PROFESSIONAL INFORMATION

DYNATOR RANGE

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

DYNATOR 10 mg film coated tablet

DYNATOR 20 mg film coated tablet

DYNATOR 40 mg film coated tablet

DYNATOR 80 mg film coated tablet

COMPOSITION:

Active ingredients:

DYNATOR 10 mg: Each tablet contains atorvastatin calcium equivalent to 10 mg atorvastatin.

DYNATOR 20 mg: Each tablet contains atorvastatin calcium equivalent to 20 mg atorvastatin.

DYNATOR 40 mg: Each tablet contains atorvastatin calcium equivalent to 40 mg atorvastatin.

DYNATOR 80 mg: Each tablet contains atorvastatin calcium equivalent to 80 mg atorvastatin.

Inactive ingredients:

Crospovidone, magnesium stearate, microcrystalline cellulose, Opadry OYL – 28900 white,

Sinespum C, sodium hydrogen carbonate, sodium lauryl sulphate.

Contains 0,02 % *w/w* butylhydroxyanisole, as a preservative.

Contains sugar.

DYNATOR 10 mg: 65,01 mg lactose monohydrate, 3,88 mg sucrose per tablet.

DYNATOR 20 mg: 130,02 mg lactose monohydrate, 7,77 mg sucrose per tablet.

DYNATOR 40 mg: 260,03 mg lactose monohydrate, 15,53 mg sucrose per tablet.

DYNATOR 80 mg: 520,05 mg lactose monohydrate, 31,07 mg sucrose per tablet.

PHARMACOLOGICAL CLASSIFICATION:

A 7.5 Serum-cholesterol reducers.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Atorvastatin is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methyl-glutaryl-coenzyme A to mevalonate, a precursor of sterols including cholesterol.

Atorvastatin reduces low-density lipoprotein cholesterol (LDL-C) production and the number of LDL-C particles. Depending on dose, atorvastatin reduces the number of apolipoprotein B particles in patients with hypercholesterolemia. The primary site of action of atorvastatin is the liver which is the principal site of cholesterol synthesis and low-density lipoprotein cholesterol (LDL-C) clearance.

In animal models atorvastatin lowers the plasma cholesterol and lipoprotein levels by inhibiting HMG-CoA reductase and cholesterol synthesis in the liver and by increasing the number of LDL-C receptors on the cell-surface of liver cells, providing for enhanced uptake and catabolism of LDL-C.

Atorvastatin reduces total cholesterol (total-C), LDL-C, apolipoprotein-B in normal volunteers, and in patients with heterozygous familial hypercholesterolaemia, non-familial hypercholesterolaemia, mixed dyslipidaemia, and in some patients with homozygous familial hypercholesterolaemia. It also reduces serum triglycerides (TG) and produces variable increases in high-density lipoprotein cholesterol (HDL-C) and apolipoprotein-A-1 in non-familial hypercholesterolaemia and mixed dyslipidaemias.

Pharmacokinetic properties:

Absorption

Following oral administration of atorvastatin, maximum plasma concentrations occur within 1 to 2 hours. The absolute bioavailability of atorvastatin is approximately 12 % and the systemic availability of HMG-CoA reductase inhibitory activity is approximately 30 %. Atorvastatin has a low systemic availability due to the presystemic clearance in gastrointestinal mucosa and/or hepatic first-pass metabolism. Food decreases the rate and extent of medicine absorption by approximately 25 % and 9 %, respectively, as assessed by C_{max} and AUC, however, LDL-C reduction is similar whether atorvastatin is given with or without food. Plasma atorvastatin concentrations are lower

(approximately 30 % for C_{max} and AUC) following evening medicine administration compared to morning administration. LDL-C reduction is however the same regardless of the time of medicine administration.

Distribution

Mean volume of distribution of atorvastatin is approximately 381 litres. Atorvastatin is 98 % or more bound to plasma proteins.

