

SCHEDULING STATUS:

S2

PROPRIETARY NAME AND DOSAGE FORM:**BAYER ASPIRIN Cardio 100**

Enteric Coated Tablets

COMPOSITION:

The active ingredient is 100mg Acetylsalicylic acid per tablet.

Excipients are: cellulose, maize starch, methacrylic acid- ethyl acrylate copolymer, talc, triethyl citrate, sodium lauryl sulphate, polysorbate 80

PHARMACOLOGICAL CLASSIFICATION: A 8 Medicines acting on the blood and haemopoietic system.

PHARMACOLOGICAL ACTION:**Pharmacodynamic properties**

Acetylsalicylic acid inhibits platelet aggregation by inactivation of platelet cyclo-oxygenase, the enzyme that produces the cyclic endoperoxide precursor of thromboxane A₂.

Pharmacokinetic properties

Following oral administration, acetylsalicylic acid is absorbed rapidly and completely from the gastro-intestinal tract. During and after absorption acetylsalicylic acid is converted into its main active metabolite, salicylic acid. Maximal plasma levels are reached after 10-20 minutes for acetylsalicylic acid and after 0.3-2 hours for salicylic acid, respectively. Due to the acid-resistant lacquer of Bayer Aspirin Cardio 100, the active substance is not released in the stomach but in the alkaline milieu of the intestine. Therefore, absorption of acetylsalicylic acid is delayed by 3-6 hours after application of Bayer Aspirin Cardio 100 in comparison to plain tablets.

Both acetylsalicylic acid and salicylic acid are extensively bound to plasma proteins and are rapidly distributed throughout the body. Salicylic acid passes into breast milk and crosses the placenta.

Salicylic acid is eliminated predominantly by hepatic metabolism. Its metabolites are salicyluric acid, salicylic phenolic glucuronide, salicylacyl glucuronide, gentisic acid, and gentisuric acid.

The elimination kinetics of salicylic acid is dose-dependent, as metabolism is limited by liver enzyme capacity. The elimination half life therefore varies from 2 to 3 hours after low doses to up to about 15 hours at high doses. Salicylic acid and its metabolites are excreted mainly via the kidneys.

INDICATIONS

Bayer Aspirin Cardio 100 is indicated for the following cardiovascular uses:

- To reduce the risk of myocardial infarction in patients with unstable angina or in patients who have had a previous myocardial infarction.
- To reduce the risk of recurrent transient ischaemic attacks or stroke in men who have had transient ischaemia of the brain due to fibrin platelet emboli.

- To reduce the risk of graft occlusion following aortocoronary by-pass surgery.
- For reducing the risk of myocardial ischaemic events in people with cardiovascular risk factors.

CONTRA-INDICATIONS:

- Hypersensitivity to acetylsalicylic acid, to other salicylates, or to any other components of the product
- A history of asthma induced by the administration of salicylates or substances with a similar action, notably non-steroidal anti-inflammatory medicines.
- Acute gastrointestinal ulcers
- Haemorrhagic diathesis
- Severe renal impairment
- Severe hepatic impairment
- Severe cardiac failure
- Combination with methotrexate at doses of 15 mg/week or more (see “Interactions”)
- Last trimester of pregnancy (see “Pregnancy & Lactation”)

WARNINGS:

Bayer Aspirin Cardio 100 should be used with particular caution in the following cases:

- hypersensitivity to analgesics,/ anti-inflammatory agents/ antirheumatic medicinal products and in the presence of other allergies.
- history of gastro-intestinal ulcers including chronic or recurrent ulcer disease or history of gastro-intestinal bleedings
- with concomitant treatment with anticoagulants (see Interactions)
- impaired renal function;
- impaired hepatic function;
- ibuprofen may interfere with the acetylsalicylic acid’s inhibitory effect on platelet aggregation. Patients should tell their doctor if they are on a Bayer Aspirin Cardio 100 regimen and take ibuprofen for pain.

