SUMMARY OF PRODUCT CHARACTERISTICS CARDISPRIN 75 MG ENTERIC COATED TABLET

1. **Name of the Medicinal Product**

   Cardisprin 75 mg enteric coated Tablets

2. **Qualitative and Quantitative Composition**

   Each enteric coated tablet contains 75 mg Aspirin.

3. **Pharmaceutical Form**

   Enteric coated Tablets

4. **Clinical Particulars**

4.1 Therapeutic Indications

For the secondary prevention of thrombotic cerebrovascular or cardiovascular disease and following by-pass surgery.

Aspirin has an antithrombotic action, mediated through inhibition of platelet activation, which has been shown to be useful in secondary prophylaxis following myocardial infarction and in patients with unstable angina or ischaemic stroke including cerebral transient attacks.

Cardisprin 75mg EC Tablets are indicated when prolonged dosage of aspirin is required. The special coating resists dissolution in gastric juice, but will dissolve readily in the relatively less acid environment of the duodenum. Owing to the delay that the coating imposes on the release of the active ingredient,

4.2 Posology and Method of administration

For oral administration.

Adults: Patients should seek the advice of a doctor before commencing therapy for the first time

The usual dosage, for long-term use, is 75-150 mg once daily. In some circumstances a higher dose may be appropriate, especially in the short term, and up to 300mg a day may be used on the advice of a doctor.

Antithrombotic action: 150mg at diagnosis and 75mg daily thereafter. Tablets taken at diagnosis should be chewed in order to gain rapid absorption

Elderly patients: The risk/benefit ratios in the elderly have not been fully established.

4.3 Contraindication

Hypoprothrombinaemia, haemophilia and other bleeding disorders.

Active peptic ulceration or a history of peptic ulceration.

Hypersensitivity to the active substance (aspirin) or to any of the excipients.

4.4 Special warnings and precautions for use

There is a possible association between aspirin and Reye's syndrome when given to children. Reye's syndrome is a very rare disease, which affects the brain and liver, and can be fatal. For this reason aspirin should not be given to children aged under 16 years unless specifically indicated (e.g. for Kawasaki's disease).Before commencing long-term aspirin therapy for the management of cardiovascular or cerebrovascular disease patients should consult their doctor who can advise on the relative benefits versus the risks for the individual patient.Aspirin decreases platelet adhesiveness and increases bleeding time. Haematological and haemorrhagic effects can occur, and may be severe. Patients should report any unusual bleeding symptoms to their physician.Care is advised when stopping antiplatelet therapy after stent insertion either after a fixed period of time or in preparation for a planned surgical procedure, as the balance between stent thrombosis and excessive bleeding has to be carefully assessed.Salicylates should be used with caution in patients with a history of peptic ulceration or coagulation abnormalities. They may also induce gastro-intestinal haemorrhage, occasionally major.They may also precipitate bronchospasm, urticaria or acute rhinitis or induce attacks of asthma in susceptible subjects.Aspirin should be used with caution in patients with impaired hepatic or renal function (avoid if severe), or in patients who are dehydrated.

Patients with hypertension should be carefully monitored. Cardisprin 75mg EC Tablets can increase the risk of bleeding after some surgical interventions such as dental surgery.This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Salicylates may enhance the effects of anticoagulants, oral hypoglycaemic agents, phenytoin and sodium valproate. They inhibit the uricosuric effect of probenecid and may increase the toxicity of sulfonamides.Aspirin may potentiate the effect of heparin and increases the risk of bleeding with oral anticoagulants, antiplatelet agents and fibrinolytics.Patients using enteric-coated aspirin should be advised against ingesting antacids simultaneously, to avoid premature drug release.

As with other NSAID's Cardisprin 75mg EC Tablets should not be used for 8-12 days after mifepristone administration, as it could affect the efficacy of mifepristone treatment.The activity of methotrexate may be markedly enhanced increasing its toxicity.The efficacy of anti-hypertensive drugs may be reduced. Patients with hypertension should be carefully monitored.Corticosteroids may increase the renal clearance of salicylate and when the corticosteroid is discontinued, serum salicylate levels may rise significantly. The risk of gastrointestinal ulceration and bleeding may be increased when aspirin and corticosteroids are co-administered.Concurrent use of aspirin and other NSAIDs should be avoided. Use of two or more NSAID preparations increases the risk of serious gastrointestinal haemorrhage.Concurrent administration of carbonic anhydrase inhibitors such as acetazolamide and salicylates may result in severe acidosis and increased central nervous system toxicity.In large doses, salicylates may also decrease insulin requirements.

4.6 Pregnancy and lactation

Use in pregnancy: Although clinical and epidemiological evidence suggests the safety of aspirin for use in pregnancy, caution should be exercised when considering use in pregnant patients.

