APO-ROSUVASTATIN TABLETS
Rosuvastatin 10mg & 20mg (as Rosuvastatin Calcium)

Product Description
10 mg: Pink, round, biconvex, film-coated tablet. Engraved "APO" on one side, "ROS" over "10" on the other side
20 mg: Pink, round, biconvex, film-coated tablet. Engraved "APO" on one side, "ROS" over "20" on the other side.

Mechanism of Action
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.

Pharmacodynamics
Rosuvastatin reduces elevated LDL-cholesterol, total cholesterol and triglycerides and increases HDL-cholesterol. It also lowers ApoB, nonHDL-C, VLDL-C, VLDL-TG and increases ApoA-I. Rosuvastatin also lowers the LDL-C/HDL-C, total C/HDL-C and nonHDL-C/HDL-C and the ApoB/ApoA-I ratios.
Rosuvastatin is effective in adults with hypercholesterolaemia, with and without hypertriglyceridaemia, regardless of race, sex, or age and in special populations such as diabetics, or patients with familial hypercholesterolaemia.

Pharmacokinetics
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.
Excretion: Approximately 90% of the rosuvastatin dose is excreted unchanged in the faeces (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 litres/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.
Linearity: Systemic exposure of rosuvastatin increases in proportion to dose. There are no changes in pharmacokinetic parameters following multiple daily doses.

Indication
APO-ROSUVASTATIN is indicated as an adjunct to diet, at least equivalent to the Adult Treatment Panel III (ATP III TLC diet), for the reduction of elevated total cholesterol, LDL-cholesterol, ApoB, the total cholesterol: HDL-cholesterol ratio and triglycerides and for increasing HDL-C, in hyperlipidemic and dyslipidemic conditions, when response to diet and exercise alone has been inadequate including: Prevention of Cardiovascular Events.
In adult patients with an increased risk of atherosclerotic cardiovascular disease based on the presence of cardiovascular disease risk markers such as an elevated hsCRP level, age, hypertension, low HDL-C, smoking or a family history of premature coronary heart disease, APO-ROSUVASTATIN is indicated to reduce total mortality and the risk of major cardiovascular events (cardiovascular death, stroke, MI, unstable angina, or arterial revascularization).
APO-ROSUVASTATIN is indicated as an adjunct to diet for the treatment of patients with primary dysbetalipoproteinemia (Type III Hyperlipoproteinemia). Primary hypercholesterolaemia (Type IIa including heterozygous familial hypercholesterolaemia and severe non-familial hypercholesterolaemia) Combined (mixed) dyslipidemia (Type IIb) Homozygous familial hypercholesterolaemia where APO- ROSUVASTATIN is used either alone or as an adjunct to diet and other lipid lowering treatment such as apheresis.
APO-ROSUVASTATIN is indicated as adjunctive therapy to diet to slow the progression of atherosclerosis in adult patients as part of a treatment strategy to lower Total-C and LDL-C to target levels. Pediatric Patients 10 to 17 years of age with Heterozygous Familial Hypercholesterolemia (HeFH): Adjunct to diet to reduce Total-C, LDL- C and ApoB levels in adolescent boys and girls, who are at least one year post-menarche, 10-17 years of age with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following findings are present: LDL-C > 190 mg/dL or > 160 mg/dL and there is a positive family history of premature cardiovascular disease (CVD) or two or more other CVD risk factors.

