

## PACKAGE INSERT TEMPLATE FOR ACETYLSALICYLIC ACID/ASPIRIN TABLET

### Brand or Product Name

[Product name] Enteric-coated tablets 100mg

[Product name] Enteric-coated tablets 300 mg

### Name and Strength of Active Substance(s)

Acetylsalicylic acid ....mg

### Product Description

[Visual description of the appearance of the product (eg colour etc)]

eg White, circular flat beveled edge tablets marked '100' on one side

### Pharmacodynamics

Acetylsalicylic acid is an analgesic, anti-inflammatory, antipyretic and an inhibitor of platelet aggregation. It prolongs the bleeding time. It inhibits fatty acid cyclo-oxygenase by acetylation of the active site of the enzyme, and most of its pharmacological effects are due to inhibition of the formation of cyclo-oxygenase products including thromboxanes, prostaglandins and prostacyclin.

Acetylsalicylic acid has an active metabolite (salicylate) which, in addition to possessing some anti-inflammatory properties in its own right, also has important effects on respiration, acid-base balance and the stomach. Salicylates stimulate respiration by a direct effect on the medulla, and at high concentrations, uncouple oxidative phosphorylation in muscle, increasing oxygen consumption and carbon dioxide production. Hyperventilation causes respiratory alkalosis which is compensated by renal excretion of bicarbonate.

### Pharmacokinetics

#### *Absorption*

In general, immediate Acetylsalicylic acid is well and completely absorbed from the gastrointestinal (GI) tract. Following absorption, Acetylsalicylic acid 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 (the presence or absence of GI antacids or buffering agents), and other physiologic factors. Enteric coated Acetylsalicylic acid products are erratically absorbed from the GI tract.

#### *Metabolism*

Acetylsalicylic acid is rapidly hydrolyzed in the plasma to salicylic acid such that plasma levels of Acetylsalicylic acid 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. Following toxic doses (10-20 grams (g)), the plasma half-life may be increased to over 20 hours.

### *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.

### *Excretion*

The elimination of salicylic acid 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.

### *Elimination Half-life*

Salicylic acid: approximately 6 h

## **Indication**

Acetylsalicylic acid is indicated for unstable angina, acute myocardial infarction, prevention of a repeat myocardial infarction after an initial myocardial infarction, and following operations or other interventions in arterial blood vessels.

It is also used for prevention of transient ischaemic attack and cerebral infarction after the onset of precursor stages.

## **Recommended Dosage**

### *Adult Dosage*

*For unstable angina pectoris and acute myocardial infarction*

100mg acetylsalicylic acid daily.

*Prevention of a repeat myocardial infarction after an initial myocardial infarction (reinfarction prophylaxis)*

300mg acetylsalicylic acid daily.

*Following operations or other interventions in arterial blood vessels (e.g. after aortocoronary venous bypass; ACVB, in percutaneous transluminal coronary angioplasty; PTCA)*

100mg acetylsalicylic acid daily.

*To prevent transient ischaemic attacks (TIA) and cerebral infarction following manifestation of the precursor stages*

100mg acetylsalicylic acid daily.

### *Pediatric and children Dosage*

Not to be given to children under 16 years of age.

## **Mode of Administration**

Oral

## **Contraindications**

Known intolerance to Acetylsalicylic acid or any of the other ingredients in the tablet. Acetylsalicylic acid is contraindicated in patients with active peptic ulceration or a history of peptic ulceration and those with haemophilia or other clotting disorders or gout. Known hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to Acetylsalicylic acid or non-steroidal; anti-inflammatory drugs.

Acetylsalicylic acid should not be taken concurrently with anti-coagulants.

## **Warnings and Precautions**

“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”.

Hypersensitivity to other anti-inflammatory/antirheumatic drugs or other allergenic substances.

Allergies (e.g. skin reactions, itching, nettle rash) or asthma, hay fever, nasal polyps, chronic respiratory tract infections.

Concomitant treatment with anticoagulant drugs.

Gastric or duodenal ulcers or a history of gastrointestinal bleeding.

Impaired liver and kidney function.

Before surgery (including minor surgery such as dental extractions); the bleeding time can be prolonged.

Habitual use of analgesics can lead to permanent kidney damage with the risk of kidney failure .The risk is particularly great when several different analgesics are taken concomitantly.

At low doses acetylsalicylic acid reduces the excretion of uric acid. This may cause a gout attack in predisposed patients.

## **Interactions with Other Medicaments**

The effects of the medicines or groups of substances below may be affected by concomitant treatment with acetylsalicylic acid.