Bayer Aspirin Cardio 100 may precipitate bronchospasm and induce asthma attacks and other hypersensitivity reactions. Risk factors are: pre-existing asthma, hay fever, nasal polyps, or chronic respiratory disease. This also applies to patients exhibiting allergic reactions (e.g. cutaneous reactions, itching, urticaria) to other substances.

Due to its inhibitory effect on platelet aggregation which persists for several days after administration, Bayer Aspirin Cardio 100 may lead to an increased bleeding tendency during and after surgical operations (including minor surgeries, e.g. dental extractions).

At low doses, acetylsalicylic acid reduces the excretion of uric acid. This can possibly trigger gout attacks in predisposed patients.

Acetylsalicylic acid containing products should not be used in children and adolescents for viral infections with or without fever without consulting a physician. In certain viral illnesses, especially influenzae A, influenzae B and varicella, there is a risk of Reye’s syndrome, a very rare but possibly life-threatening illness requiring immediate medical action. The risk may be increased when Bayer Aspirin Cardio 100 is given concomitantly.

Should persistent vomiting occur with such diseases, this may be a sign of Reye's syndrome.

INTERACTIONS

Contraindicated Interactions:

Methotrexate used at doses of 15 mg/week or more:

Increased haematological toxicity of methotrexate (decreased renal clearance of methotrexate by anti-inflammatory agents in general and displacement of methotrexate from its plasma protein binding by salicylates) (see "Contraindications").

Combinations requiring precautions for use:

Methotrexate, used at doses of less than 15 mg/week:

Increased haematological toxicity of methotrexate (decreased renal clearance of methotrexate by anti-inflammatory agents in general and displacement of methotrexate from its plasma protein binding by salicylates).

Ibuprofen:

The concomitant administration of ibuprofen antagonizes the irreversible platelet inhibition induced by acetylsalicylic acid. Treatment with ibuprofen in patients with increased cardiovascular risk may limit the cardioprotective effects of Bayer Aspirin Cardio 100.

Anticoagulants, thrombolytics/other inhibitors of platelet aggregation/hemostasis:

Increased risk of bleeding.

Other non-steroidal anti-inflammatory medicines with salicylates at high doses :

Increased risk of ulcers and gastrointestinal bleeding due to synergistic effect.

Selective Serotonin Reuptake Inhibitors (SSRIs):

Increased risk of upper gastrointestinal bleeding due to possibly synergistic effect

Digoxin:

Plasma concentrations of digoxin are increased due to a decrease in renal excretion

Antidiabetics, e.g. insulin, sulphonylureas:

Increased hypoglycemic effect by high doses of acetylsalicylic acid via hypoglycaemic action of acetylsalicylic acid and displacement of sulfonylurea from its plasma protein binding

Diuretics in combination with acetylsalicylic acid at higher doses:

Decreased glomerular filtration via decreased renal prostaglandin synthesis.

Systemic glucocorticoids, except hydrocortisone used as replacement therapy in Addison's disease:

Decreased blood salicylate levels during corticosteroid treatment and risk of salicylate overdose after this treatment is stopped via increased elimination of salicylates by corticosteroids.

Angiotensin converting enzyme inhibitors (ACE) in combination with acetylsalicylic acid at higher doses:
Decreased glomerular filtration via inhibition of vasodilator prostaglandins. Furthermore, decreased antihypertensive effect.

Valproic acid:

Increased toxicity of valproic acid due to displacement from protein binding sites.

Alcohol:

Increased damage to gastro-intestinal mucosa and prolonged bleeding time due to additive effects of acetylsalicylic acid and alcohol

Uricosurics such as benzbromarone, probenecid:

Decreased uricosuric effect (competition of renal tubular uric acid elimination).