Recommended Dosage
Patients should be placed on a standard cholesterol-lowering diet (at least equivalent to the Adult Treatment Panel III (ATP III TLC diet)) before receiving APO-ROSUVASTATIN (rosuvastatin calcium), and should continue on this diet during treatment with APO- ROSUVASTATIN. If appropriate, a program of weight control and physical exercise should be implemented. Prior to initiating therapy with APO-ROSUVASTATIN, secondary causes for elevations in plasma lipid levels should be excluded. A lipid profile should also be performed. After initiation or upon titration of APO-ROSUVASTATIN, lipid levels should be analyzed within 2-4 weeks and the dosage adjusted accordingly.
The usual recommended starting dose of APO-ROSUVASTATIN is 10 mg once daily. However, initiation of therapy with 5 mg once daily should be considered for special patient populations or patients requiring less aggressive LDL-C reductions. The choice of starting dose should take into account the individual patients' cholesterol level and future cardiovascular risk as well as the potential risk for adverse reactions.
APO-ROSUVASTATIN may be taken in the morning or evening, with or without food. The majority of patients are controlled at the 10mg dose. However, if necessary, dose adjustments to the next dose level can be made after 4-week intervals. The maximum response is usually achieved within 2-4 weeks and is maintained during chronic therapy. Increasing the dose to 40 mg should be reserved for patients with severe

hypercholesterolaemia at high cardiovascular risk (in particular those with familial hypercholesterolaemia), who do not achieve their treatment goal on 20 mg and should only be initiated under specialist supervision (see Special Warnings and Precautions for Use).
The physician who elects to use APO-ROSUVASTATIN at a dose higher than 20 mg should periodically re-evaluate the long term risk/benefit of APO-ROSUVASTATIN for the individual patient. APO- ROSUVASTATIN should be prescribed with caution in patients with pre-disposing factors for myopathy / rhabdomyolysis (see Special Warnings and Precautions for Use).
The dosage of APO-ROSUVASTATIN should be individualised according to baseline LDL-C, total-C/HDL-C ratio and/or TG levels, the recommended target lipid values (see Recommendations for the Management and Treatment of Dyslipidemia [Canada] summarised below in Table 1) and/or the Third Report of the U.S. National Cholesterol Education Program [NCEP Adult Treatment Panel III]) and the patient response. The majority of patients treated with rosuvastatin 10 mg achieved their NCEP ATP III treatment target for LDL-C levels; fewer subjects achieved target on the 5 mg dose. The difference between rosuvastatin 5 mg and 10 mg was greatest for high risk subjects, i.e. for subjects who have a lower LDL-C target. Lipid levels should be monitored periodically and, if necessary, the dose of APO-ROSUVASTATIN adjusted based on target lipid levels recommended by guidelines.
Table 1: Canadian Recommendations for Target Lipid Values Based on Level of Risk

Level of Risk (definition)	Target values		
	LDL-C (mmol/L)	Total- C/HDL-C ratio	TG (mmol/L)
Very high * (10-year risk of CAD>30%, or history of cardiovascular disease or diabetes)	<2.5	<4.0	<2.0
High * (10-year risk CAD 20% - 30%)	<3.0	<5.0	<2.0
Moderate ** (10-year risk of CAD 10% - 20%)	<4.0	<6.0	<2.0
Low *** (10-year risk of CAD <10%)	<5.0	<7.0	<3.0

*Start medication and lifestyle changes concomitantly if values are above target values
**Start medication if target values are not achieved after 3 months of lifestyle modification
***Start medication if target values are not achieved after 6 months of lifestyle modification

Dosage in patients with renal insufficiency
The usual dose range applies in patients with mild to moderate renal impairment. The use of APO-ROSUVASTATIN in patients with severe renal impairment is contraindicated.

Dosage in patients with hepatic insufficiency
There was no increase in systemic exposure to rosuvastatin in subjects with Child-Pugh scores of 7 or below. However, increased systemic exposure has been observed in subjects with Child-Pugh scores of 8 and 9. In these patients an assessment of renal function should be considered. There is no experience in subjects with Child- Pugh scores above 9.

APO-ROSUVASTATIN is contraindicated in patients with active liver disease.

Use in the elderly
The overall frequency of adverse events and types of adverse events were similar in patients above and below 65 years of age. The efficacy of rosuvastatin in the geriatric population (≥65 years of age) was comparable to the efficacy observed in the non-elderly.

