30XXXXX

CLOPIDOGREL ROSUVASTATIN

ROSUGREL®

℞

75mg / 10mg Capsule
75mg / 20mg Capsule

ANTI-PLATELET / ANTI-HYPERLIPIDEMIA

FORMULATION

Each capsule contains:

Clopidogrel (as bisulfate), USP..... 75mg
Rosuvastatin (as calcium).....10mg
Clopidogrel (as bisulfate), USP..... 75mg
Rosuvastatin (as calcium)..... 20mg

DESCRIPTION

Rosugrel® 75mg/10mg - Orange/White coloured, hard gelatin capsule of size '0' containing one light pink to pink coloured, film coated tablet of Rosuvastatin, plain on both sides and two light brown to brown coloured, film coated tablets of Clopidogrel, plain on both sides and white to off-white coloured free flowing powder.

Rosugrel® 75mg/20mg - Purple/White coloured, hard gelatin capsule of size '0' containing one light yellow to yellow coloured, film coated tablet of Rosuvastatin, plain on both sides, two light brown to brown coloured, film coated tablets of Clopidogrel, plain on both sides and white to off-white coloured free flowing powder.

INDICATIONS

The fixed dose combination of ROSUVASTATIN PLUS CLOPIDOGREL is indicated for the reduction of atherosclerotic events (Myocardial Infarction, stroke and vascular death) in patients with atherosclerosis documented by recent stroke, Myocardial Infarction or established peripheral arterial disease.

CONTRAINDICATIONS

The fixed dose combination of ROSUVASTATIN PLUS CLOPIDOGREL is contraindicated in patients who are

- hypersensitive to either rosuvastatin or clopidogrel
- In patients with active liver disease including unexplained, persistent elevations of serum transaminases and any serum transaminase elevation exceeding 3 x the upper limit of normal (ULN).
- In patients with severe renal impairment (creatinine clearance <30 ml/min).
- In patients with myopathy.
- In patients receiving concomitant ciclosporin.
- During pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures.
- Active pathological bleeding such as peptic ulcer or intracranial hemorrhage.

DOSAGE AND ADMINISTRATION

Adults and Elderly : A single daily dose of one tablet with or without food. Or as prescribed by the physician.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Rosuvastatin

Renal Effects: Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with higher doses of Rosuvastatin, in particular 40 mg, where it was transient or intermittent in most cases. Proteinuria has not been shown to be predictive of acute or progressive renal disease. The reporting rate for serious renal events in post-marketing use is higher at the 40 mg dose. An assessment of renal function should be considered during routine follow-up of patients treated with a dose of 40 mg.

Skeletal Muscle Effects: Effects on skeletal muscle e.g. myalgia, myopathy and, rarely, rhabdomyolysis have been reported in Rosuvastatin-treated patients with all doses and in particular with doses > 20 mg. Very rare cases of rhabdomyolysis have been reported with the use of ezetimibe in combination with HMG-CoA reductase inhibitors. A pharmacodynamic interaction cannot be excluded and caution should be exercised with their combined use.

As with other HMG-CoA reductase inhibitors, the reporting rate for rhabdomyolysis associated with Rosuvastatin in post-marketing use is higher at the 40 mg dose.

Creatine Kinase Measurement: Creatine Kinase (CK) should not be measured following strenuous exercise or in the presence of a plausible alternative cause of CK increase which may confound interpretation of the result. If CK levels are significantly elevated at baseline (>5xULN) a confirmatory test should be carried out within 5 – 7 days. If the repeat test confirms a baseline CK>5xULN, treatment should not be started.

Before Treatment: Rosuvastatin, as with other HMG-CoA reductase inhibitors, should be prescribed with caution in patients with pre-disposing factors for myopathy/rhabdomyolysis. Such factors include:

renal impairment
hypothyroidism
personal or family history of hereditary muscular disorders
previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate
alcohol abuse
age >70 years
situations where an increase in plasma levels may occur
concomitant use of fibrates.

In such patients the risk of treatment should be considered in relation to possible benefit and clinical monitoring is recommended. If CK levels are significantly elevated at baseline (>5xULN) treatment should not be started.