PREGNANCY AND LACTATION:

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. During the first and second trimester of pregnancy, acetyl salicylic acid containing medicines are not recommended. 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 child, at the end of pregnancy, to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even after very low doses
- inhibition of uterine contractions resulting in delayed or prolonged labour

Consequently, Bayer Aspirin Cardio 100 is contraindicated during the third trimester of pregnancy.

Lactation

Salicylates and its metabolites pass into breastmilk in small quantities. Safety is unproven. When regular use of Bayer Aspirin Cardio 100 is indicated, breastfeeding should be discontinued.

DOSAGE AND DIRECTIONS FOR USE:

100 to 300 mg to be taken every day, preferably at the same time each day:

- To reduce the risk of myocardial infarction in patients with unstable angina or in patients who have had a previous myocardial infarction.

- To reduce the risk of recurrent transient ischaemic attacks or stroke in men who have had transient ischaemia of the brain due to fibrin platelet emboli.
- To reduce the risk of graft occlusion following aortocoronary by-pass surgery.

The tablets should be swallowed whole. Do not chew, break or crush the tablets as this will destroy the protective effect of the enteric coating.

100 mg to be taken every day, preferably at the same time each day:

- For reducing the risk of myocardial ischaemic events in people with cardiovascular risk factors.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Upper and lower gastrointestinal tract disorders such as common signs and symptoms of dyspepsia, gastrointestinal and abdominal pain, rarely gastrointestinal inflammation, gastrointestinal ulcer. There have been reports of gastrointestinal ulcer hemorrhage and perforation, with the respective laboratory and clinical signs and symptoms.

Due to its inhibitory effect on platelets, Bayer Aspirin Cardio 100 may be associated with an increased risk of bleeding. Bleedings, such as perioperative hemorrhage, hematomas, epistaxis, urogenital bleedings, gingival bleedings, have been observed. Rare to very rare serious bleedings, such as gastrointestinal tract hemorrhage, cerebral hemorrhage (especially in patients with uncontrolled hypertension and/or on concomitant antihemostatic agents), which in single cases may be potentially life-threatening, have been reported (*see "Warnings"*).

Hemorrhage may result in acute and chronic posthemorrhagic anaemia / iron-deficiency anaemia (due to e.g. occult microbleeding) with respective laboratory and clinical signs and symptoms, such as asthenia, pallor, hypoperfusion.

Hypersensitivity reactions with respective laboratory and clinical manifestations include asthma syndrome, mild to moderate reactions potentially affecting skin, respiratory tract, gastrointestinal tract, and cardiovascular system, including symptoms such as rash, urticaria, oedema, pruritus, rhinitis, nasal congestion cardio-respiratory distress, and very rarely severe reactions, including anaphylactic shock.

Transient hepatic impairment with increase in liver transaminases has very rarely been reported.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT.

Poisoning must be feared in the elderly and above all in young children (therapeutic overdose or frequent accidental poisoning) in whom it may be fatal.

Symptomatology:

Moderate poisoning:

Nausea, vomiting, tinnitus, feeling of impaired hearing, headache, vertigo, and mental confusion are observed in case of overdose and can be controlled by a dosage reduction.

Severe poisoning:

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

Emergency management:

immediate transfer to hospital specialist unit,

gastric lavage, administration of activated charcoal, check of acid-base balance,

alkaline diuresis so as to obtain a urine pH between 7.5 and 8, forced alkaline diuresis should be considered when the plasma salicylate concentration is greater than: 500 mg/litre (3.6 mmol/litre) in adults or 300 mg/litre (2.2 mmol/litre) in children,

possibility of hemodialysis in severe poisoning,

fluid losses should be replaced,

symptomatic treatment.

IDENTIFICATION: White, round, coated tablets.

PRESENTATION: 100 mg tablets blister packed into packs of 30.

STORAGE INSTRUCTIONS: Store below 25°C. Keep out of reach of children.

REGISTRATION NUMBER: 31/8/ 0413

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Bayer (Pty) Ltd. Wrench Road, Isando, 1600. 1968/011192/07

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

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