Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Persantin Retard 200mg Modified-release Capsules, Hard

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains dipyridamole 200 mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Modified-release Capsules, Hard

Product imported from the UK:
Hard gelatin capsules consisting of a red cap and an orange body.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Secondary prevention of ischaemic stroke and transient ischaemic attacks either alone or in conjunction with aspirin.
As an adjunct to oral anti-coagulation for prophylaxis of thromboembolism associated with prosthetic heart valves.

4.2 Posology and method of administration

Adults, including the Elderly
One capsule twice daily, usually one in the morning and one in the evening, preferably with meals.
The capsules should be swallowed whole without chewing.
Children
Persantin Retard is not suitable for use in children.

4.3 Contraindications

Hypersensitivity to any components of the product.

4.4 Special warnings and precautions for use

Among other properties, dipyridamole acts as a potent vasodilator. It should therefore be used with caution in patients with severe coronary artery disease including unstable angina and recent myocardial infarction, left ventricular outflow obstruction or haemodynamic instability (e.g. decompensated heart failure).

Clinical experience suggests that patients being treated with oral dipyridamole who also require pharmacological stress testing with intravenous dipyridamole should discontinue drugs containing oral dipyridamole for twenty-four hours prior to stress testing. Failure to do so may impair the sensitivity of the test.

In patients with myasthenia gravis, readjustment of therapy may be necessary during treatment with dipyridamole. (See Section 4.5 Interactions with other medicinal products and other forms of interactions).

PERSANTIN should be used with caution in patients with coagulation disorders.

A small number of cases have been reported in which unconjugated dipyridamole was shown to be incorporated into gallstones to a variable extent (up to 70% by dry weight of stone). These patients were all elderly, had evidence of ascending cholangitis and had been treated with oral dipyridamole for a number of years. There is no evidence that dipyridamole was the initiating factor in causing gallstones to form in these patients. It is possible that bacterial deglucuronidation of conjugated dipyridamole in bile may be the mechanism responsible for the presence of dipyridamole in gallstones.

4.5 Interaction with other medicinal products and other forms of interaction

Dipyridamole increases the plasma levels and cardiovascular effects of adenosine. Adjustment of adenosine dosage should therefore be considered if use with dipyridamole is unavoidable.
It is possible that dipyridamole may enhance the effects of oral anti-coagulants.
There is evidence that the effects of aspirin and dipyridamole on platelet behaviour are additive.
When dipyridamole is used in combination with anti-coagulants and aspirin, the statements on intolerance and risks for these preparations must be observed.
Addition of dipyridamole to aspirin does not increase the incidence of bleeding events. When dipyridamole was administered concomitantly with warfarin, bleeding was no greater in frequency or severity than that observed when warfarin was administered alone.
Dipyridamole may increase the hypotensive effect of blood pressure lowering drugs and may counteract the anti-cholinesterase effect of cholinesterase inhibitors, thereby potentially aggravating myasthenia gravis.

4.6 Fertility, pregnancy and lactation

There is inadequate evidence of safety in human pregnancy, but dipyridamole has been used for many years without apparent ill-consequence. Animal studies have shown no hazard. Nevertheless, medicines should not be used in pregnancy, especially the first trimester unless the expected benefit is thought to outweigh the possible risk to the foetus.
Persantin Retard 200 mg should only be used during lactation if considered essential by the physician.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Adverse effects at therapeutic doses are usually mild and transient. Vomiting, diarrhoea and symptoms such as dizziness, faintness, nausea, dyspepsia, headache and myalgia have been observed. Such effects usually disappear on long-term use of Persantin Retard 200mg in most cases.

As a result of its vasodilating properties, dipyridamole may cause hypotension, hot flushes and tachycardia. Worsening of symptoms of coronary heart disease such as angina and arrhythmias has been observed.

Hypersensitivity reactions such as rash, urticaria, severe bronchospasm and angio-oedema have been reported. In very rare cases, increased bleeding during or after surgery has been observed. Isolated cases of thrombocytopenia have been reported in conjunction with treatment with PERSANTIN.

Dipyridamole has been shown to be incorporated into gallstones (see Special Warnings and Precautions for Use).

4.9 Overdose

Symptoms

Due to the low number of observations, experience with dipyridamole overdose is limited. Symptoms such as feeling warm, flushes, sweating, accelerated pulse, restlessness, feeling of weakness and dizziness, drop in blood pressure and anginal complaints may occur.

Therapy

Symptomatic therapy is recommended. A gastric decontamination procedure should be considered. Administration of xanthine derivatives (e.g. aminophylline) may reverse the haemodynamic effects of dipyridamole overdose. Due to its wide distribution to tissues and its predominantly hepatic elimination, dipyridamole is not likely to be accessible to enhanced removal procedures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dipyridamole has an anti-thrombotic action based on the ability to modify various aspects of platelet function, such as inhibition of platelet adhesion and aggregation, which have been shown to be factors associated with the initiation of thrombus formation as well as lengthening shortened platelet survival time.
Dipyridamole also produces vasodilation indirectly by the inhibition of adenosine uptake and the inhibition of cGMP-phosphodiesterase.

5.2 Pharmacokinetic properties

Persantin Retard 200 mg given twice daily has been shown to be bioequivalent to the same total daily dose of Persantin Tablets given in four divided doses. Peak plasma concentrations are reached 2-3 hours after administration.
Dipyridamole is distributed widely in the body. Metabolism occurs in the liver to form mainly a monoglucuronide.
The major route of excretion is via the bile.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

hypromellose
tartaric acid
acacia
povidone
methacrylic acid-methylmethacrylate copolymer (1:2)
hypromellose phthalate
dimethicone 350
triacetin
talc
stearic acid

Capsule Shell
gelatin
titanium dioxide (E171)
red iron oxide (E172)
yellow iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life expiry date for this product shall be the date shown on the bottle and outer package of the product on the market in the country of origin.

In use: discard any capsules remaining 6 weeks after first opening.

6.4 Special precautions for storage

Store in the original package in order to protect from moisture. Keep the bottle tightly closed.

Store below 30°C.

6.5 Nature and contents of container

White polypropylene bottles with child-resistant multi-part polypropylene/polyethylene plastic screw cap containing a desiccant made from silica gel/molecular sieves agent.
Packs containing 60 capsules.

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

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

LTT Pharma Limited
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Worcestershire B98 0RE
United Kingdom

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1562/61/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

The date of first authorisation: 26th August 2011

10 DATE OF REVISION OF THE TEXT