Whilst on Treatment

Patients should be asked to report inexplicable muscle pain, weakness or cramps immediately, particularly if associated with malaise or fever. CK levels should be measured in these patients. Therapy should be discontinued if CK levels are markedly elevated (>5xULN) or if muscular symptoms are severe and cause daily discomfort (even if CK levels are 5x ULN). If symptoms resolve and CK levels return to normal, then consideration should be given to re-introducing Rosuvastatin or an alternative HMG-CoA reductase inhibitor at the lowest dose with close monitoring. Routine monitoring of CK levels in asymptomatic patients is not warranted.

In clinical trials there was no evidence of increased skeletal muscle effects in the small number of patients dosed with Rosuvastatin and concomitant therapy. However, an increase in the incidence of myositis and myopathy has been seen in patients receiving other HMG-CoA reductase inhibitors together with fibric acid derivatives including gemfibrozil, ciclosporin, nicotinic acid, azole antifungals, protease inhibitors and macrolide antibiotics. Gemfibrozil increases the risk of myopathy when given concomitantly with some HMG-CoA reductase inhibitors. Therefore, the combination of Rosuvastatin and gemfibrozil is not recommended. The benefit of further alterations in lipid levels by the combined use of Rosuvastatin with fibrates or niacin should be carefully weighed against the potential risks of such combinations. The 40 mg dose is contraindicated with concomitant use of a fibrate.

Rosuvastatin should not be used in any patient with an acute, serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders; or uncontrolled seizures).

Liver Effects: As with other HMG-CoA reductase inhibitors, Rosuvastatin should be used with caution in patients who consume excessive quantities of alcohol and/or have a history of liver disease.

It is recommended that liver function tests be carried out prior to, and 3 months following, the initiation of treatment. Rosuvastatin should be discontinued or the dose reduced if the level of serum transaminases is greater than 3 times the upper limit of normal. The reporting rate for serious hepatic events (consisting mainly of increased hepatic transaminases) in post-marketing use is higher at the 40 mg dose.

In patients with secondary hypercholesterolemia caused by hypothyroidism or nephrotic syndrome, the underlying disease should be treated prior to initiating therapy with Rosuvastatin.

Race: Pharmacokinetic studies show an increase in exposure in Asian subjects compared with Caucasians

Protease inhibitors: The concomitant use with protease inhibitors is not recommended.

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

Interstitial lung disease: Exceptional cases of interstitial lung disease have been reported with some statins, especially with long term therapy. Presenting features can include dyspnea, non-productive cough and deterioration in general health (fatigue, weight loss and fever). If it is suspected a patient has developed interstitial lung disease, statin therapy should be discontinued.

Diabetes Mellitus: In patients with fasting glucose 5.6 to 6.9 mmol/L, treatment with rosuvastatin has been associated with an increased risk of diabetes mellitus

Clopidogrel

Bleeding and haematological disorders: Due to the risk of bleeding and haematological adverse reactions, blood cell count determination and/or other appropriate testing should be promptly considered whenever clinical symptoms suggestive of bleeding arise during the course of treatment. As with other antiplatelet agents, Clopidogrel should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery or other pathological conditions and in patients receiving treatment with ASA, heparin, glycoprotein IIb/IIIa inhibitors or non-steroidal anti-inflammatory drugs (NSAIDs) including Cox-2 inhibitors. Patients should be followed carefully for any signs of bleeding including occult bleeding, especially during the first weeks of treatment and/or after invasive cardiac procedures or surgery. The concomitant administration of Clopidogrel with oral anticoagulants is not recommended since it may increase the intensity of bleedings.

If a patient is to undergo elective surgery and antiplatelet effect is temporarily not desirable, Clopidogrel should be discontinued 7 days prior to surgery. Patients should inform physicians and dentists that they are taking Clopidogrel before any surgery is scheduled and before any new medicinal product is taken. Clopidogrel prolongs bleeding time and should be used with caution in patients who have lesions with a propensity to bleed (particularly gastrointestinal and intraocular).

Patients should be told that it might take longer than usual to stop bleeding when they take Clopidogrel (alone or in combination with ASA), and that they should report any unusual bleeding (site or duration) to their physician.

