
WINSPIRIN

Acetylsalicylic Acid Dispersible Tablet 300mg

Each tablet contains:

Aspirin 300 mg

Description:

Product Description

White, circular, biconvex, uncoated tablets with score line. Dispersible tablet gives a cloudy liquid after dispersion in water.

Pharmacodynamics

At higher doses, aspirin is an effective anti-inflammatory agent, partially due to inhibition of inflammatory mediators via cyclo-oxygenase inhibition in peripheral tissues. Acetyl salicylic acid affects platelet aggregation by irreversibly inhibiting prostaglandin cyclo-oxygenase. This effect lasts for the life of the platelet and prevents the formation of the platelet aggregating factor thromboxane A₂. Non-acetylated salicylates do not inhibit this enzyme and have no effect on platelet aggregation. At somewhat higher doses, aspirin reversibly inhibits the formation of prostaglandin I₂ (prostacyclin), which is an arterial vasodilator and inhibits platelet aggregation.

Pharmacokinetics

Absorption: Aspirin after oral administration is generally well absorbed from the gastrointestinal (GI) tract. Following absorption, aspirin is hydrolyzed to salicylic acid with peak plasma levels of salicylic acid occurring within 1-2 hours of dosing. The rate of absorption from the GI tract is dependent upon the dosage form, the presence or absence of food, gastric pH and other physiologic factors.

Distribution: Salicylic acid is widely distributed to all tissues and fluids in the body including the central nervous system (CNS), breast milk and fetal tissues. The highest concentrations are found in the plasma, liver, renal cortex, heart and lungs. The protein binding of salicylate is concentration-dependent, i.e., non-linear. At low concentrations (<100 micrograms/milliliter (mcg/ml)), approximately 90 percent of plasma salicylate is bound to albumin while at higher concentrations (> 400 mcg/ml), only about 75 percent is bound. The early signs of salicylic overdose (salicylism), including tinnitus (ringing in the ears), occur at plasma concentrations approximating 200 mcg/ml.

Metabolism: Aspirin is rapidly hydrolyzed in the plasma to salicylic acid such that plasma levels of aspirin are essentially undetectable 1-2 hours after dosing. Salicylic acid is primarily conjugated in the liver to form salicyluric acid, a phenolic glucuronide, an acyl glucuronide, and a number of minor metabolites. Salicylic acid has a plasma half-life of approximately 6 hours. Salicylate metabolism is saturable and total body clearance decreases at higher serum concentrations due to the limited ability of the liver to form both salicyluric acid and phenolic glucuronide.

Elimination: The elimination of salicylic acid follows zero order pharmacokinetics, (i.e., the rate of drug elimination is constant in relation to plasma concentration). Renal excretion of unchanged drug depends upon urine pH. As urinary pH rises above 6.5, the renal clearance of free salicylate increases from < 5 percent to > 80 percent. Following therapeutic doses, approximately 10 percent is found excreted in the urine as salicylic acid, 75 percent as salicyluric acid, 10 percent and 5 percent as the phenolic and acyl glucuronides, respectively.

Indications

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

- 1) The relief of headache, toothache, migraine, neuralgia, sore throat, dysmenorrhoea.
- 2) The symptomatic relief of influenza, feverishness, rheumatic pains, sciatica, lumbago, fibrositis, muscular aches and pains.
- 3) It also has an antithrombotic action, mediated through inhibition of platelet activation, which has been shown to be useful in secondary prophylaxis following myocardial infarction, and in patients with unstable angina and cerebral transient ischaemic attacks.

Recommended Dose

For the relief of headache, toothache, migraine, neuralgia, sore throat, dysmenorrhea and symptomatic relief of influenza, feverishness, rheumatic pains, sciatica, lumbago, fibrositis, muscular aches and pains:

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

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

Antithrombotic action: For its antithrombotic effect following myocardial infarction, transient ischaemic attack, or in patients with unstable angina, the recommended dose is 300mg daily. The suitable dose depends on treatment needs and patient's condition. Daily intake of aspirin should be under doctor's supervision.

Direction: Tablet can be dispersed in water immediately before use or swallowed whole.

Gastric irritation may be reduced by taking doses after food.

Instructions for Use

Tablet can be dispersed in water immediately before use or swallowed whole.

Route of Administration

Oral.

Contraindications

Reye's Syndrome: Aspirin should not be used in children or teenagers for viral infections, with or without fever, because of the risk of Reye's syndrome with concomitant use of aspirin in certain viral illness.