Metabolism

Atorvastatin undergoes extensive hepatic and/or extra-hepatic metabolism by cytochrome P450 3A4 to ortho- and para-hydroxylated derivatives and various beta-oxidation products.
In vitro inhibition of HMG-CoA reductase by ortho- and para-hydroxylated metabolites is equivalent to that of atorvastatin. Approximately 70 % of circulating inhibitory activity for HMG-CoA reductase is due to active metabolites.

Elimination

Atorvastatin is eliminated primarily in the faeces via the biliary route following hepatic and/or extrahepatic metabolism. Atorvastatin has a mean plasma elimination half-life in humans of approximately 14 hours, but the half-life of inhibitory activity for HMG-CoA reductase is 20 to 30 hours due to the contribution of active metabolites. Less than 2 % of a dose of atorvastatin is recovered in urine following oral administration.

Special Populations

Elderly:

In healthy elderly subjects (65 years and older) the plasma concentrations of atorvastatin are higher (approximately 40 % for C_{max} and 30 % for AUC) than in young adults. LDL-C reduction is comparable to that seen in younger patient populations given equal doses of atorvastatin.

Paediatric:

Pharmacokinetic data in the paediatric population are not available.

Gender:

There is no clinically significant difference in LDL-C reduction with atorvastatin between men and women although the plasma concentrations of atorvastatin in women differ (approximately 20 % higher for C_{max} and 10 % lower for AUC) from those in men.

Renal Insufficiency:

Renal disease has no influence on the plasma concentrations or lipid effects of atorvastatin. Thus, dose adjustment in patients with renal dysfunction is not necessary (see **DOSAGE AND DIRECTIONS FOR USE**).

Haemodialysis:

While studies have not been conducted in patients with end-stage renal disease, haemodialysis is not expected to significantly enhance clearance of atorvastatin since the medicine is extensively bound to plasma proteins.

Hepatic Insufficiency:

Plasma concentrations of atorvastatin are markedly increased in patients with chronic alcoholic liver disease (Child-Pugh B) (see **CONTRAINDICATIONS**).

INDICATIONS:

DYNATOR is indicated

- As an adjunct to diet for reduction of elevated total-cholesterol, LDL-cholesterol, apolipoprotein-B, and triglyceride levels in patients with primary hypercholesterolaemia; mixed dyslipidaemia (Fredrickson Types IIa and IIb); and heterozygous familial hypercholesterolaemia.
- To reduce total-C and LDL-C in patients with homozygous familial hypercholesterolaemia as an adjunct to other lipid-lowering treatments (e.g. LDL aphaeresis) or if such treatments are unavailable.
- As an adjunct to diet to reduce total-C, LDL-C, and apo B levels in boys and postmenarchal girls, > 10 to 17 years of age, with heterozygous familial hypercholesterolaemia, if after an adequate trial of diet therapy the following findings are present:
- LDL-C remains ≥190 mg/dL (4,98 mmol/L) or

- LDL-C remains ≥160 mg/dL (4,04 mmol/L) and:
    - there is a positive family history of premature cardiovascular disease or
    - two or more other CVD risk factors are present in the paediatric patient.
- Prevention of Cardiovascular Complications in patients without clinically evident cardiovascular disease, and with or without dyslipidaemia, but with multiple risk factors for coronary heart disease such as smoking, hypertension, diabetes, low HDL-C, or a family history of early coronary heart disease, **DYNATOR** is indicated to reduce the risk of ischaemic cardiovascular and cerebrovascular diseases.
- Secondary prevention of cardiovascular events in patients with clinically evident coronary heart disease and increased cholesterol levels.

Prior to treatment with **DYNATOR**, a lipid profile must be performed to measure total-C, LDL-C, HDL-C, and TG and additionally, secondary causes for hypercholesterolaemia (e.g. poorly controlled diabetes mellitus, hypothyroidism, nephrotic syndrome, dysproteinaemias, obstructive liver disease, other medicines, and alcoholism) should be excluded.

Lipid-altering medicines should be used in addition to a diet restricted in saturated fat and cholesterol only when the response to diet and other non-pharmacological measures has been inadequate. Therapy with lipid-lowering medicines should be a component of multiple-risk-factor intervention in individuals at increased risk of atherosclerotic vascular disease due to hypercholesterolaemia.

