ACEMAGNIL 75

Instructions for the medicinal product

Trade name: Acemagnil 75.
International Nonproprietary Name: Acetylsalicylic Acid & Magnesium Hydroxide.
Dosage form: Film-coated Tablets.
Composition: Each film coated tablet contains:

Acetylsalicylic Acid BP	75 mg
Magnesium Hydroxide BP	15.2 mg

Colour: Red Oxide of Iron
Pharmacotherapeutic group: Thrombocyte Aggregation Inhibitors in Combination.
ATC Code: B01AC30.
Pharmacologic property:
Pharmacodynamics:
Acetylsalicylic Acid inhibits platelet aggregation.
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 (81mg) a decreased effect of Acetylsalicylic Acid 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.
Magnesium hydroxide is an antacid with slow neutralising action and a mild laxative action.
Magnesium hydroxide, which is a combination of acetylsalicylic acid and magnesium hydroxide, protects the mucous membrane of the gastrointestinal tract from the effects of acetylsalicylic acid.
Pharmacokinetics:
Non ionised acetylsalicylic acid is absorbed from the stomach. There is also absorption of acetylsalicylates from the intestines.
Acetylsalicylic Acid 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.
Magnesium salts are poorly absorbed following oral administration.
Approximately one third of magnesium is absorbed from the small intestine, and excreted mainly in the urine with small amounts in breast milk and saliva.
Indications for use:
For the secondary prevention of thrombotic cerebrovascular or cardiovascular disease and following by-pass surgery for relief of the symptoms of flatulence, heartburn, dyspepsia and indigestion.
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;
- 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;
- Methotrexate used at doses >15mg/week;
- Contraindicated in severe renal failure, acute gastrointestinal conditions and in hypersensitivity to magnesium salts or any of the other ingredients.