Thrombotic Thrombocytopenic Purpura (TTP): Thrombotic Thrombocytopenic Purpura (TTP) has been reported very rarely following the use of Clopidogrel, sometimes after a short exposure. It is characterized by thrombocytopenia and microangiopathic haemolytic anaemia associated with either neurological findings, renal dysfunction or fever. TTP is a potentially fatal condition requiring prompt treatment including plasmapheresis.

Recent ischaemic stroke: In view of the lack of data, Clopidogrel cannot be recommended during the first 7 days after acute ischaemic stroke.

Cytochrome P450 2C19 (CYP2C19): Pharmacogenetics: Based on literature data, patients with genetically reduced CYP2C19 function have lower systemic exposure to the active metabolite of Clopidogrel and diminished antiplatelet responses, and generally exhibit higher cardiovascular event rates following myocardial infarction than do patients with normal CYP2C19 function.

Since Clopidogrel is metabolized to its active metabolite partly by CYP2C19, use of medicinal products that inhibit the activity of this enzyme would be expected to result in reduced drug levels of the active metabolite of Clopidogrel. The clinical relevance of this interaction is uncertain. As a precaution concomitant use of medicinal products that inhibit CYP2C19 should be discouraged.

Renal impairment: Therapeutic experience with Clopidogrel is limited in patients with renal impairment. Therefore Clopidogrel should be used with caution in these patients.

Hepatic impairment: Experience is limited in patients with moderate hepatic disease who may have bleeding diatheses. Clopidogrel should therefore be used with caution in this population.

PHARMACODYNAMICS

Mechanism of Action

Rosuvastatin

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor for cholesterol. The primary site of action of rosuvastatin is the liver, the target organ for cholesterol lowering.

Rosuvastatin increases the number of hepatic LDL receptors on the cell-surface, enhancing uptake and catabolism of LDL and it inhibits the hepatic synthesis of VLDL, thereby reducing the total number of VLDL and LDL particles

Clopidogrel

Clopidogrel is a prodrug, one of whose metabolites is an inhibitor of platelet aggregation. Clopidogrel must be metabolized by CYP450 enzymes to produce the active metabolite that inhibits platelet aggregation. The active metabolite of Clopidogrel selectively inhibits the binding of adenosine diphosphate (ADP) to its platelet P2Y12 receptor and the subsequent ADP mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation. Due to the irreversible binding, platelets exposed are affected for the remainder of their lifespan (approximately 7-10 days) and recovery of normal platelet function occurs at a rate consistent with platelet turnover. Platelet aggregation induced by agonists other than ADP is also inhibited by blocking the amplification of platelet activation by released ADP.

Repeated doses of 75 mg per day produced substantial inhibition of ADP-induced platelet aggregation from the first day; this increased progressively and reached steady state between Day 3 and Day 7. At steady state, the average inhibition level observed with a dose of 75 mg per day was between 40% and 60%. Platelet aggregation and bleeding time gradually returned to baseline values, generally within 5 days after treatment was discontinued.

PHARMACOKINETICS

ROSUVASTATIN

Absorption

Maximum Rosuvastatin plasma concentrations are achieved approximately 5 hours after oral administration. The absolute bioavailability is approximately 20%

Distribution

Rosuvastatin is taken up extensively by the liver which is the primary site of cholesterol synthesis and LDL-C clearance. The volume of distribution of Rosuvastatin is approximately 134 L. Approximately 90% of Rosuvastatin is bound to plasma proteins, mainly to albumin

Metabolism

Rosuvastatin undergoes limited metabolism (approximately 10%). In vitro metabolism studies using human hepatocytes indicate that Rosuvastatin is a poor substrate for cytochrome P450-based metabolism. CYP2C9 was the principal isoenzyme involved, with 2C19, 3A4 and 2D6 involved to a lesser extent. The main metabolites identified are the N-desmethyl and lactone metabolites. The N-desmethyl metabolite is approximately 50% less active than Rosuvastatin whereas the lactone form is considered clinically inactive. Rosuvastatin accounts for greater than 90% of the circulating HMG-CoA reductase inhibitor activity.

