Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

ASPIRIN® CARDIO

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains 100 mg acetylsalicylic acid

3. PHARMACEUTICAL FORM

Enteric-coated tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Inhibition of platelet aggregation:

- in unstable angina pectoris
- in acute myocardial infarction
- in reinfarction prophylaxis
- after vascular surgery or interventions (e.g. PTCA, CABG)
- for the prevention of transient ischaemic attacks (TIA) and cerebral infarction after the onset of precursor stages
- to prevent thrombosis of the coronary blood vessels in patients with multiple risk factors
- to prevent venous thrombosis and lung embolism.

For long-term prophylaxis of migraine.

4.2 Posology and method of administration

In unstable angina pectoris, in reinfarction prophylaxis, after arterial surgery or interventions:
Daily doses of 100-300 mg acetylsalicylic acid are recommended.

In acute myocardial infarction:
Daily doses of 100-160 mg acetylsalicylic acid are recommended.
The first tablet should be chewed in order to achieve fast absorption.

For the prevention of transient ischaemic attacks and cerebral infarction after the onset of precursor stages:
Daily doses of 30-300 mg acetylsalicylic acid are recommended.

For the prevention of thrombosis of the coronary blood vessels in patients with multiple risk factors:
Doses of 100-200 mg/daily or 300 mg every other day are recommended.

For the prevention of venous thrombosis and lung embolism:
Daily doses of 1000 - 1500 mg are recommended.

For prophylaxis of migraine:
Doses of 100-200 mg/daily or 300 mg every other day are recommended.

4.3 CONTRAINDICATIONS

Aspirin® Cardio must not be used in the following circumstances:

- Known hypersensitivity to the active substance acetylsalicylic acid or other salicylates or to any of the excipients of the product;
- In the presence of haemorrhagic diathesis;
- In the presence of gastric or duodenal ulcers;
- Last trimester of pregnancy.

4.4 Special warnings and special precautions for use

The medicinal product may be used in the following circumstances only after strict consideration of the risk-benefit ratio:

- First and second trimesters of pregnancy;
- During breast feeding when using high doses (> 300 mg/d);
- Hypersensitivity to antiinflammatory or antirheumatic drugs and other allergens;
- In the presence of concomitant treatment with anticoagulants (e.g. coumarin derivatives or heparin - except low-dose heparin therapy);
- In the presence of severe liver or kidney damage;
- In patients with a history of gastrointestinal disorders.

Medicinal products containing acetylsalicylic acid should be used in children and adolescents with febrile diseases only after careful risk-benefit-evaluation because of the possibility of Reye´s syndrome, a rare but serious illness.

Patients with bronchial asthma, chronic bronchoconstrictive (obstructive) respiratory disease, hay fever, or swelling of the nasal mucosa (nasal polyps) may react to non-steroidal analgesics with asthma attacks, localised swelling of the skin or mucosa (Quincke´s edema), or urticaria more frequently than other patients.

Surgical patients should consult with their physician concerning the use of Aspirin® Cardio.

4.5 Interaction with other medicinal products and other forms of interaction

The effects of the following are intensified:

- the action of anticoagulants
- the risk of gastrointestinal bleeding when taken simultaneously with corticosteroids or alcohol.
- the effects of non-steroidal antiinflammatory drugs,
- the action of sulfonylureas,
- the effects of methotrexate,
- the plasma concentrations of digoxin, barbiturates and lithium,
- the effects of sulfonamides and its combinations
- the effects of valproic acid.

The effects of the following are reduced:

- aldosterone antagonists and loop diuretics
- antihypertensives
- uricosurics.

At low doses, acetylsalicylic acid reduces the excretion of uric acid. This can trigger gout in patients who already tend to have a low uric acid excretion.

4.6 Pregnancy and lactation
Use of salicylates in the first 3 months of pregnancy has been associated in several epidemiological studies with an elevated risk of malformations (cleft palate, heart malformations). After normal therapeutic doses this risk seems to be low, however, as a prospective study with exposure of about 32,000 mother-child pairs has not yielded any association with an elevated rate of malformations.

Salicylates should be taken during pregnancy only after strict risk-benefit evaluation.

In the last 3 months of pregnancy administration of salicylates in high doses (> 300 mg/d) can lead to a prolongation of the gestation period, premature closure of the arterial duct and inhibition of uterine contractions. An increased haemorrhagic tendency has been observed on both mother and child.

Administration of acetylsalicylic acid in high doses (> 300 mg/d) shortly before birth can lead to intracranial haemorrhages, particularly in premature babies.

Salicylates pass into breast milk in small quantities. Since no adverse effects on the infant have been observed so far after occasional use, interruption of breast-feeding is usually unnecessary. However, on regular use of high doses (> 300 mg/d), breast feeding should be discontinued early, since risks due to inadequate detoxication by the new-born baby cannot be ruled out.

4.7 Effects on ability to drive and use machines
None.

4.8 Undesirable effects
Side effects that occasionally occur are gastrointestinal disorders such as e.g. nausea, diarrhea, vomiting and slight gastrointestinal blood losses, which in exceptional cases can lead to anaemia. Gastrointestinal ulcers may rarely develop, in some circumstances with haemorrhaging and perforation.

Rare cases of hypersensitivity reactions (e.g. attacks of dyspnoe, skin eruptions) can occur.

Isolated cases of liver (transaminases increase) and kidney function disturbances, hypoglycaemia and severe skin reactions have been described.