Dosage and directions for use:
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. Treatment should be reviewed at regular intervals.
Children: Acetylsalicylic Acid & Magnesium Hydroxide Tablet is not indicated for use in children and young people less than 16 years of age.
Method of administration:
These tablets should be taken orally with a drink of water.
Side-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: 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 disorders: Rare: Menorrhagia.
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: 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.
Overdose:
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 > 300mg/L (2.5 mmol/L). Plasma concentrations above 500mg/l in adults and 300mg/l in children generally cause severe toxicity. 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 harmful for elderly patients and particularly for small children (therapeutic overdose or frequent accidental intoxications may be fatal).
Symptoms of moderate intoxications:
Common features of salicylate poisoning include vomiting, nausea, abdominal pain, dehydration, tinnitus, headache, vertigo, deafness, sweating, warm extremities with bounding pulses.
Symptoms of severe intoxications:
Some degree of acid-base disturbance is present in most cases. In the first instance hyperventilation occurs, which results in respiratory alkalosis. Respiratory acidosis ensues due to suppression of the respiratory centre. In addition 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 as a result of the presence of salicylate. In children aged 4 years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common.
Since younger children are often not seen until they have reached a late stage of intoxication, they are usually in the stage of acidosis.
Furthermore, the following symptoms may occur: haematemesis, hyperpyrexia,
hypoglycaemia, hypokalaemia, thrombocytopaenia, increased INR/PTR, intravascular coagulation, renal failure, non-cardiac pulmonary oedema, hyperthermia and perspiration, resulting in dehydration: feelings of restlessness, convulsions and halluciations.
Central nervous system features including confusion, disorientation, convulsions may lead to coma, cardiovascular collapse or respiratory arrest are less common in adults than in children.
Treatment of overdose
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 - (50g for an adult, 1g/kg body weight for a child up to 12 years) - 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.
Drug 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 Acetylsalicylic Acid & Magnesium Hydroxide Tablet is contraindicated.
Not recommended combinations
Uricosuric agents, e.g. probenecid
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
Anti-platelet agents (e.g clopidogrel and dipyridamole) and selective serotonin reuptake 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. 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.
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
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.
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 will reduce the effect of Acetylsalicylic Acid.
Principle incompatibilities are iron salts, carbonates and alkali hydroxides.
As a precaution for antacids, in order to minimise the risk of interactions affecting pharmacokinetics of concomitantly administered products, drug administrations should be separated by approximately 2 to 3 hours.
Magnesium salts reduce the absorption of a number of other drugs taken concomitantly. These include ACE inhibitors (captopril, enalapril, and fosinapril), antibacterials and antifungals (azithromycin, cefaclor, cefpodoxime, isoniazid, itraconazole, nitrofurantoin, rifampicin, tetracyclines, ketoconazole and the quinolone group of antibacterials); antivirals (atazanavir, fosamprenavir, tipranavir); antihistamines (fexofenadine); bisphosponates, corticosteroids (deflazacort); digoxin, dipyridamole, diflunisal, antiepileptics (gabapentin and phenytoin), ulcer healing drugs (lansoprazole); levothyroxine, mycophenolate, iron preparations, lipid regulating drugs (rosuvastatin); antipsychotics (sulpiride, phenothiazines), chloroquine, hydrochloroquine, proguanil, and penicillamine.
Concomitant use with sodium polystyrene sulphonate may produce metabolic alkalosis. Alkaline urine due to some antacids increases excretion of Acetylsalicylic Acid. Antacids should be avoided with nilotinib.
Antacids possibly reduce absorption of bile acids.
Urine alkalinisation secondary to administration of magnesium hydroxide may modify excretion of some drugs; thus, increased excretion of salicylates has been seen.
Cautions:
Acetylsalicylic Acid
It is not suitable for use as an anti- inflammatory / analgesic / antipyretic.
Recommended for use in adults and adolescents from 16 years of age. This medicinal product is not recommended for use in adolescents/children under 16 years unless the expected benefits outweigh the risks. Acetylsalicylic acid may be a contributory factor in the causation of Reye's Syndrome in some children.
There is an increased risk of haemorrhage particularly during or after operative procedures (even in cases of minor procedures, e.g. tooth extraction). Use with caution before surgery, including tooth extraction. Temporary discontinuation of treatment may be necessary.
It is not recommended during menorrhagia where it may increase menstrual bleeding.
It is to be used with caution in cases of hypertension and when patients have a past history of gastric or duodenal ulcer or haemorrhagic episodes or are undergoing therapy with anticoagulants.
Patients should report any unusual bleeding symptoms to their physician. If gastrointestinal bleeding or ulceration occurs the treatment should be withdrawn.
Acetylsalicylic acid should be used with caution in patients with moderately impaired renal or hepatic function (contraindicated if severe), or in patients who are dehydrated since the use of NSAIDs may result in deterioration of renal function. Liver function tests should be performed regularly in patients presenting slight or moderate hepatic insufficiency.
Acetylsalicylic acid may promote bronchospasm and asthma attacks or other hypersensitivity reactions. Risk factors are existing asthma, hay fever, nasal polyps or chronic respiratory diseases. The same applies for patients who also show allergic reaction to other substances (e.g. with skin reactions, itching or urticaria).
Serious skin reactions, including Steven-Johnsons syndrome, have rarely been reported in association with the use of acetylsalicylic acid.
It 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. Where prolonged therapy is required, patients should be reviewed regularly.
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. 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 Acetylsalicylic Acid taken at over dosage.
Acetylsalicylic Acid should be avoided in late pregnancy and generally during breast feeding.
Magnesium Hydroxide:
Use with caution in the elderly and debilitated and in patients with impaired liver function. Also in patients with impaired kidney function as hypermagnesaemia may result.
In young children the use of magnesium hydroxide can produce a hypermagnesemia, especially if they present renal impairment or dehydration.
Pregnancy and Nursing Mother:
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 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.
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, shortterm 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.
Effects on ability to drive and use machine:
None stated.
Presentation:
10 Tablets in Alu-Alu Blister, such 3 blisters packed in a carton along with package insert.
Storage:
Keep in dry place, protected from light at a temperature below 30°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescribed medicine.