CONTRAINDICATIONS:

DYNATOR tablets are contraindicated in:

- Hypersensitivity to atorvastatin or any of the other ingredients of **DYNATOR**.
- Active liver disease or unexplained persistent elevations of serum aminotransaminase concentrations (see **WARNINGS AND SPECIAL PRECAUTIONS**).
- Pregnancy and lactation (see **HUMAN REPRODUCTION**).
- Patients with Child-Pugh B and C (liver cirrhosis).
- Concomitant use with rifampicin, diltiazem and grapefruit juice.

- Porphyria.

WARNINGS AND SPECIAL PRECAUTIONS:

The use of **DYNATOR** in active liver disease or unexplained persistent transaminase increases is contraindicated (see **CONTRAINDICATIONS**).

Liver Effects:

Persistent dose related increases in serum transaminases can occur in patients who received DYNATOR. It is recommended that liver function tests be performed before starting of treatment, following each dosage increase, and periodically thereafter. Liver enzyme changes mostly commence in the first 4 months of treatment with atorvastatin, such as DYNATOR. Patients who develop increased transaminase levels should be monitored until the abnormalities resolve. Withdrawal of DYNATOR is recommended should an increase in ALT or AST of > 3 times ULN persist.

DYNATOR should be used with caution in patients who take substantial quantities of alcohol and/or have a history of liver disease. Limit alcohol intake during **DYNATOR** treatment.

Skeletal Muscle Effects:

Myalgia has been reported in patients treated with **DYNATOR** (see **SIDE EFFECTS**).
Rhabdomyolysis with or without renal impairment has been reported with the use of HMG-CoA reductase inhibitors, such as **DYNATOR.**

SLOC1B1 polymorphism:

Hepatic uptake of all HMG-CoA reductase inhibitors including atorvastatin, involves the OATP1B1 transporter. In patients with SLCO1B1 polymorphism there is a risk of increased exposure of atorvastatin, which may lead to an increased risk of rhabdomyolysis.

Myopathy, characterised by muscle aching or muscle weakness accompanied by increases in

creatine phosphokinase (CPK) values greater than 10 times the upper limit of normal, should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should promptly report any unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. Treatment with **DYNATOR** should be discontinued if markedly elevated CPK levels are found or myopathy is suspected or diagnosed. The risk of myopathy during treatment with **DYNATOR** is increased with concomitant use of immunosuppressive medicines, including ciclosporin, fibric acid derivatives, nicotinic acid, azole antifungals or erythromycin and cytochrome P450 inhibitors (see **INTERACTIONS**).

Treatment with **DYNATOR** should be discontinued in any patient having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis, (e.g. severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures) or with an acute, serious condition indicating the presence of a myopathy.

Protease Inhibitors:

Co-administration of **DYNATOR** with protease inhibitors can lead to increased plasma concentrations of atorvastatin (see **INTERACTIONS**).

Haemorrhagic Stroke:

For patients with prior haemorrhagic stroke or lacunar infarct, and the potential risk of haemorrhagic stroke should be carefully considered before initiating treatment.

Interstitial lung disease:

Cases of interstitial lung disease including hypersensitivity pneumonitis have been reported with some statins, especially with long term therapy (see **SIDE EFFECTS**). 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, **DYNATOR** therapy should be discontinued.

Diabetes Mellitus:

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. Patients at risk (fasting glucose 5,6 to 6,9 mmol/L, BMI >30 kg/m^2, raised triglycerides, hypertension) should be monitored.

Concomitant treatment with other medicines:

Risk of rhabdomyolysis is increased when **DYNATOR** is administered concomitantly with certain medicines that may increase the plasma concentration of atorvastatin such as potent inhibitors of CYP3A4 or transport proteins (see **INTERACTIONS**).