Aspirin has the ability to alter platelet function and there may be a risk of haemorrhage in infants whose mothers have consumed aspirin during pregnancy. Prolonged pregnancy and labour, with increased bleeding before and after delivery, decreased birth weight and increased rate of stillbirth have been reported with high blood salicylate levels. With high doses there may be premature closure of the ductus arteriosus and possible persistent pulmonary hypertension in the newborn. Analgesic doses of aspirin should be avoided during the last trimester of pregnancy.

Use in nursing mothers: As aspirin is excreted in breast milk, patients who are breastfeeding should not take it.

Neonates excrete salicylates slowly and are more sensitive to the platelet inhibitory effect of aspirin in addition to the possible risk of Reye's syndrome.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Most commonly the side-effects associated with aspirin are gastrointestinal disturbances such as nausea, dyspepsia and vomiting. Irritation of the gastric mucosa with slight gastrointestinal blood loss may occur. More severe reactions including gastric erosions, ulceration and severe bleeding are less common and are often associated with high dose aspirin over prolonged periods. Anaemia may occur following chronic gastrointestinal blood loss or acute haemorrhage.Aspirin prolongs bleeding time, and bleeding disorders, such as epistaxis, haematuria, purpura, ecchymoses, haemoptysis, gastrointestinal bleeding, haematoma and cerebral haemorrhage have occasionally been reported. Fatalities have occurred.Aspirin may precipitate hypersensitivity reactions, bronchospasm, attacks of asthma in susceptible subjects, urate kidney stones, tinnitus and blood disorders including hypoprothrombinaemia and thrombocytopenia.

4.9 Overdose

Salicylate poisoning is usually associated with plasma concentrations >350 mg/L (2.5 mmol/L). Most adult deaths occur in patients whose concentrations exceed 700 mg/L (5.1 mmol/L). Single doses less than 100 mg/kg are unlikely to cause serious poisoning.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

The antiplatelet effect of aspirin is largely unrelated to its systemic bioavailability and its duration of effect does not correlate with the presence of intact salicylic acid in the circulation. The antiplatelet effect is considered to be largely pre-systemic, associated with acetylation of platelet cyclo-oxygenase in the portal circulation. Aspirin (acetylsalicylic acid) irreversibly acetylates platelet cyclo-oxygenase thereby inhibiting the biosynthesis of thromboxane, a potent

vasoconstrictor and inducer of platelet aggregation. It also inhibits the action of cyclo-oxygenase in the vascular endothelial wall preventing the synthesis of prostacyclin, a potent vasodilator and inhibitor of platelet aggregation.

However, as the endothelial cell is capable of synthesizing new cyclo-oxygenase, whereas the platelet is not, the effect on thromboxane is longer lasting.

Due to the low dose enteric-coated formulation of Cardisprin 75mg EC Tablets acetylsalicylic acid is slowly released into the portal circulation and is deacetylated by the liver to inactive salicylate before reaching the systemic circulation. It is postulated that platelets passing through the portal circulation are exposed to acetylsalicylic acid concentrations sufficient to achieve effective thromboxane inhibition, while systemic prostacyclin synthesis remains essentially unaffected.Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release aspirin (81mg), a decreased effect of aspirin on the formation of thromboxane or platelet aggregation occurred.

However, the limitations of these data and the uncertainties regarding extrapolation of *ex-vivo* data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

5.2 Pharmacokinetic Properties

Aspirin is rapidly absorbed after oral administration of conventional release preparations, with some hydrolysis to salicylate before absorption. Absorption is delayed by the presence of food and is impaired in patients suffering migraine attacks.Absorption is more rapid in patients with achlorhydria and also following administration of polysorbates and antacids. Plasma concentrations of the drug increase disproportionately to the dose; e.g. a 325 mg dose having a half-life of 2-3 hours and higher doses showing lower plasma concentrations in the presence of an increased half-life due to a disproportionate increase in the volume of distribution. Aspirin is found in saliva, milk, plasma and synovial fluid at concentrations less than in blood and crosses the placenta. Salicylate/protein binding extensive. Aspirin/protein binding to a small extent. In the blood, rapid

hydrolysis to salicylic acid; glucuronic acid/glycine conjugation to form glucuronides and salicyluronic acid. Salicylate reabsorbed by renal tubules in acid urine, and alkaline diuresis will increase the rate of excretion; 85% of dose excreted as free salicylate. The absolute bioavailability of aspirin from Cardisprin 75mg EC Tablets (compared with intravenous aspirin solution) is approximately 25%.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6 Pharmaceutical Particulars

6.1 List of Excipients

FLOCEL 101 USP

Partially Pregelatinized starch 1500

Purified Talc BP

Aerosil BP

ENTERIC COATING

Tabcoat TC

Acryl-Eze pink

Purified Water BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in a dry place below 30°C. Protect from light.

6.5 Nature and contents of container

ALU/ALU Blister Packing

6.6 Instructions for use, handling and disposal

No special requirements for disposal.

7 Registrant

Cosmos Limited

8 Manufacturer

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