Pediatric Patients (10 to 17 years of age)
In pediatric patients (10 to 17 years of age) with heterozygous familial hypercholesterolemia the usual dose range of APO-ROSUVASTATIN is 5-20 mg/day; the maximum recommended dose is 20 mg/day (doses greater than 20 mg have not been studied in this patient population). Doses should be individualized according to the recommended goal of therapy (see Clinical Efficacy and Therapeutic Indications). Adjustments should be made at intervals of 4 weeks or more.

Use in Children below 10 years
The safety and effectiveness in children have not been established. In children and adolescents with homozygous familial hypercholesterolemia experience is limited (aged 8 years and above). Dosage on Asian Patients Initiation of APO-ROSUVASTATIN therapy with 5 mg once daily should be considered for Asian patients. The potential for increased systemic exposures relative to Caucasians is relevant when considering escalation of dose in cases where hypercholesterolaemia is not adequately controlled at doses of 5, 10 or 20 mg once daily (see Special warnings and special precautions for use and Pharmacokinetic properties).

Genetic polymorphisms
Specific types of genetic polymorphisms are known that can lead to increased rosuvastatin exposure (see Pharmacokinetic Properties). For patients who are known to have such specific types of polymorphisms, a lower daily dose of APO-ROSUVASTATIN is recommended.

Dosage in patients with pre-disposing factors to myopathy
The recommended start dose is 5 mg in patients with predisposing factors to myopathy (see Special warnings and special precautions for use).

Concomitant therapy Rosuvastatin is a substrate of various transporter proteins (e.g. OATP1B1 and BCRP). The risk of myopathy (including rhabdomyolysis) is increased when APO-ROSUVASTATIN is administered concomitantly with certain medicinal products that may increase the plasma

concentration of rosuvastatin due to interactions with these transporter proteins (e.g. ciclosporin and certain protease inhibitors including combinations of ritonavir with atazanavir, lopinavir, and/or tipranavir; see Special warnings and special precautions for use and Interaction with other medicinal products and other forms of interaction). Whenever possible, alternative medications should be considered, and, if necessary, consider temporarily discontinuing APO-ROSUVASTATIN therapy. In situations where co-administration of these medicinal products with APO- ROSUVASTATIN is unavoidable, the benefit and the risk of concurrent treatment and APO-ROSUVASTATIN dosing adjustments should be carefully considered (see Interaction with Other Medicinal Products and Other Forms of Interaction).

Mode of Administration
Oral

Contraindications
APO-ROSUVASTATIN is contraindicated:
- in patients with hypersensitivity to rosuvastatin or to any of the excipients.
- 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.

Warnings and Precautions
Renal Effects Proteinuria
Skeletal Muscle Effects
Effects on skeletal muscle e.g. myalgia, myopathy and, rarely, rhabdomyolysis. Very rare cases of rhabdomyolysis with the use of ezetimibe in combination with HMG-CoA reductase inhibitors.

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
APO-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 APO-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.

There have been very rare reports of an immune-mediated necrotising myopathy (IMNM) during or after treatment with statins, including rosuvastatin. IMNM is clinically characterised by
• persistent proximal muscle weakness and elevated serum creatine kinase, which persist despite discontinuation of statin treatment;
• muscle biopsy showing necrotizing myopathy without significant inflammation;
• improvement with immunosuppressive agents.

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.
Combination with rosuvastatin and fusidic acid is not recommended. APO-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, APO-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. APO- ROSUVASTATIN should

be discontinued or the dose reduced if the level of serum transaminases is greater than 3 times the upper limit of normal.
In patients with secondary hypercholesterolaemia caused by hypothyroidism or nephrotic syndrome, the underlying disease should be treated prior to initiating therapy with APO- ROSUVASTATIN.
Protease inhibitors
The concomitant use with certain protease inhibitors is not recommended unless the dose of APO-ROSUVASTATIN is adjusted.
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
Presenting features can include dyspnoea, 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
Some evidence suggests that statins as a class raise blood glucose and in some patients, at high risk of future diabetes, may produce a level of hyperglycaemia where formal diabetes care is appropriate. This risk, however, is outweighed by the reduction in vascular risk with statins and therefore should not be a reason for stopping statin treatment.