The risk of myopathy may also be increased with the concomitant use of gemfibrozil and other fibric acid derivates, boceprevir, erythromycin, niacin, ezetimibe, telaprevir, or the combination of tipranavir/ritonavir (see I**NTERACTIONS**). If possible, alternative (non-interacting) therapies should be considered instead of these medicines.

There have been reports of an immune-mediated necrotising myopathy (IMNM) during or after treatment with some statins. IMNM is clinically characterised by persistent proximal muscle weakness and elevated serum creatine kinase, which persist despite discontinuation of statin treatment.

When patients are receiving medicines that increase the plasma concentration of atorvastatin, a lower maximum dose of **DYNATOR** is recommended. In addition, in the case of potent CYP3A4 inhibitors, a lower starting dose of **DYNATOR** should be considered and appropriate clinical monitoring of these patients is recommended (see **INTERACTIONS**).

The concurrent use of **DYNATOR** and fusidic acid is not recommended, therefore, temporary suspension of **DYNATOR** may be considered during fusidic acid therapy (see **INTERACTIONS**).

Patient monitoring of renal, hepatic and skeletal muscle (myopathy) function is critical during **DYNATOR** treatment.

Effects on ability to drive or use machines:

DYNATOR may cause dizziness and therefore may impair concentration or motor skills. Patients

should be cautioned that their ability to drive a vehicle or operate hazardous machinery when taking **DYNATOR** may be impaired.

Information on excipients of DYNATOR:

DYNATOR contains lactose. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency or glucose-galactose malabsorption should not take **DYNATOR.**

DYNATOR contains sucrose. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take **DYNATOR**.

DYNATOR contains lactose and sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

INTERACTIONS:

Diltiazem hydrochloride:

Co-administration of **DYNATOR** with diltiazem can cause an increase in atorvastatin AUC (see **CONTRAINDICATIONS**)

Grapefruit*:*

Products and juice of grapefruit should not be taken before or after administration of **DYNATOR** as significant increases in the plasma concentrations of **DYNATOR** may result (see **CONTRAINDICATIONS**). Grapefruit juice has been shown to increase the C_{max} and AUC of **DYNATOR**. It is recommended that **DYNATOR** not be administered with grapefruit juice.

The risk for the development of myopathy is increased during treatment with **DYNATOR**, with concurrent administration of immunosuppressive medicines, fibric acid derivatives (fibrates or gemfibrozil), niacin (nicotinic acid), boceprevir, ezetimibe, telaprevir, or the combination of tipranavir/ritonavir, or cytochrome P450 3A4 inhibitors such as, macrolide antibiotics, e.g. erythromycin, azole antifungals, e.g. clotrimazole (see **WARNINGS AND SPECIAL PRECAUTIONS**). If concomitant administration cannot be avoided, dose reductions of **DYNATOR** should be considered and appropriate clinical monitoring of the patient is recommended.

Inhibitors of cytochrome P450 3A4:

DYNATOR is metabolised by cytochrome P450 3A4 and therefore co-administration with inhibitors of cytochrome P450 3A4 can lead to increases in plasma concentrations of atorvastatin (**DYNATOR**).

- Co-administration of potent and moderate CYP3A4 inhibitors (e.g. ciclosporin, delavirdine, stiripentol, fluconazole, ketoconazole, voriconazole, itraconazole, posaconazole and HIV protease inhibitors including ritonavir, lopinavir, atazanavir, indinavir, darunavir), nefazandone, danazol, amiodarone, amlodipine, ranolazine and verapamil should be avoided if possible. In cases where co-administration of these medicines with **DYNATOR** cannot be avoided, lower starting and maximum doses of **DYNATOR** should be considered and appropriate clinical monitoring of the patient is recommended.
- ***Erythromycin/Clarithromycin/Telithromycin:***

  DYNATOR plasma concentrations increase approximately 40 % with co-administration of **DYNATOR** and erythromycin, a known inhibitor of cytochrome P450 3A4 (see **WARNINGS AND SPECIAL PRECAUTIONS**).

Inducers of cytochrome P450 3A4:

Concomitant administration of **DYNATOR** with inducers of cytochrome P450 3A4 (e.g. efavirenz, rifampicin, St John's Wort) can lead to variable reductions in plasma concentrations of atorvastatin (**DYNATOR**).

