For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

LOPRIN-75

1. Generic Name

Aspirin Gastro - Resistant Tablets I.P. 75 mg

2. Qualitative and quantitative composition

Each gastro-resistant tablet contains:

Aspirin I.P……75 mg

Excipients…….q.s

Colours: Lake of sunset yellow FCF, Lake of Erythrosine and Titanium Dioxide I.P.

The excipients used are Colloidal Silicon Dioxide, Triacetin, Isopropyl Alcohol, Lake of Erythrosine, Lake of Sunset Yellow, Methanol, Microcrystalline Cellulose, Starch, Stearic Acid, Talcum, Polymers and Titanium Dioxide.

3. Dosage form and strength

Dosage form: Gastro-Resistant Tablet

Strength: 75 mg

4. Clinical particulars

4.1 Therapeutic indication

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

4.2 Posology and method of administration

Posology

For the management of cardiovascular or cerebrovascular disease:

Patients should seek the advice of a doctor 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. Treatment should be reviewed at regular intervals.

Antithrombotic action:

150mg at diagnosis and 75mg daily thereafter. Tablets taken at diagnosis should be chewed in order to gain rapid absorption.

Children:

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

Method of administration

Aspirin 75 mg is for oral administration to adults only.

Take the tablet with water, do not cut, chew or crush the tablet. Swallow whole.

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), or to any of the excipients.

• Active, or history of peptic ulceration 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.

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

• Doses >100 mg/day during the third trimester of pregnancy; Methotrexate used at doses >15mg/week.

4.4 Special warnings and precautions for use

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

Caution should be exercised in patients with allergic disease, impairment of hepatic or renal function (avoid if severe) and dehydration, 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.

Aspirin may also precipitate bronchospasm or induce attacks of asthma in susceptible subjects or promote 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. Aspirin Tablets should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

The elderly may be more susceptible to the toxic effects of salicylates. Continuous prolonged use of aspirin should be avoided in the elderly because of the risk of gastrointestinal bleeding and perforation which may be fatal. Where prolonged therapy is required, patients should be reviewed regularly.

Caution should be taken in patients with glucose-6-phosphate dehydrogenase deficiency as haemolytic anaemia may occur.

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

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. Use with caution before surgery, including tooth extraction. Patients should report any unusual bleeding symptoms to their physician.

Care is advised when stopping antiplatelet therapy after stent insertion either after a fixed period of time or in preparation for a planned surgical procedure, as the balance between stent thrombosis and excessive bleeding has to be carefully assessed.

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).

Aspirin is to be used with caution in cases of hypertension and patients with a stomach ulcer or a history of stomach ulcers or duodenal ulcer or haemorrhagic episodes or 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.

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.

Concomitant treatment with Aspirin 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. 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.

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.

The risk of hypoglycaemic effect with sulfonylureas and insulins may be potentiated with Aspirin 75mg tablets taken at over dosage.

Aspirin should be avoided in late pregnancy and generally during breast feeding.

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

4.5 Drugs 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 75 mg tablets is contraindicated.

Not recommended combinations

Uricosuric agents, e.g. probenecid and sulfinpyrazone:

Salicylates reverse the effect of probenecid and sulfinpyrazone. 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.

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.

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. Patients with hypertension should be carefully monitored. 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.

Other non-steroidal anti-inflammatory drugs (NSAIDs):

Concurrent administration can increase side effects. Use of two or more NSAIDs increases risk of gastrointestinal haemorrhage.

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.

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.

Systemic Corticosteroids:

The risk of gastrointestinal bleeding and ulceration is increased when acetylsalicylic acid and corticostetoids are co-administered. Corticosteroids reduce the plasma salicylate concentration and salicylate toxicity may occur following withdrawal of corticosteroids.

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.

Carbonic anhydrase inhibitors:

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

Antacids and adsorbents:

The excretion of aspirin is increased in alkaline urine; kaolin possibly reduces absorption. Antacids will reduce the effect of aspirin. Principle incompatibilities are iron salts, carbonates and alkali hydroxides.

Mifepristone:

The manufacturer of mifepristone recommends that aspirin should be avoided until eight to twelve days after mifepristone has been discontinued.