Effects on ability to drive and use machines
Based on its pharmacodynamic properties, rosuvastatin is unlikely to affect this ability. When driving vehicles or operating machines, it should be taken into account that dizziness may occur during treatment.

Myasthenia Gravis/ Ocular Myasthenia

In few cases, statins have been reported to induce de novo or aggravate pre-existing myasthenia gravis or ocular myasthenia. Apo-Rosuvastatin should be discontinued in case of aggravation of symptoms. Recurrences when the same or different statin was (re-)administered have been reported.

Interactions with Other Medicaments
Effect of co-administered medicinal products on rosuvastatin Transporter protein inhibitors: Rosuvastatin is a substrate for certain transporter proteins including the hepatic uptake transporter OATP1B1 and efflux transporter BCRP. Concomitant administration of APO-ROSUVASTATIN with medicinal products that are inhibitors of these transporter proteins may result in increased rosuvastatin plasma concentrations and an increased risk of myopathy.
Ciclosporin: APO-ROSUVASTATIN is contraindicated in patients receiving concomitant ciclosporin. Concomitant administration did not affect plasma concentrations of ciclosporin.
Protease inhibitors: Although the exact mechanism of interaction is unknown, concomitant protease inhibitor use may strongly increase rosuvastatin exposure. The concomitant use of APO-ROSUVASTATIN and some protease inhibitor combinations may be considered after careful consideration of APO-ROSUVASTATIN dose adjustments based on the expected increase in rosuvastatin exposure.
Gemfibrozil and other lipid-lowering products: Concomitant use of APO-ROSUVASTATIN and gemfibrozil resulted in a 2-fold increase in rosuvastatin C_{max} and AUC. Concurrent use of fibrates may cause severe myositis and myoglobinuria. These patients should also start with the 5 mg dose.
Ezetimibe: Concomitant use of 10 mg APO-ROSUVASTATIN and 10 mg ezetimibe resulted in a 1.2 fold increase in AUC of rosuvastatin in hypercholesterolaemic subjects.
Antacid: The simultaneous dosing of APO-ROSUVASTATIN with an antacid suspension containing aluminium and magnesium hydroxide resulted in a decrease in rosuvastatin plasma concentration of approximately 50%.
Erythromycin**:** Concomitant use of APO-ROSUVASTATIN and erythromycin may be caused by the increase in gut motility caused by erythromycin.
Cytochrome P450 enzymes: Rosuvastatin is a poor substrate for these isoenzymes. Therefore, drug interactions resulting from cytochrome P450-mediated metabolism are not expected.
Interactions requiring rosuvastatin dose adjustments: When it is necessary to co-administer APO-ROSUVASTATIN with other medicinal products known to increase exposure to rosuvastatin, doses of APO- ROSUVASTATIN should be adjusted. The maximum daily dose of APO- ROSUVASTATIN should be adjusted so that the expected rosuvastatin exposure would not likely exceed that of a 40 mg daily dose of APO- ROSUVASTATIN taken without interacting medicinal products.
Effect of rosuvastatin on co-administered medicinal products
Vitamin K antagonists: As with other HMG-CoA reductase inhibitors, the initiation of treatment or dosage up-titration of APO- ROSUVASTATIN in patients treated concomitantly with vitamin K antagonists (e.g. warfarin or another coumarin anticoagulant) may result in an increase in International Normalised Ratio (INR). Discontinuation or down-titration of Crestor may result in a decrease in INR. In such situations, appropriate monitoring of INR is desirable. Oral contraceptive/ hormone replacement therapy (HRT): Concomitant use of APO-ROSUVASTATIN and an oral contraceptive resulted in an increase in ethinyl estradiol and norgestrel AUC. These increased plasma levels should be considered when selecting oral contraceptive doses.
Other medicinal products:
Digoxin: No clinically relevant interaction with digoxin is expected. Fusidic Acid: The combination rosuvastatin and fusidic acid is not recommended. If possible, temporary suspension of rosuvastatin treatment is recommended. If unavoidable, patients should be closely monitored.