Combination of protease inhibitors:

Concomitant administration of **DYNATOR** 40 mg with protease inhibitors ritonavir plus saquinavir (400 mg twice daily) resulted in a 3-fold increase in atorvastatin AUC. Concomitant administration of **DYNATOR** 20 mg with lopinavir plus ritonavir (400 mg + 100 mg twice daily) resulted in 5,9-fold increase in atorvastatin AUC (see **WARNINGS AND SPECIAL PRECAUTIONS**)

Cimetidine:

DYNATOR plasma concentrations and LDL-C reduction were not altered by co-administration of

cimetidine.

Ezetimibe:

The use of ezetimibe alone is associated with muscle related events, including rhabdomyolysis. The risk of these events may therefore be increased with concomitant use of ezetimibe and **DYNATOR**. Appropriate clinical monitoring of these patients is recommended.

Fusidic acid:

Muscle related events, including rhabdomyolysis, have been reported in post-marketing experience with **DYNATOR** and fusidic acid given concurrently. The mechanism of this interaction is not known. Patients should be closely monitored and temporary suspension of **DYNATOR** treatment may be appropriate.

Antacid:

Plasma concentration of atorvastatin is approximately 35 % decreased with co-administration of oral antacids containing magnesium and aluminium hydroxides, however, LDL-C reduction was not altered.

Warfarin:

DYNATOR had no clinically significant effect on prothrombin time when administered to patients receiving combined **DYNATOR** and warfarin therapy for two weeks. Nevertheless, patients receiving **DYNATOR** should be closely monitored when **DYNATOR** is combined with warfarin therapy.

Colestipol:

LDL-C reduction was greater when **DYNATOR** and colestipol are co-administered than when either medicine was given alone, although plasma concentrations of atorvastatin decreased by approximately 25 % when colestipol and **DYNATOR** were co-administered.

Cholestyramine*:*

No data is available.

Digoxin:

Co-administration of multiple doses of **DYNATOR** and digoxin increased steady-state plasma digoxin concentrations by approximately 20 %. Patients taking digoxin should be monitored appropriately.

Oral contraceptives:

Co-administration of **DYNATOR** and an oral contraceptive increased AUC values of norethindrone and ethinyl estradiol approximately 30 % and 20 %, respectively. These increases should be considered when selecting an oral contraceptive for a woman taking **DYNATOR.**

HUMAN REPRODUCTION:

DYNATOR is contraindicated in pregnancy and in women of childbearing potential not using adequate contraceptive measures. An interval of one month should be allowed from stopping **DYNATOR** treatment to conception in the event of planning a pregnancy (see **CONTRAINDICATIONS**).

Adequate protection is essential to prevent pregnancy during **DYNATOR** treatment (see **CONTRAINDICATIONS**).

Maternal treatment with **DYNATOR** may reduce the foetal levels of mevalonate which is a precursor of cholesterol biosynthesis.

DYNATOR is contraindicated in breastfeeding mothers.

DOSAGE AND DIRECTIONS FOR USE

A standard cholesterol-lowering diet should be implemented for patients before receiving **DYNATOR** and patients should continue on this diet during treatment with **DYNATOR**.

The usual oral starting dose is 10 mg once a day at any time of the day with or without food. The goal of therapy will determine the individualised dose for each patient according to the baseline LDL-

C levels, and patient response. Adjustment of dosage should only be made following measurement of lipid concentrations after an interval of 4 weeks or more. The maximum recommended dose will depend on the indication (see below).

Primary non-familial hypercholesterolaemia and combined (mixed) hyperlipidaemia:

Adults:

The majority of patients are controlled with 10 mg **DYNATOR** once a day. A therapeutic response is evident within 2 weeks, and the maximum response is usually achieved within 4 weeks.

Heterozygous familial hypercholesterolaemia:

Adults:

A starting dose with **DYNATOR** 10 mg daily. Doses should be individualised for each patient and adjusted every 4 weeks up to 40 mg daily.

