**SUMMARY PRODUCT CHARACTERISTIC (SPC)**

# CARDIOLIFE
**Coated tablets**

**1.1 TRADE NAME** – Cardiolife
**1.2 COMBINATION OF WELL-KNOWN GENERICS** – Acetylsalicylic acid / Magnesium hydroxide

## 2. COMPOSITION
Each tablet contains:
***active ingredients:*** Acetylsalicylic acid – 75 mg, Magnesium hydroxide – 15.2 mg;
*For a full list of excipients, see section 6.1.*

## 3. PHARMACEUTICAL FORM
White heart-shaped coated tablets

## 4.CLINICAL PARTICULARS
### 4.1 Therapeutic indications
- Primary prevention of cardiovascular diseases such as thrombosis and acute heart failure in the presence of risk factors (eg, diabetes, hyperlipidemia, hypertension, obesity, smoking, old age);
- Prevention of recurrent myocardial infarction and thrombosis of blood vessels;
- Prevention of thromboembolic events after vascular surgery (coronary artery bypass grafting, percutaneous transluminal coronary angioplasty);
- Unstable angina.

### 4.2 Posology and method of administration
The tablets should be swallowed whole with water.
*For primary prevention of cardiovascular diseases such as thrombosis and acute heart failure in the presence of risk factors (eg, diabetes, hyperlipidemia, hypertension, obesity, smoking, older age)* appoint 2 tablets of Cardiolife containing acetylsalicylic acid at a dose of 75 mg the first day, followed by 1 tablet of Cardiolife 1 time / day.
*For the prevention of repeated myocardial infarction and thrombosis of blood vessels* appoint Cardiolife at a dose of 75-150 mg 1 time / day.
*For the prevention of thromboembolic events after vascular surgery (coronary artery bypass grafting, percutaneous transluminal coronary angioplasty)* appoint Cardiolife at a dose of 75-150 mg 1 time / day.
*In unstable angina* appoint Cardiolife at a dose of 75-150 mg 1 time / day.

### 4.3 Contraindications
- Bleeding in the brain;
- Tendency to bleeding (vitamin K deficiency, thrombocytopenia, hemorrhagic diathesis);
- Asthma induced by intake of salicylates and NSAIDs;
- Erosive and ulcerative lesions GIT (exacerbation);
- Gastro-intestinal bleeding;
- Renal failure, severe stage (creatinine clearance <10 ml / min);
- Lack of glucose-6-phosphate dehydrogenase;
- Concomitant use of methotrexate (> 15 mg per week);
- I and III trimesters of pregnancy;
- Lactation (breastfeeding);
- Children and teens age under 18;
- Hypersensitivity to acetylsalicylic acid, the drug auxiliary substances and other NSAIDs.

**4.4 Special warnings and precautions for use**

Drug should be taken after doctor prescription.

Aspirin may provoke bronchospasm and induce asthma attacks or other hypersensitivity reactions. Risk factors include the presence of asthma in anamnesis, hay fever, nasal polyposis, chronic respiratory diseases and allergic reactions (e.g., skin reactions, pruritus, urticaria) to other drugs.

Aspirin can cause bleeding of varying severity during and after surgery.

A few days before the planned surgery should be assess the risk of bleeding compared to the risk of ischemic complications in patients taking low doses of acetylsalicylic acid. If the risk of bleeding is significant, taking of aspirin should be temporarily discontinued.

The combination of aspirin with anticoagulants, thrombolytic and antiplatelet agents associated with an increased risk of bleeding.

Acetylsalicylic acid in low doses can trigger the development of gout in susceptible individuals (with decreased excretion of uric acid).

The combination of aspirin with methotrexate is accompanied by an increased incidence of side effects of the hemopoietic organs.

Admission of acetylsalicylic acid in high doses has a hypoglycemic effect, it is necessary to bear in mind when assigning it to patients with diabetes receiving hypoglycemic agents for oral intake and insulin.