Enhanced effects ranging up to an increased risk of side effects:

Anticoagulants (e.g. coumarin, heparin) and thrombolytic drugs: acetylsalicylic acid can increase the risk of bleeding if taken before anticoagulant treatment.

Other platelet aggregation inhibitors (drugs that inhibit the clumping together of blood platelets), e.g. ticlopidine, Clopidogrel: increased bleeding risk.

Drug product containing cortisone or cortisone-like substances (with the exception of products that are applied topically or cortisone replacement therapy for Addison's disease): increased risk for gastrointestinal side effects.

Alcohol: increased risk of gastrointestinal ulcers and bleeding.

Other analgesics and anti-inflammatory medicines (nonsteroidal anti-inflammatory drugs) and other antirheumatic medicines in general: increased risk for gastrointestinal ulcers and bleeding.

Antidiabetics: the blood glucose level can be reduced.

Digoxin (a drug to strengthen the heart muscle contraction).

Methotrexate (a drug used to treat cancer and certain rheumatic disorders).

Valproic acid (a drug used to treat convulsions of the brain).

Selective Serotonin Re-uptake inhibitors (certain medicines for treatment of depression): increased risk for gastrointestinal bleeding.

Certain antibiotics (sulphonamides and sulphonamide combinations, e.g. sulphamethoxazole / trimethoprim).

Triiodothyronine (a medicine for treating hypothyroidism).

Weakening of effects:

Certain medicines that increase the excretion of urine (diuretics so-called aldosterone antagonists, e.g. spironolactone and canrenoate, and loop diuretics, e.g. furosemide).

Certain antihypertension drugs (in particular angiotensin converting enzyme inhibitors).

Gout remedies that promote the excretion of uric acid (e.g. probenecid, benzbromarone).

**Statement on Usage During Pregnancy and Lactation**

### *Pregnancy*

Acetylsalicylic acid used during the third trimester of pregnancy should be avoided because of the known effects of NSAIDs on the fetal cardiovascular system. Salicylate have also been associated with alterations in maternal and neonatal hemostasis mechanisms, decreased birth weight, and with perinatal mortality.

### *Lactation*

Nursing mothers should avoid using Acetylsalicylic acid. Use of high doses may lead to rashes, platelet abnormalities, and bleeding in nursing infants.

## **Adverse Effects / Undesirable Effects**

### *Gastrointestinal Effects*

Gastrointestinal disorders such as heartburn, nausea, vomiting, abdominal pain. Gastrointestinal bleeding which in very rare cases can lead to iron deficiency anaemia. Gastrointestinal ulcers which in very rare cases can lead to perforation. Elevated liver values have been reported.

### *Neurologic Effects*

Headache, dizziness, impaired hearing ability, tinnitus can be signs of an overdose.

### *Hematologic effect:*

Bleeding, e.g. nosebleeds or bleeding gums, possibly with prolongation of the bleeding time.

### *Dermatologic Effects:*

Hypersensitivity reactions such as skin reactions.

### *Hepatic Effects*

Elevated liver values.

### *Renal Effects*

Very rare cases of renal impairment and acute renal failure.

### *Otic: Tinnitus*

*Respiratory:* Bronchospasm

*Other:* Angioedema, Reye's syndrome

## **Overdose and Treatment**

### *Symptoms*

Moderate intoxication:

Tinnitus, hearing disorders, headache and vertigo are reported in all cases of overdosage

Severe intoxication:

Fever, hyperventilation, ketosis, respiratory alkalosis, metabolic acidosis, coma, cardiovascular shock, respiratory failure, severe hypoglycaemia.

### *Treatment*

The moderate intoxication can be eliminated by reducing the dose. Meanwhile for the severe intoxication need to be treated at hospital. Gastric lavage and administration of activated carbon, monitoring of the acid-base balance. Alkaline diuresis to attain a urine pH of between 7.5 and 8;

increased alkaline diuresis must be considered if the plasma Salicylate concentration exceeds 500 mg/l (3.6 mmol/l) in adults or 300 mg/l (2.2 mmol/l) in children. Optionally haemodialysis in cases of severe intoxication. Fluid loss must be compensated and Symptomatic treatment.

**Storage Conditions**

*[ Store below 30° C , protect from light and moisture ]*

**Dosage Forms and Packaging Available**

*[ Packaging type & pack size]*

**Name and Address of Manufacturer**

*[ Name & full address of manufacturer ]*

**Name and Address of Marketing Authorization Holder**

*[ Name & full address of marketing authorization holder ]*

**Date of Revision of Package Insert**

*[ day/month/year ]*