BIOEQUIVALENT TO ASASANTIN®

Molita®
Modified-Release Capsules, Hard
Dipyridamol and Aspirin

200mg/25mg
100 Capsules (2 x 50)

Indications: Secondary prevention of ischaemic stroke and transient ischaemic attacks.

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>STRENGTH</th>
<th>PACK SIZE</th>
<th>PIP CODE</th>
<th>EAN CODE</th>
<th>LEGAL CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molita® Dipyridamole/Aspirin Modified Release Hard Capsules</td>
<td>200mg/25mg</td>
<td>100</td>
<td>118-6576</td>
<td>5036072005310</td>
<td>POM</td>
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</table>

Order now from your local wholesaler
200mg/25mg

Presentation: Yellow to orange coloured pellets filled in hard gelatin capsules with an orange coloured cap and white to off-white coloured body

Carton Dimensions: 102 x 52 x 106mm

Format: 1 carton, containing two child resistant white bottles of 50 capsules, with a patient information leaflet

Originator Brand Name: Asasantin®

Patent Expiry Date: Expired

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Bioequivalence Data

Dr. Reddy's Molita® Dipyridamole/Aspirin 200mg/25mg modified release capsules is equivalent to Asasantin® Retard 200mg/25mg modified release capsules.

Plasma Concentration Profile
Bioequivalence studies comparing Dr. Reddy's Molita® Dipyridamole/Aspirin 200mg/25mg modified release capsules with Asasantin® Retard 200mg/25mg modified release capsules have been conducted. The tables opposite show the plasma concentration profiles following a single oral dose in healthy adults under fed conditions.

Bioequivalence was demonstrated as Cmax and AUC ratios of Dr Reddy's Molita® Dipyridamole/ Aspirin 200mg/25mg modified release capsules to Asasantin® Retard 200mg/25mg modified release capsules were found to be within the range of 80 to 125%.

The graphs clearly provide confidence that suitable patients have the potential to be switched to Dr. Reddy's Molita® Dipyridamole/Aspirin 200mg/25mg modified release capsules from Asasantin® capsules. Patients being prescribed Dipyridamole/Aspirin 200mg/25mg modified release capsules for the first time can also be initiated on the Dr. Reddy's Molita® product.
Fed Conditions: Dipyridamole

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Dr. Reddy’s Molita® Dipyridamole/Aspirin 200mg/25mg MR capsules</th>
<th>Asasantin® Dipyridamole/Aspirin 200mg/25mg MR capsules</th>
<th>Ratio</th>
<th>90% Confidence Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/mL)</td>
<td>1779.724</td>
<td>1600.764</td>
<td>111.18</td>
<td>102.36 - 120.76</td>
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<tr>
<td>AUC 0-t (ng.hr/mL)</td>
<td><strong>13661.694</strong></td>
<td>13134.905</td>
<td>104.01</td>
<td>95.38 - 113.43</td>
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<tr>
<td>AUC 0-∞(ng.hr/mL)</td>
<td><strong>13907.180</strong></td>
<td>13342.980</td>
<td>104.23</td>
<td>95.39 - 113.88</td>
</tr>
</tbody>
</table>

Fed Conditions: Salicylic acid (Aspirin)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Dr. Reddy’s Molita® Dipyridamole/Aspirin 200mg/25mg MR capsules</th>
<th>Asasantin® Dipyridamole/Aspirin 200mg/25mg MR capsules</th>
<th>Ratio</th>
<th>90% Confidence Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/mL)</td>
<td><strong>1083.16</strong></td>
<td>1075.80</td>
<td>100.68</td>
<td>95.97 - 105.63</td>
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<tr>
<td>AUC 0-t (ng.hr/mL)</td>
<td><strong>4441.01</strong></td>
<td>4389.81</td>
<td>101.17</td>
<td>98.11 - 104.31</td>
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<tr>
<td>AUC 0-∞(ng.hr/mL)</td>
<td><strong>4820.20</strong></td>
<td>4720.13</td>
<td>102.12</td>
<td>98.86 - 105.49</td>
</tr>
</tbody>
</table>
Dipyriramole/Aspirin Modified Release Hard Capsules

Molita® 200mg/25mg modified release capsules

Refer to full Summary of Product Characteristics before prescribing.

Presentation:
Modified release capsules containing 200mg dipyriramole and 25mg acetylsalicylic acid (aspirin).

Indications:
Secondary prevention of ischaemic stroke and transient ischaemic attack.

Dosage and administration:
Adults/elderly: one capsule twice daily. Usually one in the morning and one in the evening. In the event of intolerable headaches during treatment initiation, switch to one capsule at bedtime and low-dose acetylsalicylic acid in the morning. Patients should return to the usual regimen as soon as possible, usually within one week. Molita® is contraindicated in patients with severe renal or hepatic impairment. Caution should be exercised in patients with mild or moderate renal or hepatic impairment. They should not be taken with alcohol.

Children: Not recommended.

Contraindications:
Hypersensitivity to any component of Molita® or salicylates. Peanut or soy allergies. History of haemorrhagic cerebrovascular accident. Gastric symptoms or patients who have experienced gastric pain when previously using the medicine. Active peptic ulcer and/or gastrointestinal bleeding. Severe hepatic or renal insufficiency. Haemorrhagic diabetes or coagulation disorders. Glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency).

Methotrexate used at doses > 15 mg/week. Warning and precautions:
Use caution in patients at increased bleeding risk, patients should be followed for any signs of bleeding, including occult bleeding.

Caution should be advised in patients receiving concomitant medication which may increase the risk of bleeding, such as antiplatelet agents or SSRIs. Headache or migraine-like headaches should not be treated with analgesic doses of acetylsalicylic acid. Dipyriramole acts as a vasodilator. Use 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. decompenated heart failure).