Elimination

Approximately 90% of the Rosuvastatin dose is excreted unchanged in the feces (consisting of absorbed and non-absorbed active substance) and the remaining part is excreted in urine. Approximately 5% is excreted unchanged in urine. The plasma elimination half-life is approximately 19 hours. The elimination half-life does not increase at higher doses. The geometric mean plasma clearance is approximately 50 liters/hour (coefficient of variation 21.7%). As with other HMG-CoA reductase inhibitors, the hepatic uptake of Rosuvastatin involves the membrane transporter OATP-C. This transporter is important in the hepatic elimination of Rosuvastatin.

CLOPIDOGREL

Absorption

After single and repeated oral doses of 75 mg per day, Clopidogrel is rapidly absorbed. Mean peak plasma levels of unchanged Clopidogrel (approximately 2.2 2.5 ng/mL after a single 75 mg oral dose) occurred approximately 45 minutes after dosing. Absorption is at least 50%, based on urinary excretion of Clopidogrel metabolites.

Distribution

Clopidogrel and the main circulating (inactive) metabolite bind reversibly in vitro to human plasma proteins (98% and 94% respectively). The binding is non saturable in vitro over a wide concentration range.

Metabolism

Clopidogrel is extensively metabolized by the liver. In vitro and in vivo, Clopidogrel is metabolized according to two main metabolic pathways: one mediated by esterases and leading to hydrolysis into its inactive carboxylic acid derivative (85% of circulating metabolites), and one mediated by multiple cytochromes P450. Clopidogrel is first metabolized to a 2-oxo-clopidogrel intermediate metabolite. Subsequent metabolism of the 2-oxo-clopidogrel intermediate metabolite results in formation of the active metabolite, a thiol derivative of Clopidogrel. In vitro, this metabolic pathway is mediated by CYP3A4, CYP2C19, CYP1A2 and CYP2B6. The active thiol metabolite which has been isolated in vitro, binds rapidly and irreversibly to platelet receptors, thus inhibiting platelet aggregation.

Elimination
Following an oral dose of 14C labeled Clopidogrel in man, approximately 50% was excreted in the urine and approximately 46% in the feces in the 120 hour interval after dosing. After a single oral dose of 75 mg, Clopidogrel has a half-life of approximately 6 hours. The elimination half life of the main circulating (inactive) metabolite was 8 hours after single and repeated administration.

Special populations
The pharmacokinetics of the active metabolite of Clopidogrel is not known in these special populations.

RENAL IMPAIRMENT

Rosuvastatin
In a study in subjects with varying degrees of renal impairment, mild to moderate renal disease had no influence on plasma concentration of Rosuvastatin or the N-desmethyl metabolite. Subjects with severe impairment (CrCl <30 mL/min) had a 3-fold increase in plasma concentration and a 9-fold increase in the N-desmethyl metabolite concentration compared to healthy volunteers. Steady-state plasma concentrations of Rosuvastatin in subjects undergoing haemodialysis were approximately 50% greater compared to healthy volunteers

Clopidogrel
After repeated doses of 75 mg Clopidogrel per day in subjects with severe renal disease (creatinine clearance from 5 to 15 ml/min), inhibition of ADP induced platelet aggregation was lower (25%) than that observed in healthy subjects, however, the prolongation of bleeding time was similar to that seen in healthy subjects receiving 75 mg of Clopidogrel per day. In addition, clinical tolerance was good in all patients.

HEPATIC IMPAIRMENT

Rosuvastatin
In a study with subjects with varying degrees of hepatic impairment there was no evidence of increased exposure to Rosuvastatin in subjects with Child-Pugh scores of 7 or below. However, two subjects with Child-Pugh scores of 8 and 9 showed an increase in systemic exposure of at least 2-fold compared to subjects with lower Child-Pugh scores. There is no experience in subjects with Child-Pugh scores above 9.

Clopidogrel
After repeated doses of 75 mg clopidogrel per day for 10 days in patients with severe hepatic impairment, inhibition of ADP induced platelet aggregation was similar to that observed in healthy subjects. The mean bleeding time prolongation was also similar in the two groups.

