SUMMARY OF PRODUCT CHARACTERISTICS

APPROVED
By Geeta at 1:43 pm, Dec 09, 2016

1 NAME OF THE MEDICINAL PRODUCT

Aspirin 300mg Tablets BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains aspirin 300 mg
Excipient with known effect: Also contains Lactose Monohydrate 18.0 mg
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablets

White biconvex tablets; breakline on one side and debossed <A> on other side

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Aspirin has analgesic, antipyretic and anti-inflammatory actions. It is indicated for:

1. The relief of mild to moderate pain, including headaches, migraine, neuralgia, toothache, sore throat, period pains, aches and pains.
2. The symptomatic relief of influenza, feverishness, feverish colds, symptomatic relief of sprains, strains, rheumatic pain, sciatica, lumbago, fibrositis, muscular aches and pains, joint swelling & stiffiness.

4.2 Posology and method of administration

For Oral use
If symptoms persist for more than 3 days, consult your doctor.
Adults including elderly:
Analgesic, antipyretic and anti-inflammatory actions:

1-2 tablets (300-600mg) every 3-4 hours as required, to a maximum of 12 tablets (3.6g) daily in divided doses.

Elderly:
Analgesic, antipyretic and anti-inflammatory actions: As for adults. The elderly are more likely to experience gastric side-effects and tinnitus.
Children: Do not give to children under 16 years, unless specifically indicated (e.g. for Kawasaki's Disease). See Section 4.4

4.3 Contraindications

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

- Children under 16 years unless specifically indicated (e.g. for Kawasaki's disease).
- Active peptic ulceration or a past history of peptic ulceration or dyspepsia.
- Haemophilia or other haemorrhagic disorder (including thrombocytopenia) coagulopathies or concurrent anticoagulant therapyas there is an increased risk of bleeding
- Known hypersensitivity to aspirin, any other NSAIDs (a patient may have developed anaphylaxis, angiodema, asthma, rhinitis or urticaria induced by aspirin or other NSAIDs),, or any of the excipients (See section 6.1)
- Gout
- Nasal polyps associated with asthma (high risk of severe sensitivity reactions)
- Severe renal impairment
- Severe hepatic impairment
- Third trimester of pregnancy
- Methotrexate used at doses> 15mg/week (see section 4.5)
- Severe cardiac failure

4.4 Special warnings and precautions for use:

- Caution should be exercised in patients with impairment of hepatic function, allergic disease and in patients with asthma (as they may 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).
- anaemia (may be exacerbated by GI blood loss)
- cardiac failure (conditions which predispose to fluid retention)
- dehydration
- gout (serum urate may be increased)
- 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)

- 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.
- Vaccine recipients should avoid use of salicylates for 6 weeks after varicella vaccination (see section 4.5).
- Acetylsalicylic acid is not recommended during menorrhagia where it may increase menstrual bleeding.
- Acetylsalicylic acid 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
- Serious skin reactions, including Steven-Johnsons syndrome, have rarely been reported in association with the use of acetylsalicylic acid (see section 4.8). Acetylsalicylic acid should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- Concomitant treatment with acetylsalicylic acid 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)
- Where analgesics are used long-term (>3 months) with administration every two days or more frequently, headache may develop or worsen. Headache induced by overuse of analgesics (MOH medication-overuse headache) should not be treated by dose increase. In such cases, the use of analgesics should be discontinued in consultation with the doctor.
- The elderly may be more susceptible to the toxic effects of NSAIDs, including salicylates. Continuous, prolonged use of aspirin should be avoided in the elderly because of the risk of gastrointestinal bleeding and perforation. Salicylates should be used with caution in patients with a history of coagulation abnormalities. They may also induce gastro-intestinal haemorrhage, occasionally major.
- Aspirin should not be taken by patients with a stomach ulcer or history of stomach ulcers (see section 4.3)
- Caution should be used in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency as haemolytic anaemia may occur.

- Aspirin may interfere with insulin and glucagon in diabetes. The risk of hypoglycaemic effect with sulfonylureas and insulins may be potentiated with acetylsalicylic acid taken at over dosage (see section 4.5).

- Aspirin prolongs bleeding time, mainly by inhibiting platelet aggregation and therefore it should be discontinued several days before scheduled surgical procedures. Haematological and haemorrhagic effects can occur, and may be severe. Patients should report any unusual bleeding symptoms to their physician.

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

- Aspirin should be used with caution in patients with impaired renal or hepatic function (avoid 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..

- 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).

- Acetylsalicylic acid is not suitable for use as an anti-inflammatory/analgesic/ antipyretic

  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.

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*
Aspirin may potentiate the effect of heparin and increase the 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).
Antiplatelet agents (e.g. clopidogrel and dipyridamole), Selective serotonin reuptake inhibitors (SSRIs such as sertraline and paroxetine) and fibrinolytics: increased risk of gastrointestinal bleeding (see section 4.4)

Antidiabetics, e.g. sulphonylurea, insulin

Salicylics may increase the hypoglycaemic effect of sulphonylureas and insulin.

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.

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.

Ciclosporin, tacrolimus

Concomitant use of NSAIDs and ciclospoin 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

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.

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)
Alcohol: Some of the effects of aspirin on the gastrointestinal tract are enhanced by alcohol. (See Section 4.4)
Systemic Corticosteroids: The risk of gastrointestinal bleeding and ulceration is increased. Corticosteroids reduce the plasma salicylate concentration. Salicylate toxicity may occur following withdrawal of the corticosteroids.
Carbonic anhydrase inhibitors (acetazolamide):: Reduced excretion of acetazolamide with an increased risk of toxicity. Salicytate intoxication has occurred in patients on high dose salicylate regimens and carbonic anhydrase inhibitors.