At concomitant use of systemic corticosteroids and salicylates should be remembered that during treatment the concentration of salicylates in the blood is reduced, and after the abolition of systemic GCS possible overdose of salicylates.

Not recommended combination with acetylsalicylic acid ibuprofen in patients with an increased risk of cardiovascular disease: the simultaneous use of ibuprofen observed decrease antiplatelet action of acetylsalicylic acid in doses up to 300 mg, which reduces the cardioprotective effects of acetylsalicylic acid.

Excess of dose of acetylsalicylic acid over the recommended therapeutic dose is associated with a risk of gastrointestinal bleeding.

With prolonged use of aspirin in low doses as an antiplatelet therapy, caution is necessary in elderly patients due to the risk of gastrointestinal bleeding.

At the same time taking acetylsalicylic acid and ethanol increased risk of damage to the gastrointestinal mucosa and prolonged bleeding.

***Precautions for use***

Precautions should be appoint a drug in gout, hyperuricemia, ulcers or gastrointestinal bleeding from the gastrointestinal tract in anamnesis, renal and / or liver failure, asthma, hay fever, nasal polyps, allergic conditions, in the II trimester of pregnancy.

**4.5 Interaction with other medicinal products and other forms of interaction**

With simultaneous application of acetylsalicylic acid increases the effect of these drugs:

- Methotrexate (due to reduction in renal clearance and ousting him from association with proteins);
- Heparin and indirect anticoagulants (due to platelet dysfunction and displacing anticoagulants from binding protein);
- Thrombolytic and antiplatelet and anticoagulant drugs (ticlopidine);
- Digoxin (due to the decrease of its renal excretion);
- Hypoglycemic agents for oral use (sulfonylurea derivatives) and insulin (due hypoglycemic properties of the acetylsalicylic acid in high doses and sulfonylurea derivatives of displacement due to plasma proteins);
- Valproic acid (due to displacement from its association with proteins).

Concomitant use of aspirin with ibuprofen reduces the cardioprotective effects of acetylsalicylic acid.

An additive effect is observed while taking aspirin and ethanol (alcohol).

Aspirin reduces the effect of uricosuric agents (benzbromarone) due to competitive tubular elimination of uric acid.

Leveraging the elimination of salicylates, systemic corticosteroids weaken their effect.

Antacids and cholestyramine while applying Cardiolife reduce absorption of the drug.

**4.6 Fertility, pregnancy and lactation**

The use of salicylates in high doses in the I trimester of pregnancy is associated with increased frequency of malformations of the fetus. In the II trimester salicylates can be given only with the rigorous assessment of the risks and benefits. In the III trimester of pregnancy salicylates at high doses (> 300 mg / day) cause inhibition of labor, premature closure of the ductus arteriosus in the fetus, increased bleeding in the mother and fetus, and the appointment just before birth may cause intracranial hemorrhage, especially in preterm infants. Appointment of salicylates in III trimester of pregnancy is contraindicated.

The available clinical data is insufficient to establish the ability or inability to use during breastfeeding. Before the appointment of acetylsalicylic acid during breastfeeding should assess the potential benefits of therapy with respect to the potential risk to the infant.

**4.7 Effects on ability to drive and use machines**

During the period of treatment with acetylsalicylic acid, patients should be careful when driving and activities potentially hazardous activities that require high concentration and speed of psychomotor reactions.

**4.8 Undesirable effects**

*Allergic reactions:* often - urticaria, angioedema;

*Immune system:* sometimes - anaphylactic reactions.

*From the digestive system:* very often - heartburn; often - nausea, vomiting; sometimes - pain in the stomach area, ulceration of the mucous membrane of the stomach and duodenal ulcers, gastrointestinal bleeding; rarely - ulcer perforation of the stomach or duodenal ulcers, elevated liver enzymes; very rarely - stomatitis, esophagitis, erosive lesions of upper gastrointestinal strictures, colitis, irritable bowel syndrome.

*From respiratory system*: often - bronchospasm.