DRUG INTERACTIONS

Oral anticoagulants : it may increase the intensity of bleedings.
Glycoprotein IIb/IIIa inhibitors, Acetylsalicylic acid, Heparin, NSAIDs : may increase the risk of bleeding.
Drugs that inhibiting CYP2C19 : may cause reduced drug levels of the active metabolite of clopidogrel
Ciclosporin : rosuvastatin AUC values may increase
Vitamin K antagonists : may result in an increase in International Normalised Ratio (INR).
Gemfibrozil and other lipid-lowering products : may result in increase of rosuvastatin C_{max} and AUC.
Protease inhibitors : may strongly increase rosuvastatin exposure.
Antacid : antacid suspension containing aluminum and magnesium hydroxide may result in a decrease in rosuvastatin plasma concentration
Erythromycin : may result in decrease in AUC (0-t) and a Cmax of rosuvastatin.
Oral contraceptive/hormone replacement therapy (HRT) : may result in an increase in ethinyl estradiol and norgestrel AUC of 26% and 34%, respectively. These increased plasma levels should be considered when selecting oral contraceptive doses.

Effects on ability to drive and use machines
Studies to determine the effect of the product on the ability to drive and use machines have not been conducted. However, based on its pharmacodynamic properties, this product is unlikely to affect this ability. When driving vehicles or operating machines, it should be taken into account that dizziness may occur during treatment.

ADVERSE EFFECTS

Rosuvastatin
The adverse events seen with Rosuvastatin are generally mild and transient. In controlled clinical trials, less than 4% of Rosuvastatin-treated patients were withdrawn due to adverse events.
The frequencies of adverse events are ranked according to the following: Common (>1/100, <1/10); Uncommon (>1/1,000, <1/100); Rare (>1/10,000, <1/1000); Very rare (<1/10,000); Not known (cannot be estimated from the available data).

Immune system disorders
Rare: hypersensitivity reactions including angioedema
Endocrine disorders
Common: diabetes mellitus1
Nervous system disorders
Common: headache, dizziness
Gastrointestinal disorders
Common: constipation, nausea, abdominal pain
Rare: pancreatitis
Skin and subcutaneous tissue disorders
Uncommon: pruritus, rash and urticaria
Musculoskeletal, connective tissue and bone disorders
Common: myalgia
Rare: myopathy (including myositis) and rhabdomyolysis
General disorders
Common: asthenia
1 Observed in the JUPITER study (reported overall frequency 2.8% in Rosuvastatin and 2.3% in placebo) mostly in patients with fasting glucose 5.6 to 6.9 mmol/L.
As with other HMG-CoA reductase inhibitors, the incidence of adverse drug reactions tends to be dose dependent.
Renal effects: Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with Rosuvastatin. Shifts in urine protein from none or trace to ++ or more were seen in <1% of patients at some time during treatment with 10 and 20 mg, and in approximately 3% of patients treated with 40 mg. A minor increase in shift from none or trace to + was observed with the 20 mg dose. In most cases, proteinuria decreases or disappears spontaneously on continued therapy. Review of data from clinical trials and post-marketing experience to date has not identified a causal association between proteinuria and acute or progressive renal disease.
Haematuria has been observed in patients treated with Rosuvastatin and clinical trial data show that the occurrence is low.
Skeletal muscle effects: Effects on skeletal muscle e.g. myalgia, myopathy (including myositis) and, rarely, rhabdomyolysis with and without acute renal failure have been reported in Rosuvastatin-treated patients with all doses and in particular with doses> 20 mg.
A dose-related increase in CK levels has been observed in patients taking rosuvastatin; the majority of cases were mild, asymptomatic and transient. If CK levels are elevated (>5xULN), treatment should be discontinued.
Liver effects: As with other HMG-CoA reductase inhibitors, a dose-related increase in transaminases has been observed in a small number of patients taking Rosuvastatin; the majority of cases were mild, asymptomatic and transient.
Post marketing experience: In addition to the above, the following adverse events have been reported during post marketing experience for Rosuvastatin:
Nervous system disorders: Very rare: polyneuropathy, memory loss.
Respiratory, thoracic and mediastinal disorders: Not known: cough, dyspnea.
Gastrointestinal disorders: Not known: diarrhea.
Hepatobiliary disorders: Very rare: jaundice, hepatitis; rare: increased transaminases.
Skin and subcutaneous tissue disorders: Not known: Stevens-Johnson syndrome.
Musculoskeletal disorders: Very rare: arthralgia.
Renal disorders: Very rare: haematuria.
General disorders and administration site conditions: Not known: edema.
The following adverse events have been reported with some statins: depression, sleep disturbances, including insomnia and nightmares, sexual dysfunction, exceptional cases of interstitial lung disease, especially with long term therapy.
The reporting rates for rhabdomyolysis, serious renal events and serious hepatic events (consisting mainly of increased hepatic transaminases) are higher at the 40 mg dose.
Pediatric population: Creatine kinase elevations>10xULN and muscle symptoms following exercise or increased physical activity were observed more frequently in a 52-week clinical trial of children and adolescents compared to adults. In other respects, the safety profile of Rosuvastatin was similar in children and adolescents compared to adults.