The following drug interactions should be considered when prescribing aspirin:

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

• Alkalizers of urine (*eg* antacids, citrates) - increased excretion of aspirin.

• Metoclopramide and domperidone - increased rate of absorption of aspirin.

• 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.

• Laboratory investigations - aspirin may interfere with some laboratory tests such as urine 5-hydroxyindoleacetic acid determinations and copper sulphate urine sugar tests.

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

• 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.

• 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.

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 acetylsalicylic acid is contraindicated (see section 4.3).

Not recommended combinations

Uricosurics: Effect of probenecid and sulfinpyrazone reduced. The combination should be avoided.

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:

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.

Maternal use of aspirin prior to birth may increase the risk of intracranial haemorrhage in premature or low birth weight infants.

Regular or high dose use of salicylates late in pregnancy may result in:

- kernicterus in jaundiced neonates

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: Low quantities of salicylates and of their metabolites are excreted in human milk. Aspirin should not be taken by patients who are breast-feeding, as there is a risk of Reye's syndrome in the infant. In cases of long-term use and/or administration of higher doses, breastfeeding should be discontinued. Regular use of high doses may impair platelet function and produce hypoprothrombinaemia in the infant neonatal vitamin K stores are low.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed with Acetylsalicylic acid.

Based on the pharmacodynamic properties and the side effects of acetylsalicylic acid, no influence on the reactivity and the ability to drive or use machines is expected.

4.8 Undesirable effects

Investigations: Aspirin may interfere with thyroid function test.
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, agranulocytosis, 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). anaemia, haemolytic anaemia in patients with glucose 6 phosphate dehydrogenase deficiency (G6PD), hypoprothrombinaemia, pancytopenia, occult blood loss, elevated transaminase levels
Immune system disorders	*Rare:* Hypersensitivity reactions (bronchospasm, asthma, rhinitis), 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:* Haemorrhagic vasculitis.
Respiratory, thoracic and mediastinal disorders	*Uncommon:* Rhinitis, dyspnoea. *Rare:* Bronchospasm, asthma attacks.
Reproductive systemand mammary disorders	*Rare:* Menorrhagia
Gastrointestinal disorders	*Common:* Dyspepsia. *Rare:* Severe gastrointestinal haemorrhage, nausea, vomiting. *Not known:* Gastric or duodenal ulcers and perforation which can occasionally be major (may develop bloody or black tarry stools, severe stomach pain and vomiting blood), gastrointestinal irritation (mild stomach pain), erosions, gastritis, heartburn, Fatalities have occurred.
Hepatobiliary disorders	*Not known:* Hepatic insufficiency, hepatitis (particularly in patients with SLE or connective tissue disease)
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, Urate kidney stones
Body as a whole – general disorders	*Not known:* 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)

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 the 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

Although considerable inter-individual variations are involved, it can be considered that the toxic dose is about 200 mg/kg in adults and 100 mg/kg in children. The lethal dose of acetylsalicylic acid is 25-30 grams. Salicylate poisoning is usually associated with plasma concentrations >350mg/L (2.5mmol/L). Plasma concentrations above 500 mg/l in adults and 300 mg/l in children generally cause severe toxicity. 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.

Plasma salicylate concentrations should be measured urgently for patients who are thought to have ingested more than 125 mg/kg of aspirin. The sample should be taken at least 2 hours (symptomatic patients) or 4 hours (asymptomatic patients) after ingestion, since it may take several hours for peak plasma concentrations to occur and up to 12 hours for enteric-coated preparations. A repeat sample should be taken in ALL symptomatic patients and those with concentrations greater than 500 mg/L after a further 2 hours because of the possibility of continuing absorption. Under these circumstances, measurements should be repeated every 3 hours until concentrations are falling.

a) 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, thrombocytopenia, increased INR/PTR, intravascular coagulation, renal failure and non-cardiac pulmonary oedema.
Other symptoms may include: headache, nausea, or abdominal pain.
Central nervous system features including confusion, restlessness, hallucinations, disorientation, coma, cardiovascular collapse, respiratory arrest and convulsions are less common in adults than in children.

b) Treatment

If a toxic dose has been ingested, hospital admission is required

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 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 >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.
Other symptoms to be treated symptomatically.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

N02B A01- (Nervous system- analgesics/ antipyretics)
Aspirin is an analgesic, an inhibitor of platelet aggregation and antipyretic with anti-inflammatory properties. 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.
It also has antithrombotic action, which is mediated through inhibition of platelet activation.
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.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, absorption of non-ionised aspirin occurs in the stomach and intestine. Aspirin is rapidly absorbed after oral administration, with some hydrolysis to salicylate in the gut wall before absorption. 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. 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

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. 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 l5mcg/ml of aspirin are attained in about one hour and peak plasma concentrations of approximately) 130mcg/ml of salicylate are attained in 2 to 4 hours.

Distribution

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.

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

Salicylate is mainly eliminated by hepatic metabolism; the metabolites include salicyluric acid, salicyl phenolic glucuronide, salicylic acyl glucuronide, gentisic acid, and gentisuric 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; 85% of dose excreted as free salicylate. 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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch
Lactose monohydrate
Purified talc (E553b)

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 bottle tightly closed.

6.5 Nature and contents of container

Blister packs: 20, 24, 28, 30 or 32 as Pharmacy.

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

Polypropylene/polyethylene Containers: 25 tablets as Pharmacy.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

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