the first and second trimester aspirin should not be given unless necessary.

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 labour
• complicated deliveries and increased risk of maternal or fetal haemorrhage
• possibly persistent pulmonary hypertension of newborn
• kernicterus in jaundiced neonates
• renal dysfunction, which may progress to renal failure with oligohydramnios

Administration is contraindicated in the last trimester of pregnancy and should be avoided during the late stages of labour and during the delivery of a premature infant.

**Fertility**

Aspirin should not be given to women wishing to become pregnant, since it is thought that prostaglandin synthesis inhibitors can reduce fertility. The effect on fertility is reversible.

**Breastfeeding**

Aspirin appears in breast milk, and regular high doses may affect neonatal clotting. Not recommended while breast feeding due to possible risk of Reye's Syndrome as well as neonatal bleeding due to hypoprothrombinaemia.

### 4.7. Effects on ability to drive and use machines

None stated.

### 4.8 Undesirable effects

Adverse effects of aspirin treatment which have been reported include:

**Blood and lymphatic system disorders** - anaemia, haemolytic anaemia, hypoprothrombinaemia, thrombocytopenia, aplastic anaemia, pancytopenia, prolonged bleeding time, occult blood loss, elevated transaminase levels, agranulocytosis.

**Gastrointestinal disorders** - gastrointestinal bleeding, erosions, perforations or ulceration which can occasionally be major (may develop bloody or black tarry stools, severe stomach pain and vomiting blood), high incidence of gastrointestinal irritation (mild stomach pain, heartburn, vomiting and nausea) with slight asymptomatic blood loss. Fatalities have occurred. It may precipitate gout in susceptible individuals.
Hepatic disorders - hepatitis (particularly in patients with SLE or connective tissue disease)

Renal and urinary disorders – disturbances of renal function

Ear and labyrinth disorders - tinnitus.

Salicylism - mild chronic salicylate intoxication may occur after repeated administration of large doses, symptoms include dizziness, tinnitus, deafness, sweating, nausea, vomiting, headache and mental confusion, and may be controlled by reducing the dose.

Skin and subcutaneous tissue disorders - Allergic reactions - rhinitis, urticaria, purpura, angioneurotic oedema, angio-oedema (gout), Stevens-Johnson syndrome.

Respiratory disorders – asthma, worsening of asthma, bronchospasms.

Children- Aspirin may be associated with the development of Reye's Syndrome (encephalopathy and hepatic failure) in children presenting with an acute febrile illness.

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 Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms:

Common:
Nausea, vomiting, dehydration, tinnitus, lethargy or dizziness, restlessness, vertigo, deafness
Sweating
Warm extremities with bounding pulses
Increased respiratory rate
Hyperventilation
Acid base disturbance
Mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) in adults and children aged over 4 years.

In children aged 4 years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common.

Acidosis can increase salicylate transfer across the blood brain barrier.

**Uncommon:**
Haematemesis, Hyperpyrexia
Hypoglycaemia, Hypokalaemia
Thrombocytopenia, Increased INR/PTR
Intravascular coagulation, Renal failure
Non-cardiac pulmonary oedema

Confusion, disorientation, coma and convulsions are more common in children than adults.

**Treatment:**

Consider oral activated charcoal (50g for an adult, 1g/kg for a child) in adults and children who have ingested more than 250mg/kg body weight salicylate, or any amount of methyl salicylate, less than 1 hour previously.

Consider urinary alkalinisation by 1.26% sodium bicarbonate. For metabolic acidosis treat with intravenous 8.4% sodium bicarbonate.

Plasma salicylate, U & Es, INR/PTR, blood glucose, pH and electrolytes should be measured.

Fluid losses replaced and forced alkaline diuresis (eg with sodium bicarbonate) should be considered when the plasma salicylate concentration is greater than 500mg/l⁻¹ (3.6mmol l⁻¹) in adults or 300mg/l⁻¹ (2.2mmol l⁻¹) in children.

In very severe cases of poisoning haemodialysis may be needed.

5 **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

**ATC code:** N02BA01

Aspirin is an anti-inflammatory analgesic and antipyretic.
Aspirin is analgesic, anti-inflammatory, antipyretic and an inhibitor of platelet aggregation. It prolongs the bleeding time. It inhibits fatty acid cyclo-oxygenase by acetylation of the active site of the enzyme, and most of its pharmacological effects are due to inhibition of the formation of cyclo-oxygenase products including thromboxanes, prostaglandins and prostacyclin. The effect on platelets is cumulative over their 8-day life span because they have no capacity to resynthesize the cyclo-oxygenase enzyme. Aspirin has an active metabolite (salicylate) which, in addition to possessing some anti-inflammatory properties in its own right, also has important effects on respiration, acid-base balance and the stomach. Salicylates stimulate respiration by a direct effect on the medulla, and at high concentrations, uncouple oxidative phosphorylation in muscle, increasing oxygen consumption and carbon dioxide production. Hyperventilation causes respiratory alkalosis which is compensated by renal excretion of bicarbonate. When large toxic doses of salicylate are ingested and carbohydrate metabolism is deranged, lactic and pyruvic acids accumulate and renal function is impaired, resulting in metabolic acidosis. Salicylates have a direct irritant effect on the gastric mucosa and further predispose to ulceration by inhibiting synthesis of vasodilator and cytoprotective prostaglandins.

Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid 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 acetylsalicylic acid 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.

5.2 Pharmacokinetic properties:

Following oral administration, absorption of non-ionised aspirin occurs in the stomach and intestine. Some aspirin is hydrolysed salicylate in the gut wall. After absorption aspirin is rapidly converted to salicylate but during the first twenty minutes following oral administration, aspirin is the predominant form of the drug in the plasma. Aspirin is bound to plasma proteins and is widely distributed. Plasma-aspirin concentrations decline rapidly (half-life 15-20 minutes) as plasma salicylate concentrations increase. Salicylates are extensively bound to plasma proteins and are rapidly distributed to all body parts. Salicylates appear in breast milk and cross the placenta. Salicylate is mainly eliminated by hepatic metabolism; the metabolites include salicyluric acid, salicyl phenolic glucuronide, salicylic acyl glucuronide, gentisic acid, and gentisuric acid. Following a 325mg aspirin dose, elimination is a first-order process and the serum-salicylate half-life is about two to three hours; at high aspirin doses, the half-life increases to fifteen to thirty 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. Salicylates are removed by haemodialysis.

5.3 Preclinical safety data

Not applicable.
6. **Pharmaceutical Particulars**

6.1. **List of excipients**

   Starch
   Purified Talc

6.2. **Incompatibilities**

   None stated.

6.3. **Shelf life**

   2 years.

6.4. **Special precautions for storage**

   Store in a cool dry place protected from bright light.

6.5. **Nature and contents of container**

   Dispensing pack – A polypropylene container with snap lid. Supplied in packs of 50, 100, 250, 500, 1000. (POM).


6.6. **Instructions for use, handling and disposal**

   Dose is orally.

**ADMINISTRATION DATA**
7  MARKETING AUTHORISATION HOLDER

Pharmvit Limited
177 Bilton Road,
Perrivale
Greenford
Middlesex UB6 7HQ

8.  MARKETING AUTHORISATION NUMBER

PL  4556/0015

9  DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

1 October 1985 / 29 January 2004

10  DATE OF REVISION OF THE TEXT

27/04/2017