# Aspirin

**Aspilets®-EC**
**80 mg Enteric-Coated Tablet**
**antithrombotic**

## FORMULATION
Each enteric-coated tablet contains:
Aspirin ……..……80 mg

## PRODUCT DESCRIPTION
Yellow, round 9/32” diameter, biconvex tablet, plain on both sides

## CLINICAL PHARMACOLOGY
***Pharmacodynamics***
Aspirin is a nonsteroidal anti-inflammatory agent. The antithrombotic activity of aspirin is due to its inhibitory effect on platelets which is mediated via irreversible acetylation of platelet cyclooxygenase with subsequent blockade of platelet thromboxane synthesis. The inhibitory effect of aspirin on platelet thromboxane production persists for the lifespan of the platelet, around 7 to 10 days. As a result, acetylation of platelet cyclooxygenase and consequent inhibition of thromboxane formation is cumulative on repeated dosing.

Low doses of aspirin inhibit platelet aggregation and may be more effective than higher doses. Larger doses inhibit cyclooxygenase in arterial walls, interfering with prostacyclin production, a potent vasodilator and inhibitor of platelet aggregation.

***Pharmacokinetics***
Aspirin is rapidly absorbed from the gastrointestinal tract. After oral administration, absorption of non-ionized aspirin occurs in the stomach. Aspirin, in an acid-resistant coating, is not released in the stomach but in the alkaline environment of the intestine. Therefore, absorption of aspirin is delayed by 3 to 6 hours and time to achieve mean peak aspirin concentration is 4 to 6 hours after administration of the enteric-coated tablet.

Aspirin is rapidly and widely distributed into most body tissues and fluids. Aspirin’s volume of distribution is 0.15 to 0.2 L/kg. Aspirin is poorly bound to plasma proteins; the unhydrolyzed drug is 33% bound at a serum salicylate concentration of 120 mcg/mL.

Aspirin’s elimination half-life is about 15 to 20 minutes. Unlike salicylate, unhydrolyzed aspirin does not undergo capacity-limited metabolism and does not accumulate in plasma after multiple doses. Aspirin is partially hydrolyzed to salicylate during absorption by esterases in the gastrointestinal mucosa after oral administration. After absorption, unhydrolyzed aspirin is rapidly and almost completely hydrolyzed by esterases principally in the liver but also in plasma, erythrocytes, and synovial fluid; hydrolysis occurs more slowly in synovial fluid since the amounts of esterases in synovial fluid are lower. Aspirin may be hydrolyzed more slowly in women since women apparently have lower amounts of plasma aspirin esterases. About 1% of an oral aspirin dose is excreted unhydrolyzed in urine. The remainder is excreted in urine as salicylate and its metabolites.

## INDICATIONS
**For the prevention of cardiovascular disease:** Encourage aspirin use in men (age 45 to 79 years old) and women (age 55 to 79 years old) when potential benefit (i.e., prevention of myocardial infarction in men and prevention of ischemic stroke in women) outweighs potential harm of gastrointestinal hemorrhage.

| Risk Level at which CVD Events Prevented (Benefit) Exceeds GI Harms | | | |
|---|---|---|---|
| Men | | Women | |
| Age (years) | 10-year CHD Risk (%) | Age (years) | 10-year Stroke Risk (%) |
| 45 to 59 | ≥ 4 | 55 to 59 | ≥ 3 |
| 60 to 69 | ≥ 9 | 60 to 69 | ≥ 8 |
| 70 to79 | ≥ 12 | 70 to 79 | ≥ 11 |

Legend: CVD = cardiovascular disease; GI = gastrointestinal CHD = coronary heart disease

- **For primary prevention of thromboembolic disorders and cardiovascular events:**
  - ⇒ Ischemic stroke
  - ⇒ Transient ischemic attack (TIA)
  - ⇒ Prevention of recurrent MI
  - ⇒ Unstable angina pectoris
  - ⇒ Chronic stable angina pectoris

- **For secondary prevention of cardiovascular disease in persons with diabetes mellitus especially in the following subgroups:**
  - ⇒ History of myocardial infarction, vascular bypass procedure, stroke or transient ischemic attack, and angina.
  - ⇒ Persons with additional risk factors: hypertension, smoking, dyslipidemia, and family history of cardiovascular disease.