Patients being treated with Molita® should not receive additional intravenous dipyriramole. In patients with myocardial ischaemia readjustment of therapy may be necessary after changes in dipyriramole dosage.

Uncomplicated dipyriramole was shown to be incorporated into gallbladder.

Use caution in patients with asthma, allergic rhinitis, nasal polyps, chronic or recurring gastric or duodenal complaints, impaired renal or hepatic function (contraindicated if severe). Caution is advised in patients hypersensitive to other NSAIDs.

Not indicated for use in children and young people. Molita® should not be given to children aged under 18 years unless specifically indicated.

The dose of acetylsalicylic acid in Molita® has not been studied in secondary prevention of myocardial infarction.

Prior to surgical procedures, discontinuation of treatment with Molita® should be considered. Typically, treatment should be discontinued 7 days before surgery.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Molita® capsules contain ponceau 4R (E124) and sunset yellow (E110) colouring agents, which may cause allergic reactions. Molita® capsules also contain methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E218) which may cause allergic reactions (possibly delayed).

Interactions:
When dipyriramole is used in combination with acetylsalicylic acid or with warfarin, the statements regarding precautions, warnings and tolerances for these preparations must be observed.

Acetylsalicylic acid has been shown to enhance the effect of anticoagulants, antihypertensive drugs and SSRI's and may increase the risk of bleeding.

Acetylsalicylic acid may enhance the effect of warfarin and phenytoin with possible increased risk of side effects.

Gastrointestinal side effects may increase when acetylsalicylic acid is administered concomitantly with NSAIDs, corticosteroids or chronic alcohol use. The addition of dipyriramole to acetylsalicylic acid does not increase the incidence of bleeding events. In concomitant administration of dipyriramole with warfarin, bleeding was no greater in frequency or severity than that observed when warfarin was administered alone.

Dipyriramole increases the plasma levels and cardiovascular effects of acetylsalicylic acid. Adjustment of anticoagulant dosage should be considered if dipyriramole is unsuitable.

Dipyriramole may increase the hypotensive effect of blood pressure lowering drugs and may counteract the antihypertensive effect of chlorthalidone inhibitors thereby potentially aggravating myasthenia gravis.

The effect of hypoglycaemic agents and the toxicity of methylxanthine may be increased by the concomitant administration of acetylsalicylic acid. Concomitant use with methylxanthine > 15 mg/week is contraindicated. For lower doses weekly blood count tests should be carried out during the first weeks of treatment. Enhanced monitoring is recommended in the presence of impaired renal function, as well as in elderly.

Acetylsalicylic acid may decrease the natriuretic effect of dopamine. This combination should be avoided because of the known increased risk of gastrointestinal toxicity. When such a combination is necessary the balance of gastrointestinal and cardiovascular risks should be considered.

Molita® capsules should not be taken at the same time as alcohol, as alcohol may increase the rate of release of dipyriramole from the modified-release preparation.

Fertility, pregnancy and lactation:
There is limited data from the use of dipyriramole and acetylsalicylic acid in pregnant women. Studies in animals have shown reproductive toxicity. From the beginning of the sixth month of pregnancy, acetylsalicylic acid may expose the foetus to cardiopulmonary toxicity, renal dysfunction, inhibition of the thromboxane function, and the mother and the neonate at the end of pregnancy, to possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses, inhibition of uterine contractions resulting in delayed or prolonged labour. This is reversible on withdrawal of treatment. Intake of acetylsalicylic acid within 5 days of estimated parturition gives an increased tendency to bleeding in the mother and the foetus/newborn.

Molita® is not recommended during pregnancy and in women of childbearing potential not using contraception.

Dipyriramole and salicylates are excreted in breast milk. Adverse effects on the suckling child cannot be excluded. Therefore a decision should be made whether to discontinue breast-feeding or to discontinue/abstain from Molita® therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Antibiotics and studies covering the peri-postnatal period have not been performed with the combination. Undesirable effects:
Refer to the Summary of Product Characteristics for full list.

Suspected adverse reactions reported as very common: <10%, common: 1-10%, uncommon: 0.1-1%, rare: 0.01-0.1% and very rare: < 0.01%.

Very common: headache, dizziness, Dyspepsia (epigastric distress), Diarrhoea, Nausea, Abdominal pain.

Common: anorexia, hypersensitivity reactions (rash, urticaria, severe bronchospasm, angioedema), haemorrhagic intracranial, migraine-like headache, worsening of symptoms of coronary heart disease (coronary artery disease), syncope, palpitations, vomiting, (severe) gastrointestinal haemorrhage, myalgia.

Uncommon: uvea haemorrhage (intravitreal haemorrhage), lachrymalgia, hypotension, hot flush, gastric ulcer, duodenal ulcer.

Rare: thrombocytopenia (reduction of platelet count), iron deficiency anaemia due to occult gastrointestinal bleeding, gastritis erosive. Not known: skin haemorrhage (contusion, ecchymosis, haematoma), bleeding time prolonged, post procedural haemorrhage, operative haemorrhage.

In addition to those side effects listed for dipyriramole/acetylsalicylic acid, for the relevant monocompounds additional side effects are established; however, have not been reported for dipyriramole/acetylsalicylic acid yet.

Legal category: POM-G.

Pack:
One pack of two white HDPE bottles, each of 50 capsules.

Price:
£9.84 per pack.

Packing:
Packs of 100 capsules: £9.84

Marketing Authorisation number:
Molita® 200 mg/25 mg Modified-Release Capsules, Hard PL 005/00496.

Marketing Authorisation Holder:
Dr. Reddy’s Laboratories (UK) Ltd.

Full prescribing information is available from:
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