Alcohol:

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

Antiemetics:

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

Anti-epileptics:

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

Leukotriene antagonists:

The plasma concentration of zafirlukst is increased.

Antibacterials:

The toxicity of sulphonamides may be increased.

Thyroid function tests:

Aspirin may interfere with thyroid function tests.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

CAUTION: Do not take this product during the last three months of pregnancy unless directed by a doctor. Aspirin taken near the time of delivery may cause bleeding problems to both mother and child.

Not to be used in children below 12 years of age except under medical advice.

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.

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

• 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

As aspirin is excreted in breast milk, Aspirin should not be taken by patients who are breast-feeding, as there is a risk of Reye's syndrome in the infant. High maternal doses may impair platelet function in the infant.

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 (≥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, haematuria, purpura, ecchymoses, haemoptysis, haematoma, cerebral haemorrhage and 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. Aspirin decreases platelet adhesiveness and, in large doses, may cause hypoprothrombinaemia. Existing (haematemesis, melaena) or occult gastrointestinal bleeding, which may lead to iron deficiency anaemia (more common at higher doses). Haemolytic anaemia can occur in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.
Immune system disorders	*Rare*: Hypersensitivity reactions, skin rashes, urticarial, asthma, bronchospasm, 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 disorders	*Rare*: Menorrhagia.
Gastrointestinal disorders	*Common*: Dyspepsia. *Rare*: Severe gastrointestinal haemorrhage, nausea, vomiting, gastritis.

	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, Lyell's syndrome, purpura, erythema nodosum, erythema multiforme.
Renal and urinary tract disorders	*Not known*: Impaired renal function, salt and water retention, urate kidney stones.

4.9 Overdose

Salicylate poisoning is usually associated with plasma concentrations >350 mg/L (2.5 mmol/L). Most adult deaths occur in patients whose concentrations exceed 700 mg/L (5.1 mmol/L). Single doses less than 100 mg/kg are unlikely to cause serious poisoning.

Symptoms

Common features include vomiting, dehydration, tinnitus, vertigo, deafness, sweating, warm extremities with bounding pulses, increased respiratory rate and hyperventilation.

Some degree of acid-base disturbance is present in most cases.

A mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) is usual in adults or 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.

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 present within one hour of ingestion of more than 250 mg/kg. The plasma salicylate concentration should be measured, although the severity of poisoning cannot be determined from this alone and the clinical and biochemical features must be taken into account. Elimination is increased by urinary alkalinisation, which is achieved by the administration of 1.26% sodium bicarbonate.

The urine pH should be monitored. Correct metabolic acidosis with intravenous 8.4% sodium bicarbonate (first check serum potassium). Forced diuresis should not be used since it does not enhance salicylate excretion and may cause pulmonary oedema.

Haemodialysis is the treatment of choice for severe poisoning and should be considered in patients with plasma salicylate concentrations >700 mg/L (5.1 mmol/L) or lower concentrations associated with severe clinical or metabolic features. Patients under ten years or over 70 have increased risk of salicylate toxicity and may require dialysis at an earlier stage.

5. Pharmacological properties

5.1 Mechanism of Action

Aspirin (acetylsalicylic acid) irreversibly acetylates platelet cyclo-oxygenase thereby inhibiting the biosynthesis of thromboxane, a potent vasoconstrictor and inducer of platelet aggregation. It also inhibits the action of cyclo-oxygenase in the vascular endothelial wall preventing the synthesis of prostacyclin, a potent vasodilator and inhibitor of platelet aggregation.

However, as the endothelial cell is capable of synthesising new cyclo-oxygenase, whereas the platelet is not, the effect on thromboxane is longer lasting.

5.2 Pharmacodynamicproperties

Pharmacotherapeutic group: Platelet Aggregation Inhibitor excl. Heparin, *ATC code*: B01AC06

The antiplatelet effect of aspirin is largely unrelated to its systemic bioavailability and its duration of effect does not correlate with the presence of intact salicylic acid in the circulation. The antiplatelet effect is considered to be largely pre-systemic, associated with acetylation of platelet cyclo-oxygenase in the portal circulation.