**Revascularization procedures**
For patients who have undergone revascularization procedures such as coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty (PTCA), and carotid endarterectomy when there is a pre-existing condition for which aspirin is already indicated.

**Pregnancy-induced hypertension**
For primary prevention of pregnancy-induced hypertension, preeclampsia and intrauterine growth retardation particularly in pregnant women with pre-existing chronic hypertension, auto-immune disorders like systemic lupus erythematosus (SLE), positive cardiolipin antibody test, history of recurring toxemia in successive pregnancies, and hypotension developing before the 20$^{th}$ week of gestation.

**DOSAGE AND ADMINISTRATION**
***General Dosing Recommendations:***
- Take each dose of aspirin with a full glass of water unless patient is fluid restricted.
- The tablet must be swallowed whole with a glass of water. Do not chew, crush, or bite the enteric-coated tablet since this may cause inappropriate release and absorption of the drug.

| INDICATIONS | INITIAL DOSE | MAINTENANCE DOSE |
|---|---|---|
| **Ischemic Stroke and TIA** | 50 to 325 mg once daily | Continue therapy indefinitely |
| **Prevention of Recurrent MI** | 75 to 325 mg once daily | Continue therapy indefinitely |
| **Unstable Angina Pectoris and Chronic Stable Angina Pectoris** | 75 to 325 mg once daily | Continue therapy indefinitely |
| **Primary and Secondary Prevention of Cardiovascular Events in Patients with Type 1 or Type 2 Diabetes Mellitus** | 75 to 325 mg once daily | Continue therapy indefinitely |
| **Coronary Artery Bypass (CABG)** | 325 mg once daily starting 6 hours post-procedure | Continue therapy for 1 year post-procedure |
| | | |

| | | |
|---|---|---|
| **Percutaneous Transluminal Coronary Angioplasty (PTCA)** | 325 mg given 2 hours pre-angioplasty | 160 to 325 mg once daily Continue therapy indefinitely |
| **Carotid Endarterectomy** | 80 mg once daily to 650 mg twice daily, started pre-surgery | Continue therapy indefinitely |
| **Prevention of Complications of Pregnancy**<br>• Pregnancy-induced hypertension<br>• Preeclampsia<br>• Intrauterine growth retardation<br>• Pregnancy with existing conditions (e.g., SLE, positive cardiolipin antibody test) | 80 mg daily from 13$^{th}$ to 26$^{th}$ weeks of gestation | |
| Or, as prescribed by a physician. | | |

**CONTRAINDICATIONS**

- Known hypersensitivity to aspirin
- Patients with asthma, rhinitis, and nasal polyps. Aspirin may cause severe urticaria, angioedema, or bronchospasm.
- Avoid use 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 illnesses.

**WARNINGS AND PRECAUTIONS**

***Gastrointestinal Bleeding Warning:*** This product contains an NSAID, which may cause severe gastrointestinal bleeding. The chance is higher if you:

- Are age 60 years or older
- Have had gastrointestinal ulcers or bleeding problems
- Take an anticoagulant or steroid medicine
- Take other medicines containing prescription or nonprescription NSAIDs (ibuprofen, naproxen, or others)
- Take more or for a longer time than prescribed

***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:*** Aspirin can inhibit platelet function leading to an increase in bleeding time. Avoid its use in patients with inherited (hemophilia) or acquired (liver disease or vitamin K deficiency) bleeding disorders.

***General:***

- Do not use in patients with severe renal failure (glomerular filtration rate >10 mL/minute) and severe hepatic insufficiency.
- Avoid aspirin use one week prior to and during labor, delivery, and any surgical procedure because it can result in excessive blood loss.