Allergy: Aspirin is contraindicated in patients with known allergy to nonsteroidal anti-inflammatory drug products and in patients with the syndrome of asthma, rhinitis, and nasal polyps. Aspirin may cause severe urticaria, angioedema, or bronchospasm (asthma).

Warning and Precautions

Warning: NOT TO BE GIVEN TO CHILDREN UNDER 16 YEARS OF AGE.

Amaran: TIDAK BOLEH DIBERI KEPADA KANAK-KANAK BERUMUR KURANG DARIPADA 16 TAHUN.

Compulsory Warning (NSAIDs)

Risk of GI Ulceration, Bleeding and Perforation with NSAID

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID therapy. Although minor upper GI problems (e.g. dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDs even in the absence of previous GI tract symptoms.

Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Patients with prior history of serious GI events and other risk factors associated with peptic ulcer disease (e.g. alcoholism, smoking and corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

Warnings

Alcohol Warning: Patients who consume three or more alcoholic drinks every day should be counseled about the bleeding risks involved with chronic, heavy alcohol use while taking aspirin.

Coagulation Abnormalities: Even low doses of aspirin can inhibit platelet function leading to an increase in bleeding time. This can adversely affect patients with inherited (hemophilia) or acquired (liver disease or vitamin K deficiency) bleeding disorders.

GI Side Effects: GI side effects include stomach pain, heartburn, nausea, vomiting and gross GI bleeding. Although minor upper GI symptoms, such as dyspepsia, are common and can occur anytime during therapy, physicians should remain alert for signs of ulceration and bleeding, even in the absence of previous GI symptoms. Physicians should inform patients about the signs and symptoms of GI side effects and what steps to take if they occur.

Peptic Ulcer Disease: Patients with a history of active peptic ulcer disease should avoid using aspirin, which can cause gastric mucosal irritation and bleeding.

- 1) Aspirin combined with anticoagulant therapy was associated with no reduction in stroke, systemic embolism, or myocardial infarction in patients with AF. Aspirin combined with warfarin was associated with an incremental rate of major bleeding of 1.6% per year. No increased major bleeding occurred with aspirin and ximelagatran. These results suggest that the risks associated with addition of aspirin to anticoagulation in patients with AF outweigh the benefit.
- 2) Aspirin reduce blood flow to your kidneys. If your kidneys are already not filtering properly, the additional decrease in blood flow could send you into acute renal failure.
Patients with bronchial asthma, chronic bronchoconstrictive (obstructive) respiratory disease, hay fever, or swelling of the nasal mucous (nasal polyps) may react to non-steroidal analgesics with asthma attacks, localized swelling of the skin or mucous (Quincke's edema), or urticaria more frequently than other patients.: "Barbiturates and other sedatives may mask the respiratory symptoms of aspirin over dosage and have been reported to enhance its toxicity."

Avoid food/beverages containing alcohol.

Interactions with Other Medicaments

Anticoagulant Therapy (Heparin and Warfarin): Patients on anticoagulation therapy are at increased risk for bleeding because of drug-drug interactions and the effect on platelets. Aspirin can displace warfarin from protein binding site, leading to prolongation of both the prothrombin time and the bleeding time. Aspirin can increase the anticoagulant activity of heparin, increasing bleeding risk.

Acetazolamide: Concurrent use of aspirin and acetazolamide can lead to high serum concentrations of acetazolamide (and toxicity) due to competition at the renal tubule for secretion.

Angiotensin Converting Enzyme (ACE) Inhibitors: The hyponatremic and hypotensive effects of ACE inhibitors may be diminished by the concomitant administration of aspirin due to its indirect effect on the renin-angiotensin conversation pathway.

Beta Blockers: The hypotensive effects of beta blockers may be diminished by the concomitant administration of aspirin due to inhibition of renal prostaglandins, leading to decreased renal blood flow, and salt and fluid retention.

Anticonvulsants: Salicylate can displace protein-bound phenytoin and valproic acid, leading to decrease in the total concentration of phenytoin and an increase in serum valproic acid levels.

Methotrexate: Salicylate can inhibit renal clearance of methotrexate, leading to bone marrow toxicity, especially in the elderly or renal impaired.

Diuretics: The effectiveness of diuretics in patients with underlying renal or cardiovascular disease may be diminished by the concomitant administration of aspirin due to inhibition of renal prostaglandins, leading to decreased renal blood flow, and salt and fluid retention.