Due to the low dose enteric-coated formulation of Aspirin 75mg Gastro-Resistant Tablets acetylsalicylic acid is slowly released into the portal circulation and is deacetylated by the liver to inactive salicylate before reaching the systemic circulation. It is postulated that platelets passing through the portal circulation are exposed to acetylsalicylic acid concentrations sufficient to achieve effective thromboxane inhibition, while systemic prostacyclin synthesis remains essentially unaffected.

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 dosing (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 occasional ibuprofen use.

5.3 Pharmacokinetic properties

Aspirin is rapidly absorbed after oral administration of conventional release preparations, with some hydrolysis to salicylate before absorption. Absorption is delayed by the presence of food and is impaired in patients suffering migraine attacks.

Absorption is more rapid in patients with achlorhydria and also following administration of polysorbates and antacids. Plasma concentrations of the drug increase disproportionately to the dose; e.g. a 325 mg dose having a half-life of 2-3 hours and higher doses showing lower plasma concentrations in the presence of an increased half-life due to a disproportionate increase in the volume of distribution.

Aspirin is found in saliva, milk, plasma and synovial fluid at concentrations less than in blood and crosses the placenta. Salicylate/protein binding extensive. Aspirin/protein binding to a small extent. In the blood, rapid hydrolysis to salicylic acid; glucuronic acid/glycine conjugation to form glucuronides and 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.

The absolute bioavailability of aspirin from Aspirin 75mg Gastro-Resistant Tablets (compared with intravenous aspirin solution) is approximately 25%.

6. Nonclinical properties

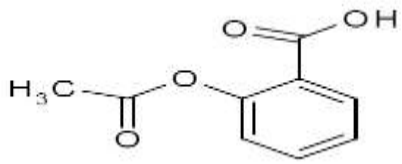
6.1 Animal Toxicology or Pharmacology

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

7. Description

Aspirin

The antiplatelet agent aspirin (acetylsalicylic acid) is chemically known as benzoic acid, 2-(acetyloxy)-, and has the following structural formula:



Aspirin IP is colourless crystals or a white, crystalline powder; odourless or almost odourless. It is freely soluble in ethanol (95 per cent) and soluble in chloroform and in ether; slightly soluble in water. The empirical formula of aspirin is $C_9H_8O_4$ and its molecular weight is 180.2.

Aspirin Gastro-resistant tablets are light orange to orange coloured round biconvex gastro-resistant tablets. The excipients used are Colloidal Silicon Dioxide, Triacetin, Isopropyl Alcohol, Lake of Erythrosine, Lake of Sunset Yellow, Methanol, Microcrystalline Cellulose, Starch, Stearic Acid, Talcum, Polymers and Titanium Dioxide.

8. Pharmaceutical particulars

8.1 Incompatibilities

Not applicable

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

LOPRIN-75 is available in blister strip of 14 tablets.

8.4 Storage and handing instructions

Store in a cool, dry & dark place. Keep all medicines out of reach of children.

Tablets should be swallowed whole and not chewed.

Not to be used in children below 12 years of age except under medical advice.

9. Patient Counselling Information

LOPRIN 75mg tablets

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

· Keep this leaflet. You may need to read it again.

· If you have any further questions, ask your doctor or pharmacist.

· This medicine has been prescribed for you only. Do not pass it on to others; it may harm them, even if their signs of illness are the same as yours.

· If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

9.1 What LOPRIN 75 and what they are used for

9.2 What you need to know before you take LOPRIN 75

9.3 How to take LOPRIN 75 Tablets

9.4 Possible side effects

9.5 How to store LOPRIN 75 Tablets

9.6 Contents of the pack and other information

9.1 What LOPRIN 75 are and what they are used

LOPRIN 75 contain acetylsalicylic acid, which in low doses belong to a group of medicines called anti-platelet agents. Platelets are tiny cells in the blood that cause the blood to clot and are involved in thrombosis. When a blood clot occurs in an artery it stops the blood flowing and cuts off the oxygen supply. When this happens in the heart it can cause a heart attack or angina; in the brain it can cause a stroke.

LOPRIN 75 are taken For the secondary prevention of thrombotic cerebrovascular or cardiovascular disease and following by-pass surgery.