**INTERACTIONS WITH OTHER MEDICAMENTS**

***Angiotensin-converting enzyme (ACE) inhibitors*:** Hyponatremic and hypotensive effects of ACE inhibitors may be diminished

***Acetazolamide:*** Increased serum acetazolamide concentrations and toxicity due to competition at the renal tubule for secretion

***Anticoagulant therapy (Heparin, Warfarin):*** Increased risk of bleeding because of drug-drug interactions and the effect on platelets

***Anticonvulsants:*** Salicylate can displace protein-bound phenytoin and valproic acid, leading to decreased total concentration of phenytoin and increased serum valproic acid levels

***Beta-blockers:*** Diminished hypotensive effects of beta-blockers due to inhibition of renal prostaglandins, leading to decreased renal blood flow, and salt and fluid retention

***Diuretics:*** Diminished effectiveness of diuretics in patients with underlying renal or cardiovascular disease due to inhibition of renal prostaglandins, leading to decreased renal blood flow and salt and fluid retention

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

***NSAIDs:*** Increased bleeding or may lead to decreased renal function

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

***Uricosuric agents (Probenecid, Sulfinpyrazone):*** Salicylates antagonize the uricosuric action of these agents

**STATEMENT ON USAGE FOR HIGH-RISK GROUPS**

***Pregnancy:*** Pregnant women should only take aspirin if clearly needed. Avoid use during the third trimester of pregnancy because of aspirin's known effect on the fetal cardiovascular system (i.e., closure of the ductus arteriosus).

***Lactation:*** Breastfeeding 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 breastfed infants.

**UNDESIRABLE EFFECTS**

***Body as a Whole:*** Fever, hypothermia, thirst

***Cardiovascular:*** Dysrhythmias, hypotension, tachycardia

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

***Gastrointestinal:*** Dyspepsia, gastrointestinal bleeding, ulceration and perforation, nausea, vomiting, transient elevations of hepatic enzymes, hepatitis, Reye's Syndrome, pancreatitis

***Hematologic:*** Prolongation of prothrombin time, disseminated intravascular coagulation, coagulopathy, thrombocytopenia

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

***Metabolism:*** Hypoglycemia (in children), hyperglycemia

***Muskuloskeletal:*** Rhabdomyolysis

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

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

***Respiratory:*** Hyperpnea, pulmonary edema, tachypnea

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

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

**OVERDOSE AND TREATMENT**

In salicylate overdosage resulting from acute ingestion of aspirin, little or no toxicity generally occurs in individuals ingesting less than 150 mg/kg, mild to moderate toxicity in those ingesting 150 to 300 mg/kg, severe toxicity in those ingesting 300 to 500 mg, and potentially lethal toxicity in those ingesting greater than 500 mg/kg. A single lethal dose of aspirin in adults is not known with certainty but death may be expected at 30 g.

The principal toxic effects of salicylate overdosage are extension of pharmacologic actions and include local gastrointestinal irritation, direct central nervous system stimulation of respiration, severe acid-base and electrolyte disturbances and are complicated by hyperthermia and dehydration. Respiratory alkalosis occurs early while hyperventilation is present, but is quickly followed by metabolic acidosis.

Treatment consists primarily of supporting vital functions, increasing salicylate elimination, and correcting the acid-base disturbance. Gastric emptying and/or lavage is recommended as soon as possible after ingestion, even if the patient has vomited spontaneously. After lavage and/or emesis, administration of activated charcoal (as a 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 be maintained.

Hemodialysis and peritoneal dialysis may be performed to reduce the body drug content. Dialysis is usually required in patients with renal insufficiency or in cases of life-threatening intoxication.

**CAUTION**
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph **AND** Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

**AVAILABILITY**
**Aspirin (Aspilets®-EC) 80 mg Enteric-Coated Tablet**, in flex foil x 10s (box of 150s)

**STORE AT TEMPERATURES NOT EXCEEDING 30°C**
**KEEP THE PRODUCT OUT OF SIGHT AND REACH OF CHILDREN**

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