Dizziness and tinnitus can occur as symptoms of overdose, especially in children and in elderly patients.

Due to the effect on platelet aggregation acetylsalicylic acid may be associated with an increased risk of bleeding.

4.9 Overdose
There is a difference between chronic overdose with predominantly central nervous disturbances ("salicylism") and acute intoxication, the main feature of which is a severe disturbance of the acid-base equilibrium.

In addition to disturbances of the acid-base equilibrium and the electrolyte balance (e.g. potassium loss), hypoglycaemia, skin eruptions, and gastrointestinal haemorrhage, the symptoms can include hyperventilation, tinnitus, nausea, vomiting, impairment of vision and hearing, headache, dizziness and confusion.

In severe intoxication delirium, tremor, dyspnoea, sweating, exsiccosis, hyperthermia and coma can occur.

In intoxications with lethal outcome, death usually occurs through respiratory failure.

The methods used to treat intoxication with acetylsalicylic acid depend on the extent, stage and clinical symptoms of the intoxication. They correspond to the usual measures for reducing absorption of an active ingredient: acceleration of excretion and monitoring of the water and electrolyte balance, disturbed temperature regulation and respiration.

5. PHARMACOLOGICAL PROPERTIES

ATC Classification: B01A C06

5.1 Pharmacodynamic properties

As a salicylate, acetylsalicylic acid belongs to the group of acidic non-steroidal analgesics/antiinflammatories. As an ester of salicylic acid, acetylsalicylic acid is a substance with analgesic, antipyretic and antiinflammatory properties. The active principle described comprises inhibition of cyclooxygenase and therefore inhibition of the prostanoids prostaglandin E 2, prostaglandin I 2 , and thromboxane A 2 .

Acetylsalicylic acid has a pronounced and inhibitory effect on platelet aggregation. The irreversible cyclooxygenase inhibition is especially pronounced in platelets, because platelets are unable to resynthesize this enzyme. Acetylsalicylic acid is also thought to have other inhibitory effects on platelets.

5.2 Pharmacokinetic properties

The absorption of acetylsalicylic acid takes place rapidly and completely after oral administration, depending on the drug form. After intake of solid, fast-release dosage forms, maximal plasma levels are reached after 0.3-2 h (total salicylate). Due to the acid-resistant lacquer of Aspirin® Cardio enteric-coated tablets, 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 the enteric-coated tablets in comparison to plain tablets.

Acetylsalicylic acid is converted into its main metabolite salicylic acid during and after absorption. The acetyl group of acetylsalicylic acid begins to be split off hydrolytically even during passage through the gastrointestinal mucosa, but mainly this process takes place in the liver.

Plasma protein binding in man is concentration-dependent; values of 66-98% (salicylic acid) have been found.

After the administration of high doses, acetylsalicylic acid is detectable in the cerebral, spinal and synovial fluid. Salicylic acid crosses the placenta and passes into breast milk.

The elimination kinetics of salicylic acid are dose-dependent, as the metabolism is limited by the capacity of liver enzymes. The elimination half-life varies between 2 to 3 hours after low doses to about 12 hours after usual analgesic doses.

The main metabolites are the glycine conjugate of salicylic acid (salicyluric acid), the ether and ester glucuronides of salicylic acid (salicylphenol glucuronide and salicylacetyl

glucuronide), and gentisic acid and its glycine conjugate. Salicylic acid and its metabolites are excreted mainly via the kidneys.

5.3 Preclinical safety data

a) Acute toxicity

Acute ingestion of doses > 10 g acetylsalicylic acid in adults and > 4 g in children can be lethal. Death usually occurs as a result of respiratory failure.

Plasma concentrations from 300-350 µg salicylic acid/ml can result in toxic symptoms and concentrations from about 400-500 µg salicylic acid/ml lead to comatose-lethal states.

b) Chronic toxicity

Acetylsalicylic acid and its metabolite salicylic acid have a local irritant action on mucous membranes.

If ulcers are present in the gastrointestinal tract, the increased bleeding tendency creates the risk of serious haemorrhage. In addition to these adverse effects, kidney damage has been found in animal studies after acute and chronic administration of high doses.

c) Mutagenic and tumorigenic potential

Acetylsalicylic acid has been adequately tested for mutagenicity and cancerogenicity; no relevant evidence of a mutagenic or cancerogenic potential was found.

d) Reproductive toxicity

Salicylates have been found to have teratogenic effects in a number of animal species. There have been reports of implantation disturbances, embryotoxic and fetotoxic effects, and disturbances of learning capacity in the offspring after prenatal exposure.

For experience on use in man please refer to 4.6 Pregnancy and lactation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powdered cellulose
Corn starch

Lacquer coating:
Methacrylic acid-ethyl acrylate copolymer, Sodium lauryl sulphate, Polysorbat 80, Talc, Triethyl Citrate NF

6.2 Incompatibilities

Not known

6.3 Shelf life

The shelf-life varies between 2 and 5 years depending on product, climatic zone and packaging material.

6.4 Special precautions for storage

None

6.5 Nature and contents of container
Country-specific

6.6 Instructions for use/handling
The tablets should preferably be taken after meals, with plenty of liquid.
When using this product in acute myocardial infarction, the first tablet should be chewed in order to achieve fast absorption.

Note:
Keep drug out of the reach of children.

6.7 Name or style and permanent address or registered place of business of the holder of the marketing authorisation
Country-specific

7. MARKETING AUTHORISATION NUMBER
Country-specific