Pregnancy and Lactation
APO-ROSUVASTATIN is contraindicated in pregnancy and lactation. Women of child bearing potential should use appropriate contraceptive measures.
Since cholesterol and other products of cholesterol biosynthesis are essential for the development of the foetus, the potential risk from inhibition of HMG-CoA reductase outweighs the advantage of treatment during pregnancy. If a patient becomes pregnant during use of this product, treatment should be discontinued immediately. Rosuvastatin is excreted in the milk of rats. There are no data with respect to excretion in milk in humans.

Adverse Effects / Undesirable Effects

The adverse reactions seen with APO-ROSUVASTATIN are generally mild and transient.

Tabulated list of adverse reactions

The frequencies of adverse reactions are ranked according to the following convention: Common; Uncommon; Rare; Very rare; Not known.

Table-Adverse reactions based on data from clinical studies and post- marketing experience

System organ class	Common	Uncommon	Rare	Very rare	Not known
Blood and lymphatic system disorders			Thrombocytopenia		
Immune system disorders			Hypersensitivity reactions including angioedma		
Endorcrine disorders	Diabetes mellitus				
Psychiatric disorders					Depression
Nervous system disorders	Headache Dizziniess			Polyneuropathy Memory Loss	Peripheral neuropathy Sleep disturbances (including insomnia and nightmares)
Respiratory, thoracic and mediastinal disorders					Cough Dyspnoea
Gastrointestinal disorders	Constipation Nausea Abdominal Pain		Pancreatitis		Diarrhoea
Hepatobiliary disorders			Increased hepatic transaminases	Jaundice Hepatitis	
Skin and subcutaneous tissue disorders		Pruritus Rash Urticaria			Stevens-Johnson syndrome
Musculoskeletal and connective tissue disorders	Myalgia		Myopathy (including myositis) Rhabdomyolysis	Arthralgia	Tendon disorders, sometimes complicated by rupture Immune-mediated necrotizing myopathy
Renal and urinary disorders				Haematouria	
Reproductive system and breast disorders				Gynaecomastia	
General disorders and administration site conditions	Asthenia				Oedema

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. Haematuria has also been observed.

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.

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.

The following adverse events have been reported with some statins: 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) is higher at the 40 mg dose.

Paediatric population: The safety profile of rosuvastatin was similar in children and adolescents compared to adults.

There have been rare post-marketing reports of cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use. These cognitive issues have been reported for all statins. The reports are generally non-serious and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptom resolution (median of 3 weeks).
Increase in HbA1c and fasting blood glucose have been reported with statins. The risk of hyperglycemia, however, is outweighed by the reduction in vascular risk with statins.

Nervous system disorders
Frequency 'not known': myasthenia gravis

Eye disorders
Frequency 'not known': ocular myasthenia

Overdose and Treatment
There is no specific treatment in the event of overdosage. Should an overdose occur, the patient should be treated symptomatically and supportive measures instituted as required. Hemodialysis does not significantly enhance clearance of rosuvastatin. Liver function and CK levels should be monitored.

Storage Conditions
Store below 30°C. Protect from moisture.

Dosage Forms and Packaging Available
10 mg: Available in bottles of 100 and 500 tablets and in unit dose blister packages of 30 (3 x 10) tablets.
20 mg: Available in bottles of 100 and 500 tablets and in unit dose blister packages of 30 (3 x 10) tablets.
Not all pack size is marketed.

Name and Address of Manufacturer
Apotex Inc.
150 Signet Drive Toronto, Ontario Canada M9L 1T9

Name and Address of Product Registration Holder
Pharmaforte (M) Sdn Bhd
2, Jalan PJU 3/49, Sunway Damansara, 47810 Petaling Jaya, Selangor, Malaysia.

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