

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Dipyridamole 50mg/5ml Oral Suspension

2. Qualitative and Quantitative Composition

Dipyridamole 50mg/5ml

Excipient(s) with known effect:

Liquid maltitol (E965) 2500mg/5ml

Propylene glycol (E1520) 136.3mg/5ml

Ethanol 10.4mg/5ml

Methyl hydroxybenzoate (E218) 6mg/5ml

Propyl hydroxybenzoate (E216) 1.5mg/5ml

For excipients see section 6.1

3. Pharmaceutical Form

Oral Suspension

Bright yellow suspension with odour of almond.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

An adjunct to oral anticoagulation for prophylaxis of thromboembolism associated with prosthetic heart valves.

4.2. Posology and Method of Administration

Administration:

For oral use only.

Dipyridamole suspension should usually be taken before meals.

Adults: 300mg to a maximum of 600mg daily in three or four doses.

Children: Dipyridamole is not recommend for children.

4.3. Contra-indications

Hypersensitivity to any of the ingredients in the product.

4.4. Special Warnings and Special Precautions for Use

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

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

In patients with myasthenia gravis, readjustment of therapy may be necessary after changes in dipyridamole dosage (see Drug Interactions).

Patients treated with regular oral doses of dipyridamole should not receive additional intravenous dipyridamole. If pharmacological stress testing with intravenous dipyridamole for coronary artery disease is considered necessary, then oral dipyridamole should be discontinued 24 hours prior to testing.

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 the bile may be the mechanism responsible for the presence of dipyridamole in gallstones.

Excipients in the formulation:

- Liquid maltitol (E965) 2500mg in each 5 ml. Patients with a rare hereditary problem of fructose intolerance should not take this medicine.
- Propylene glycol (E1520). This medicine contains 136.3mg in each 5 ml. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates.
- Ethanol. This medicine contains 10.4 mg of alcohol (ethanol) in each 5 ml. The amount in 5 ml of this medicine is equivalent to less than 3 ml beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

- The medicine also contains parahydroxybenzoates which are known to cause urticaria, generally delayed type reactions such as contact dermatitis and rarely, immediate reaction with urticaria and bronchospasm.
- This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially 'sodium-free'.

4.5. Interaction with other Medicinal Products and other forms of Interaction

Adenosine:

Dipyridamole increases plasma levels and cardiovascular effects of adenosine. Adjustment of adenosine dosage should be considered if use with dipyridamole is unavoidable.

Aspirin:

There is evidence that the effects of aspirin and dipyridamole on platelet behaviour are additive.

Antacids:

The administration of antacids may reduce the efficacy of dipyridamole.

Anticoagulants:

It is possible that dipyridamole may enhance the effects of oral anticoagulants. When dipyridamole is used in combination with anticoagulants and acetylsalicylic acid, the statements on intolerance and risks for these preparations must be observed. Addition of dipyridamole to acetylsalicylic acid 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.

Anti-Hypertensives:

Dipyridamole may increase the hypotensive effect of drugs which reduce blood pressure.

Anti-cholinesterases:

Dipyridamole may counteract the anticholinesterase effect of cholinesterase inhibitors thereby potentially aggravating myasthenia gravis.

4.6. Fertility, pregnancy and lactation

Pregnancy

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. Medicines should not be used in pregnancy, especially in the first trimester, unless the expected benefit is thought to outweigh the possible risk to the foetus.

Lactation

Dipyridamole is excreted in breast milk at levels approximately 6% of the plasma concentration. Therefore, dipyridamole should only be used during lactation if considered essential by the physician.

Fertility

No studies on the effect on human fertility have been conducted with Dipyridamole. Non-clinical studies with dipyridamole did not indicate direct or indirect harmful effects with respect to fertility.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

However, patients should be advised that they may experience undesirable effects such as dizziness during treatment with Dipyridamole. If patients experience dizziness they should avoid potentially hazardous tasks such as driving or operating machinery.

4.8. Undesirable Effects

Adverse effects at therapeutic doses are usually mild and transient.

The following side effects have been reported, frequencies have been assigned based on a clinical trial (ESPS-2) in which 1654 patients received dipyridamole alone.

If side effects do occur, it is usually during the early part of treatment.

Frequencies

Very common $\geq 1/10$

Common $\geq 1/100 < 1/10$

Uncommon $\geq 1/1,000 < 1/100$

Rare $\geq 1/10,000 < 1/1,000$

Very rare $< 1/10,000$

Blood and the lymphatic system disorders

Thrombocytopenia not known

Immune system disorders

Hypersensitivity not known

Angioedema not known

Nervous system disorders

Headache very common

Dizziness very common

Cardiac Disorders

Angina pectoris	common
Tachycardia	not known

Vascular Disorders

Hypotension	not known
Hot flushes	not known

Respiratory, thoracic and mediastinal disorders

Bronchospasm	not known
--------------	-----------

Gastrointestinal disorders

Diarrhoea	very common
Nausea	very common
Vomiting	common

Skin and subcutaneous tissue disorders

Rash	common
Urticaria	not known

Musculoskeletal, connective tissue and bone disorder

Myalgia	common
---------	--------

Injury, poisoning and procedural complications

Post procedural haemorrhage	not known
Operative haemorrhage	not known

Dipyridamole has been shown to be incorporated into gallstones (please refer to section 4.4 Special warnings and precautions for use).

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

Due to the low number of observations, experience with dipyridamole overdose is limited. Symptoms such as a warm feeling, flushes, sweating, restlessness, feeling of weakness, dizziness and anginal complaints can be expected. A drop in blood pressure and tachycardia might be observed.

Symptomatic therapy is recommended. 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 antithrombotic action based on its ability to modify various aspects of platelet function, such as platelet aggregation, adhesion and survival, which have been shown to be factors associated with the initiation of thrombus formation. Dipyridamole also has coronary vasodilator properties.

5.2. Pharmacokinetic Properties

Oral administration of dipyridamole gives a peak plasma level 0.5 - 2 hours after dosing. The drug has an apparent bioavailability of 37-66%. These figures were obtained with other oral immediate release forms of dipyridamole.

The volume of distribution is $2.43 \pm 1.11/\text{kg}$. When given orally the elimination half life is 9 –12 hours. The major route of excretion of dipyridamole is in the bile.

5.3. Preclinical Safety Data

There are no preclinical data of relevance to the prescriber additional to those already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl hydroxybenzoate (E218)
Propyl hydroxybenzoate (E216)
Propylene glycol (E1520)
Xanthan gum (E415)
Ammonium glycyrrhizinate
Almond flavour (including propylene glycol and ethanol)
Levomenthol
Liquid maltitol (E965)

Polysorbate 80 (E433)
Simethicone emulsion
Aluminium magnesium silicate
Disodium hydrogen phosphate (E339)
Citric acid monohydrate (E330)
Purified water

6.2. Incompatibilities

Not applicable.

6.3. Shelf Life

24 months
1 month - once open

6.4. Special Precautions for Storage

Do not store above 25°C.

6.5 Nature and Contents of Container

Bottle: Amber (Type III) glass
Closure: HDPE, EPE wadded, tamper evident child resistant closure.
Capacity: 150ml or 500ml

Not all pack sizes may be marketed

6.6. Instruction for Use/Handling

This product may settle during storage. Please shake the bottle thoroughly before use.

7. MARKETING AUTHORISATION HOLDER

Rosemont Pharmaceuticals Ltd
Rosemont House
Yorkdale Industrial Park
Braithwaite Street
Leeds
LS11 9XE

United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

PL 00427/0133

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

8 August 2002

10 DATE OF REVISION OF THE TEXT

09/07/2020