Clopidogrel
Adverse reactions that occurred either during clinical studies or that were spontaneously reported are presented in the table below. Their frequency is defined using the following conventions: common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000). Within each system organ class, adverse drug reactions are presented in order of decreasing seriousness.

System Organ Class	Common	Uncommon	Rare	Very rare
Blood and the lymphatic system disorders		Thrombocytopenia, leucopenia, eosinophilia	Neutropenia, including severe neutropenia	Thrombotic thrombocytopenic purpura (TTP), aplastic anemia, pancytopenia, agranulocytosis, severe thrombocytopenia, granulocytopenia, anemia
Immune system disorders				Serum sickness, anaphylactoid reactions
Psychiatric disorders				Hallucinations, confusion
Nervous system disorders		Intracranial bleeding (some cases were reported with fatal outcome), headache, paresthesia, dizziness		Taste disturbances
Eye disorders		Eye bleeding (conjunctival, ocular, retinal)		
Ear and labyrinth disorders			Vertigo	
Vascular disorders	Hematoma			Serious hemorrhage, hemorrhage of operative wound, vasculitis, hypotension
Respiratory, thoracic and mediastinal disorders	Epistaxis			Respiratory tract bleeding (haemoptysis, pulmonary hemorrhage), bronchospasm, interstitial pneumonitis
Gastrointestinal disorders	Gastrointestinal hemorrhage, diarrhea, abdominal pain, dyspepsia	Gastric ulcer and duodenal ulcer, gastritis, vomiting, nausea, constipation, flatulence	Retroperitoneal hemorrhage	Gastrointestinal and retroperitoneal hemorrhage with fatal outcome, pancreatitis, colitis (including ulcerative or lymphocytic colitis), stomatitis
Hepato-biliary disorders				Acute liver failure, hepatitis, abnormal liver function test
Skin and subcutaneous tissue disorders	Bruising	Rash, pruritus, skin bleeding (purpura)		Bullous dermatitis (toxic epidermal necrolysis, Stevens Johnson Syndrome, erythema multiforme), angioedema, rash erythematous, urticaria, eczema, lichen planus
Musculoskeletal connective tissue and bone disorders				Musculo-skeletal bleeding (haemarthrosis), arthritis, arthralgia, myalgia
Renal and urinary disorders		Hematuria		Glomerulonephritis blood creatinine increased
General disorders and administration site conditions	Bleeding at puncture site			Fever
Investigations		Bleeding time prolonged, neutrophil count decreased, platelet count decreased		

OVERDOSE AND TREATMENT
Overdose may lead to prolonged bleeding time and subsequent bleeding complications. Appropriate therapy should be considered if bleedings are observed. No antidote to the pharmacological activity of Clopidogrel has been found. If prompt correction of prolonged bleeding time is required, platelet transfusion may reverse the effects of Clopidogrel.
The patient should be treated symptomatically and supportive measures instituted as required. Liver function and CK levels should be monitored. Hemodialysis is unlikely to be of benefit.

USE IN PREGNANCY AND LACTATION
The product is contraindicated in pregnancy and lactation.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without a prescription.

STORE AT TEMPERATURES NOT EXCEEDING 30°C.

AVAILABILITY
Clopidogrel plus Rosuvastatin 75mg/10mg Capsule alu-alu blister pack x 10's (box of 30's)
Clopidogrel plus Rosuvastatin 75mg/20mg Capsule alu-alu blister pack x 10's (box of 30's)

Rosugrel® is a registered trademark of Ajanta Pharma Philippines, Inc.

FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA : www.fda.gov.ph . Seek medical attention immediately at the first sign of any adverse drug reaction.

Registration No.: 75mg/10mg - DR-XY45780
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