9.2 What you need to know before you take LOPRIN 75

Do not take LOPRIN 75 if you

• are allergic to acetylsalicylic acid or any of the ingredients of this medicine.

• are allergic to other salicylates or non-steroidal anti-inflammatory drugs (NSAIDs).

NSAIDs are often used for arthritis or rheumatism and pain

• have had an asthma attack or swelling of some parts of the body e.g. face, lips, throat or tongue (angioedema) after taking salicylates or NSAIDs

• currently have or have ever had an ulcer in your stomach or small intestine or any other type of bleeding like a stroke

• have ever had the problem of your blood not clotting properly

• have severe liver or kidney problems

• suffer from gout

• are in your last 3 months of pregnancy; you must not use higher doses than 100mg per day (see section “Pregnancy and breast-feeding”)

• are taking a medicine called methotrexate (e.g. for cancer or rheumatoid arthritis) in doses higher than 15mg per week.

Warnings and precautions

Talk to your doctor or pharmacist before taking Aspirin Tablets if you:

• have trouble with your kidneys, liver or heart

• have or have ever had problems with your stomach or small intestine

• have high blood pressure

• are asthmatic, have hay fever, nasal polyps or other chronic respiratory diseases; acetylsalicylic acid may induce an asthma attack

• have ever had gout

• have heavy menstrual periods.

You must immediately seek medical advice, if your symptoms get worse or if you experience severe or unexpected side effects e.g. unusual bleeding symptoms, serious skin reactions or any other sign of serious allergy (see section "Possible side

effects"). Inform your doctor if you are planning to have an operation (even a minor one such as tooth extraction) since acetylsalicylic acid is blood-thinning there may be an increased risk of bleeding.

Acetylsalicylic acid may cause Reye's syndrome when given to children. Reye's Syndrome is a very rare disease which affects the brain and liver and can be life-threatening. For this reason, Aspirin Tablets should not be given to children aged under 16 years, unless on the advice of a doctor.

You should take care not to become dehydrated (you may feel thirsty with a dry mouth) since the use of acetylsalicylic acid at the same time may result in deterioration of kidney function. This medicinal product is not suitable as a pain killer or fever reducer. If any of the above applies to you, or if you are not sure, speak to your doctor or pharmacist.

Other medicines and Aspirin Tablets

Tell your doctor or pharmacist if you are taking, have recently taken or might take

any other medicines.

The effect of treatment may be influenced if acetylsalicylic acid is taken at the same

time as some other medicines for:

• thinning of the blood/prevention of clots (e.g. warfarin, heparin, clopidogrel)

• rejection of organ after transplantation (ciclosporin, tacrolimus)

• high blood pressure (e.g. diuretics and ACE-inhibitors)

• regulation of the heart beat (digoxin)

• manic-depressive illness (lithium)

• pain and inflammation (e.g. NSAIDs such as ibuprofen or steroids)

• gout (e.g. probenecid)

• glaucoma (acetazolamide)

• cancer or rheumatoid arthritis (methotrexate; in doses lower than 15mg per week)

• diabetes (e.g. glibenclamide)

• depression (selective serotonin re-uptake inhibitors (SSRIs) such as sertraline or

paroxetine)

• use as hormone replacement therapy when the adrenal glands or pituitary gland have been destroyed or removed, or to treat inflammation, including rheumatic diseases and inflammation of the intestines (corticosteroids)

• antacids (indigestion medicine).

LOPRIN 75 with alcohol

Drinking alcohol may possibly increase the risk of gastrointestinal bleeding and prolong bleeding time.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Acetylsalicylic acid should not be taken during pregnancy unless advised by a doctor.

You should not take Aspirin Tablets if you are in the last 3 months of pregnancy, unless you are advised to do so by your doctor and then the daily dose should not exceed 100mg."Do not take Aspirin Tablets"). Regular or high doses of this medicinal product during late pregnancy can cause serious complications in the mother or baby.

You should not take acetylsalicylic acid during breast-feeding unless advised by your doctor.

Driving and using machines

LOPRIN 75 should not affect your ability to drive and use machines.