*From hemopoiesis system:* very often - increased bleeding; rarely - anemia; very rarely - hypoprothrombinemia, thrombocytopenia, neutropenia, aplastic anemia, eosinophilia, agranulocytosis.

*CNS:* sometimes - dizziness, drowsiness; often - headache, insomnia; rarely - ringing in the ears, intracerebral hemorrhage.

**4.9 Overdose**

*Overdose symptoms of moderate severity:* nausea, vomiting, tinnitus, hearing loss, dizziness, confusion.

*Treatment:* should be made gastric lavage, should be appoint activated charcoal, symptomatic therapy.

*Overdose symptoms of severe:* fever, hyperventilation, ketosis, respiratory alkalosis, coma, cardiovascular and respiratory insufficiency, severe hypoglycemia.

*Treatment:* immediate hospitalization in specialized departments for emergency therapy - gastric lavage, determination of the acid-alkaline balance, alkaline and forced alkaline diuresis, hemodialysis, introduction of saline solution, activated carbon, symptomatic therapy. During the alkali diuresis is necessary to achieve a pH between 7.5 and 8. Forced alkali diuresis should be performed when the salicylate concentration in plasma is greater than 500 mg /l (3.6 mmol/l) in adults and 300 mg/l (2.2 mmol/l) in children.

**5. PHARMACOLOGICAL ACTION**

**5.1 Pharmacodynamic properties**

*ATC code:* B01AC30.

*Pharmacotherapeutic Group:* Antiagregant.

NSAIDs, antiplatelet agents. The mechanism of action of aspirin is irreversible inhibition of the enzyme COX-1, resulting in blocked the synthesis of thromboxane $A_2$ and inhibiting platelet aggregation. It is believed that acetylsalicylic acid also has other mechanisms of inhibition of platelet

aggregation that expands the scope of its application in various vascular diseases. Aspirin also has anti-inflammatory, analgesic and antipyretic activity.
Magnesium hydroxide, which is part of Cardiolife, protect the gastrointestinal mucosa against acetylsalicylic acid.

**5.2 Pharmacokinetic properties**

***Absorption***

After oral administration, acetylsalicylic acid is absorbed from the gastrointestinal tract almost completely.
Bioavailability of acetylsalicylic acid is about 70%, but this value is characterized by considerable individual variability due to first-pass hydrolysis in the gastrointestinal mucosa and in the liver with the formation under the action of enzymes of salicylic acid. Bioavailability of salicylic acid is 80-100%.

***Metabolism and excretion***

$T_{1/2}$ of acetylsalicylic acid is about 15 minutes, because the participation of enzymes, it is rapidly hydrolyzed to salicylic acid in the intestine, liver, and blood plasma. $T_{1/2}$ of Salicylic acid - about 3 hours, but when taking aspirin at high doses (> 3 g), this figure could be increased significantly as a result of saturation of enzyme systems.
Magnesium hydroxide (used in doses) does not affect the bioavailability of acetylsalicylic acid.

**5.3 Preclinical safety data**

No relevant information.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

***Tablet core:***

Microcrystalline cellulose;
Sodium starch glycolate;
Magnesium stearate;

***Tablet coating :***

Titanium dioxide;
Hypromellose;
Talc purified;
Propylenglycol.

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 years

**6.4 Storage conditions**

Store at a room temperature (15-25$^0$C), in a dry place, out of the reach of children. Protect from light.

**6.5 Presentation**

4 blister packets with 24 tablets in each in the cardboard box.

**6.6 Special precautions for disposal and other handling**

No special requirements for disposal.

**7. MANUFACTURER**

**“ARPIMED” LLC**

Bldg. 19, mcr 2$^{-nd}$, Abovyan, Kotayki Marz, Republic of Armenia

Tel.: (374) 222 21703 Fax: (374) 222 21924

**8. MARKETING AUTHORIZATION HOLDER**
**“ARPIMED” LLC**
Bldg. 19, mcr 2-nd, Abovyan, Kotayki Marz, Republic of Armenia
Tel.: (374) 222 21703 Fax: (374) 222 21924