The holder of Trade Mark and Marketing Authorisation:
BELINDA LABORATORIES LLP.
London, UK

Manufactured by:
Akums Drugs & Pharmaceuticals Ltd.,
Plot No. 19, 20 & 21, Sector-6A, IIE, SIDCUL, Ranipur,
Haridwar-249403, Uttarakhand, India

02Z

ACEMAGNIL 150

Instructions for the medicinal product

Trade name: Acemagnil 150.
International Nonproprietary Name: Acetylsalicylic Acid & Magnesium Hydroxide.
Dosage form: Film-coated Tablets.
Composition: Each film coated tablet contains:

Acetylsalicylic Acid BP	150 mg
Magnesium Hydroxide BP	30.39 mg .

Colour: Red Oxide of Iron
Pharmacotherapeutic group: Thrombocyte Aggregation Inhibitors in Combination.
ATC Code: B01AC30.
Pharmacologic property:
Pharmacodynamics:
Acetylsalicylic Acid inhibits platelet aggregation.
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 (81mg) a decreased effect of Acetylsalicylic Acid 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.
Magnesium hydroxide is an antacid with slow neutralising action and a mild laxative action.
Magnesium hydroxide, which is a combination of acetylsalicylic acid and magnesium hydroxide, protects the mucous membrane of the gastrointestinal tract from the effects of acetylsalicylic acid.
Pharmacokinetics:
Non ionised acetylsalicylic acid is absorbed from the stomach. There is also absorption of acetylsalicylates from the intestines.
Acetylsalicylic Acid 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.
Magnesium salts are poorly absorbed following oral administration.
Approximately one third of magnesium is absorbed from the small intestine, and excreted mainly in the urine with small amounts in breast milk and saliva.
Indications for use:
For the secondary prevention of thrombotic cerebrovascular or cardiovascular disease and following by-pass surgery for relief of the symptoms of flatulence, heartburn, dyspepsia and indigestion.
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;
- 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;
- Methotrexate used at doses >15mg/week;
- Contraindicated in severe renal failure, acute gastrointestinal conditions and in hypersensitivity to magnesium salts or any of the other ingredients.

