Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Caprin 75 mg Gastro-resistant Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 75 mg of Aspirin (acetylsalicylic acid).

Excipients: Each tablet contains 62mg of Anhydrous Lactose.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Gastro-resistant tablets.

Pink enteric coated, round, biconvex tablets printed with "75" in black ink.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

CAPRIN 75mg may be used to reduce the risk of myocardial infarction in patients with unstable angina or ischaemic stroke and in patients with a previous history of myocardial infarction. The enteric coating makes Caprin unsuitable for short term pain relief.

4.2 Posology and method of administration

Adults (including the elderly)

One tablet daily.
In cases where a rapid onset of action is required e.g. immediately following acute myocardial infarction, then three tablets should be given for the first two days of treatment.

Children and adolescents under 16 years
Do not give to children and adolescents under 16 years, except on medical advice, where the benefit outweighs the risk.

CAPRIN 75mg tablets must not be chewed or crushed.
The tablets are best taken before meals.

Undesirable effects may be minimised by using the shortest duration necessary to control symptoms (see section 4.4).

4.3 Contraindications

CAPRIN 75mg tablets are contraindicated in the following:
History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy. Active, or history of recurrent peptic ulcer / haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
Severe heart failure
Coagulation deficiency disorders
Hypersensitivity to aspirin or to other non-steriodal anti-inflammatory drugs.

4.4 Special warnings and precautions for use

The use of Caprin with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (See section 4.2).

Gastrointestinal bleeding, ulceration and perforation: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (See section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (See below and 4.5).

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents (See section 4.5).

When GI bleeding or ulceration occurs in patients receiving Caprin, the treatment should be withdrawn.

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated (See section 4.8 – undesirable effects).

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDSs (see 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Caprin should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Undesirable effects may be minimised by using the shortest duration necessary to control symptoms (see section 4.2).

Cardiovascular and cerebrovasular effects
Appropriate monitoring and advice are required for patients with a history of hypertension and / or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical trial and epidemiology data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for aspirin.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and / or cerebrovascular disease should only be treated with aspirin after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

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 and adolescents aged under 16 years unless specifically indicated.

Aspirin should be used with caution in patients with impaired renal function or hepatic function (avoid if severe), or in patients who are dehydrated.

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interactions

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (See section 4.4)

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (See section 4.4).
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (See section 4.4).

CAPRIN 75 mg may enhance the effects of phenytoin and sodium valproate.
The activity of methotrexate may he markedly enhanced and its toxicity increased.
CAPRIN 75mg may inhibit action of uricosurics.
The toxicity of sulphonamides may also be increased.
CAPRIN 75mg may reduce the efficacy of antihypertensive drugs.
Aspirin is pharmaceutically incompatible with iron salts and alkalis.
Patients using enteric-coated aspirin should be advised against ingesting antacids simultaneously, to avoid premature drug release.

Care should be taken in patients treated with any of the following drugs as interactions have been reported:
Diuretics: reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.
Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.
Lithium: decreased elimination of lithium.
Methotrexate: decreased elimination of methotrexate.
Ciclosporin: increased risk of nephrotoxicity with NSAIDs.
Other NSAIDs: avoid concomitant use of two or more NSAIDs.
Aminoglycosides: reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentrations.

Metamizole may reduce the effect of acetylsalicylic acid on platelet aggregation, when taken concomitantly. Therefore, this combination should be used with caution in patients taking low dose aspirin for cardioprotection.

Probenecid: reduction in metabolism and elimination of NSAID and metabolites.
Oral hypoglycaemic agents: inhibition of metabolism of sulphonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. 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 (see section 5.1).

4.6 Fertility, pregnancy and lactation

Aspirin should not be used routinely during pregnancy.
Aspirin may prolong labour and contribute to maternal and neonatal bleeding, and is best avoided at term. It is excreted in breast milk and breast feeding should be avoided because of possible risk of Reye's syndrome.
Regular use of high doses could impair platelet function and produce hypoprothrombinaemia in the infant if neonatal Vitamin K stores are low.

4.7 Effects on ability to drive and use machines

Aspirin does not usually affect the ability to drive or operate machinery.

4.8 Undesirable effects

Gastrointestinal: The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (See section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (See section 4.4 - Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed.

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare).

Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Aspirin may precipitate bronchospasm, and induce attacks of asthma in susceptible subjects.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

Dizziness, tinnitus, deafness, vasodilation and sweating, nausea and vomiting, headache and mental confusion. If more severe hyperventilation, fever, restlessness, ketosis, respiratory alkalosis and metabolic acidosis. Coma, if severe, with cardiovascular collapse and respiratory failure. Hypoglycaemia may be severe in children.

Overdosage should be treated initially by gastric lavage and forced alkaline diuresis. Haemodialysis may sometimes be necessary. The patient should be observed for at least 72 hours to allow for possible delayed release from the enteric coated system. Restoration of acid-base balance may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Aspirin is an analgesic and antipyretic with anti-inflammatory properties.
Aspirin inhibits prostaglandin synthetase.
Aspirin inhibits platelet aggregation.

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 h before or within 30 min after immediate release aspirin dosing (81mg), a decreased effect of ASA 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

Absorption: Aspirin is rapidly absorbed after oral administration, 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.
To prevent stomach irritation, CAPRIN 75mg tablets have a special enteric coating so that aspirin is not released until it has passed through the stomach.

Distribution: Aspirin is found in the saliva, milk, plasma and synovial fluid at concentration less than blood and crosses the placenta.
Salicylate/extensive protein binding.
Aspirin/protein binding to a small extent.

Metabolism: In the blood, rapid hydrolysis to salicylic acid; glucuronic acid/glycine conjugation to form glucuronides and salicyluronic acid, oxidation of a small proportion.

Excretion: Excreted in the urine mainly as 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.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous Lactose
Collodial Anhydrous Silica
Pregelatinised Starch
Zinc Stearate
Titanium Dioxide (E171)
Polyvinyl Acetate Phthalate
Acetylated Vegetable Oil Monoglyceride
Hydroxypropyl Cellulose
Red Iron Oxide (E172)

Colorcon Black Ink S-1-17823 consisting of:
Shellac glaze
Black iron oxide (E172)
n-Butyl alcohol
Isopropyl alcohol
Propylene glycol
Ammonium hydroxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 25°C.

Keep the container tightly closed to protect from moisture.

6.5 Nature and contents of container

White polypropylene container (securitainer) and lid, containing 20 or 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Ltd,
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0281/130/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 23 June 2010

10 DATE OF REVISION OF THE TEXT

January 2020