9.3 How to take LOPRIN 75

Always use this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Adults

Prevention of heart attacks:

• The recommended dose is 75-160mg once daily. Prevention of strokes:

• The recommended dose is 75-325mg once daily.

Prevention of cardiovascular problems in patients who suffer from stable or unstable angina (a type of chest pain):

• The recommended dose is 75-160mg once daily. Prevention formation of blood clots after certain types of heart surgery:

• The recommended dose is 75-160mg once daily. Acute heart attack:

• The recommended dose is 150-450mg, taken as soon as possible after onset of symptoms.

Elderly

As for adults. In general, acetylsalicylic acids should be used with caution in elderly patients who are more prone to adverse events. Treatment should be reviewed at regular intervals.

Use in children and adolescents

Acetylsalicylic acid should not be administered to children and adolescents younger than 16 years, unless prescribed by a doctor (see section "Warnings and precautions").

Method of administration

For oral use.

If you take more LOPRIN 75 than you should

If you (or someone else) accidentally take too many tablets, you should tell your doctor at once or contact immediately the nearest casualty department. Show any leftover medicines or the empty packet to the doctor. Symptoms of overdose may include ringing in ears, hearing problems, headache, dizziness, confusion, nausea, vomiting and abdominal pain. A large overdose can lead to more rapid breathing than normal (hyperventilation), fever, excess sweating, restlessness, seizures, hallucinations, low blood sugar, coma and shock.

If you forget to take LOPRIN 75

If you miss a dose, wait until it is time for your next dose, then go on as normal.

Do not take a double dose to make up for a forgotten tablet.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice any of the following serious side effects, stop taking Aspirin Tablets and contact a doctor immediately:

• Sudden wheezing, swelling of your lips, face or body, rash, fainting or difficulties swallowing (severe allergic reaction).

• Reddening of the skin with blisters or peeling and may be associated with a high fever and joint pains. This could by erythema multiforme, Stevens-Johnson syndrome or Lyell's syndrome.

• Unusual bleeding, such as coughing up blood, blood in your vomit or urine, or black stools.

Common side effects (may affect up to 1 in 10 people):

• Indigestion.

• Increased tendency for bleeding

Uncommon side effects (may affect up to 1 in 100 people):

• Hives.

• Runny noses.

• Breathing difficulty.

Rare side effects (may affect up to 1 in 1000 people):

• Severe bleeding in the stomach or intestines, brain haemorrhage; altered number of blood cells.

• Nausea and vomiting.

• Cramps in the lower respiratory tract, asthma attack.

• Inflammation in the blood vessels.

• Bruising with purple spots (cutaneous bleeding).

• Severe skin reactions such as rash known as erythema multiforme and it's life threatening forms Stevens-Johnson syndrome and Lyell's syndrome.

• Hypersensitivity reactions, such as swelling of e.g. lips, face or body, or shock.

• Abnormal heavy or prolonged menstrual periods.

Side effects with unknown frequency (frequency cannot be estimated from the available data)

• Ringing in your ears (tinnitus) or reduced hearing ability.

• Headache.

• Vertigo.

• Ulcers in stomach or small intestine and perforation.

• Prolonged bleeding time.

• Impaired kidney function.

• Salt or water retention which may cause swelling of hands, feet, legs, stomach, breasts or face.

• Impaired liver function.

• High level of uric acid in the blood.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 . How to store LOPRIN 75**.**

Store in a cool, dry & dark place.

Keep all medicines out of reach of children.

9.6 Contents of the pack and other information

Aspirin I.P 75 mg

The excipients used are Colloidal Silicon Dioxide, Triacetin, Isopropyl Alcohol, Lake of Erythrosine, Lake of Sunset Yellow, Methanol, Microcrystalline Cellulose, Starch, Stearic Acid, Talcum, Polymers and Titanium Dioxide.

10. Details of manufacturer

Manufactured in India by:

Sidmak Laboratories (India) Pvt Ltd.

Post Box No. 121, National Highway No.8,

Abrama, Valsad – 396001, Gujarat India.

11. Details of permission or licence number with date

Mfg Lic. No. G/660 issued on 13.11.2016.

12. Date of revision

Not applicable

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/ LOPRIN-75 mg/Jun-20/1/PI