Dosage and directions for use:
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. Treatment should be reviewed at regular intervals.
Children: Acetylsalicylic Acid & Magnesium Hydroxide Tablet is not indicated for use in children and young people less than 16 years of age.
Method of administration:
These tablets should be taken orally with a drink of water.
Side-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: 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 disorders: Rare: Menorrhagia.
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: 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.
Overdose:
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 > 300mg/L (2.5 mmol/L). Plasma concentrations above 500mg/l in adults and 300mg/l in children generally cause severe toxicity. 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 harmful for elderly patients and particularly for small children (therapeutic overdose or frequent accidental intoxications may be fatal).
Symptoms of moderate intoxications:
Common features of salicylate poisoning include vomiting, nausea, abdominal pain, dehydration, tinnitus, headache, vertigo, deafness, sweating, warm extremities with bounding pulses.
Symptoms of severe intoxications:
Some degree of acid-base disturbance is present in most cases. In the first instance hyperventilation occurs, which results in respiratory alkalosis. Respiratory acidosis ensues due to suppression of the respiratory centre. In addition 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 as a result of the presence of salicylate. In children aged 4 years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common.
Since younger children are often not seen until they have reached a late stage of intoxication, they are usually in the stage of acidosis.
Furthermore, the following symptoms may occur: haematemesis, hyperpyrexia,
hypoglycaemia, hypokalaemia, thrombocytopaenia, increased INR/PTR, intravascular coagulation, renal failure, non-cardiac pulmonary oedema, hyperthermia and perspiration, resulting in dehydration: feelings of restlessness, convulsions and halluciations.
Central nervous system features including confusion, disorientation, convulsions may lead to coma, cardiovascular collapse or respiratory arrest are less common in adults than in children.
Treatment of overdose
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 - (50g for an adult, 1g/kg body weight for a child up to 12 years) - 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.
Drug 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 Acetylsalicylic Acid & Magnesium Hydroxide Tablet is contraindicated.
Not recommended combinations
Uricosuric agents, e.g. probenecid
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
Anti-platelet agents (e.g clopidogrel and dipyridamole) and selective serotonin reuptake 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. 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.
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
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.
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 will reduce the effect of Acetylsalicylic Acid.
Principle incompatibilities are iron salts, carbonates and alkali hydroxides.
As a precaution for antacids, in order to minimise the risk of interactions affecting pharmacokinetics of concomitantly administered products, drug administrations should be separated by approximately 2 to 3 hours.
Magnesium salts reduce the absorption of a number of other drugs taken concomitantly. These include ACE inhibitors (captopril, enalapril, and fosinapril), antibacterials and antifungals (azithromycin, cefaclor, cefpodoxime, isoniazid, itraconazole, nitrofurantoin, rifampicin, tetracyclines, ketoconazole and the quinolone group of antibacterials); antivirals (atazanavir, fosamprenavir, tipranavir); antihistamines (fexofenadine); bisphosponates, corticosteroids (deflazacort); digoxin, dipyridamole, diflunisal, antiepileptics (gabapentin and phenytoin), ulcer healing drugs (lansoprazole); levothyroxine, mycophenolate, iron preparations, lipid regulating drugs (rosuvastatin); antipsychotics (sulpiride, phenothiazines), chloroquine, hydrochloroquine, proguanil, and penicillamine.
Concomitant use with sodium polystyrene sulphonate may produce metabolic alkalosis. Alkaline urine due to some antacids increases excretion of Acetylsalicylic Acid. Antacids should be avoided with nilotinib.
Antacids possibly reduce absorption of bile acids.
Urine alkalinisation secondary to administration of magnesium hydroxide may modify excretion of some drugs; thus, increased excretion of salicylates has been seen.
Cautions:
Acetylsalicylic Acid
It is not suitable for use as an anti- inflammatory / analgesic / antipyretic.
Recommended for use in adults and adolescents from 16 years of age. This medicinal product is not recommended for use in adolescents/children under 16 years unless the expected benefits outweigh the risks. Acetylsalicylic acid may be a contributory factor in the causation of Reye's Syndrome in some children.
There is an increased risk of haemorrhage particularly during or after operative procedures (even in cases of minor procedures, e.g. tooth extraction). Use with caution before surgery, including tooth extraction. Temporary discontinuation of treatment may be necessary.
It is not recommended during menorrhagia where it may increase menstrual bleeding.
It is to be used with caution in cases of hypertension and when patients have a past history of gastric or duodenal ulcer or haemorrhagic episodes or are undergoing therapy with anticoagulants.
Patients should report any unusual bleeding symptoms to their physician. If gastrointestinal bleeding or ulceration occurs the treatment should be withdrawn.
Acetylsalicylic acid should be used with caution in patients with moderately impaired renal or hepatic function (contraindicated if severe), or in patients who are dehydrated since the use of NSAIDs may result in deterioration of renal function. Liver function tests should be performed regularly in patients presenting slight or moderate hepatic insufficiency.
Acetylsalicylic acid may promote bronchospasm and asthma attacks or other hypersensitivity reactions. Risk factors are existing asthma, hay fever, nasal polyps or chronic respiratory diseases. The same applies for patients who also show allergic reaction to other substances (e.g. with skin reactions, itching or urticaria).
Serious skin reactions, including Steven-Johnsons syndrome, have rarely been reported in association with the use of acetylsalicylic acid.
It 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. Where prolonged therapy is required, patients should be reviewed regularly.
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. 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 Acetylsalicylic Acid taken at over dosage.
Acetylsalicylic Acid should be avoided in late pregnancy and generally during breast feeding.
Magnesium Hydroxide:
Use with caution in the elderly and debilitated and in patients with impaired liver function. Also in patients with impaired kidney function as hypermagnesaemia may result.
In young children the use of magnesium hydroxide can produce a hypermagnesemia, especially if they present renal impairment or dehydration.
Pregnancy and Nursing Mother:
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 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.
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, shortterm 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.
Effects on ability to drive and use machine:
None stated.
Presentation:
10 Tablets in Alu-Alu Blister, such 3 blisters packed in a carton along with package insert.
Storage:
Keep in dry place, protected from light at a temperature below 30°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescribed medicine.

The holder of Trade Mark and Marketing Authorisation:
BELINDA LABORATORIES LLP.
London, UK

Manufactured by:
Akums Drugs & Pharmaceuticals Ltd.,
Plot No. 19, 20 & 21, Sector-6A, IIE, SIDCUL, Ranipur,
Haridwar-249403, Uttarakhand, India

02Z