Uricosuric Agents (Probenecid and Sulfinpyrazone): Salicylates antagonize the uricosuric action of uricosuric agents.

Oral Hypoglycemics: Moderate doses of aspirin may increase the effectiveness of oral hypoglycemic drugs, leading to hypoglycemia.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs): The concurrent use of aspirin with other NSAIDs should be avoided because this may increase bleeding or lead to decreased renal function.

Pregnancy & Lactation

Pregnant women should only taken aspirin if clearly needed. Because of the known effects of NSAIDs on the fetal cardiovascular system (closure of the ductus arteriosus), use during the third trimester of pregnancy should be avoided. Salicylate products have also been associated with alterations in maternal and neonatal hemostasis mechanisms, decreased birth weight, and with perinatal mortality.

Labor and Delivery

Aspirin should be avoided 1 week prior to and during labor and delivery because it can result in excessive blood loss at delivery. Prolonged gestation and prolonged labor due to prostaglandin inhibition have been reported.

Nursing Mothers

Nursing mothers should avoid using aspirin because salicylate is excreted in breast milk. Use of high doses may lead to rashes, platelet abnormalities, and bleeding in nursing infants.

Side Effects

Central Nervous System: Agitation, cerebral edema, coma, confusion, dizziness, headache, subdural or intracranial hemorrhage, lethargy, seizures.

Cardiovascular: Dysrhythmias, hypotension, tachycardia.

Fluid and Electrolyte: Dehydration, hyperkalemia, metabolic acidosis, respiratory alkalosis.

Gastrointestinal: Dyspepsia, GI bleeding, ulceration and perforation, nausea, vomiting, transient elevations of hepatic enzymes, hepatitis, Reye's syndrome, pancreatitis.

Respiratory: Hyperpnea, pulmonary edema, tachypnea.

Urogenital: Interstitial nephritis, papillary necrosis, proteinuria, renal insufficiency and failure.

Hematologic: Prolongation of the prothrombin time disseminated intravascular coagulation, coagulopathy and thrombocytopenia.

Hypersensitivity: Acute anaphylaxis, angioedema, asthma, bronchospasm, laryngeal edema, urticaria.

Musculoskeletal: Rhabdomyolysis.

Metabolism: Hypoglycemia (in children), hyperglycemia.

Reproductive: Prolonged pregnancy and labor, stillbirths, lower birth weight infants, antepartum and postpartum bleeding.

Special Senses: Hearing loss, tinnitus, Patients with higher frequency hearing loss may have difficulty perceiving tinnitus. In these patients, tinnitus cannot be used as a clinical indicator of salicylism.

Symptoms and Treatment of Overdose

Signs and Symptoms: In acute overdose, severe acid-base and electrolyte disturbances may occur and are complicated by hyperthermia and dehydration. Respiratory alkalosis occurs early while hyperventilation is present, but is quickly followed by metabolic acidosis.

Treatment: Treatment consists primarily of supporting vital functions, increasing salicylate elimination, and correcting the acid-base disturbance. Gastric emptying and/or lavage are recommended as soon as possible after ingestion, even if the patient has vomited

spontaneously. After lavage and/or emesis, administration of activated charcoal, as slurry, is beneficial, if less than 3 hours have passed since ingestion. Charcoal adsorption should not be employed prior to emesis and lavage.

Severity of aspirin intoxication is determined by measuring the blood salicylate level. Acid-base status should be closely followed with serial blood gas and serum pH measurements. Fluid and electrolyte balance should also be maintained. In severe cases, hyperthermia and hypovolemia are the major immediate threats to life. Children should be sponged with tepid water. Replacement fluid should be administered intravenously and augmented with correction of acidosis. Plasma electrolytes and pH should be monitored to promote alkaline diuresis of salicylate if renal function is normal. Infusion of glucose may be required to control hypoglycemia.

Hemodialysis and peritoneal dialysis can be performed to reduce the drug content. In patients with renal insufficiency or in cases of life-threatening intoxication, dialysis is usually required. Exchange transfusion may be indicated in infants and young children.

Storage Condition

Store below 30°C. Protect from light and moisture.

Presentation

WINSPIRIN is packed in Alu-Alu blister pack. Each blister pack contains 10 tablets.

The blister are packed into 3 x10's, 10 x10's, 50 x 10's and 100 x 10's, in a carton along with a package insert.

Registration Number

MAL18066046XZ

Manufactured by & Product Registration Holder

KCK Pharmaceutical Industries Sdn. Bhd.

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