Children (10 – 17 years of age):

Patients should be started with **DYNATOR** 10 mg daily. The maximum recommended dose is 20 mg/day.

Homozygous familial hypercholesterolaemia:

Adults:

In a compassionate-use, controlled study of 29 patients with homozygous familial hypercholesterolaemia, most patients responded to a dose of 80 mg of atorvastatin with a mean reduction in LDL-C of 20 % (range 7 % - 53 %), although in some patients an increase in LDL-C occurred.

Prevention of primary and secondary cardiovascular events:

The usual initial dose is 10 mg to 20 mg of **DYNATOR** once daily.

Dosage in patients with renal insufficiency:

No adjustment of dose is required in patients with renal disease as there is no influence on the

plasma concentrations or the lipid effects of **DYNATOR**.

Dosage in patients with hepatic dysfunction:

The therapeutic response to **DYNATOR** is unaffected in patients with moderate to severe hepatic dysfunction; but plasma concentration levels of atorvastatin are greatly increased. The plasma concentrations of atorvastatin are markedly increased in patients with chronic alcoholic liver disease, with the C_{max} and AUC are each 4-fold greater in patients with Child-Pugh A disease. The C_{max} and AUC are approximately 16-fold and 11-fold increased, respectively, in patients with Child-Pugh B disease. In patients who consume substantial quantities of alcohol and/or have a history of liver disease caution should be exercised with the dosage (see **CONTRAINDICATIONS** and **WARNINGS AND SPECIAL PRECAUTIONS**).

SIDE EFFECTS:

System Organ Class	Frequency	Side effects
Infections and infestations	*Frequent* *Frequency unknown*	Infection, nasopharyngitis Urinary tract infection
Blood and the lymphatic system disorders	*Frequency unknown*	Thrombocytopenia, lymphadenopathy, anaemia
Immune system disorders	*Less frequent*	Allergic reactions (including anaphylaxis)
Endocrine disorders	*Less frequent*	Pancreatitis
Metabolism and nutrition disorders	*Less frequent*	Hyperglycaemia, hypoglycaemia,

		weight gain, anorexia, increased appetite
Psychiatric disorders	*Frequent* *Less frequent* *Frequency unknown*	Insomnia Nightmares Depression, emotional lability, somnolence, amnesia, reversible cognitive impairment
Nervous system disorders	*Frequent* *Less frequent* *Frequency unknown*	Headache Dysgeusia Dizziness, facial paralysis, hypoaesthesia, incoordination, migraine, paraesthesia, peripheral neuropathy, syncope, taste loss, taste perversion, torticollis
Eye disorders	*Less frequent* *Frequency unknown*	Blurred vision Amblyopia, dry eyes, glaucoma, eye haemorrhage, refraction disorder,

		visual disturbance
Ear and labyrinth disorders	*Less frequent* *Frequency unknown*	Tinnitus Deafness
Cardiac disorders	*Frequency unknown*	Angina pectoris, dysrhythmia, palpitations, chest pain
Vascular disorders	*Frequency unknown*	Phlebitis, postural hypotension, vasodilation, flushing, vasculitis
Respiratory, thoracic and mediastinal disorders	*Frequent* *Frequency unknown*	Sinusitis, pharyngolaryngeal pain, epistaxis Asthma, bronchitis, dyspnoea, rhinitis, pharyngitis, pneumonitis, interstitial lung disease
Gastrointestinal disorders	*Less frequent* *Frequency unknown*	Diarrhoea, abdominal pain, dyspepsia, constipation, flatulence Oesophagitis, gastritis, gastroenteritis,

		melaena, colitis, nausea, vomiting, tenesmus, upper and lower abdominal pain, eructation, dysphagia, dry mouth, glositis
Hepato-biliary disorders	*Frequent* *Less frequent*	Liver function test abnormal Hepatitis, cholestatic jaundice, increase in transaminases, hepatic failure, alanine aminotransferase increased
Skin and subcutaneous tissue disorders	*Less frequent* *Frequency unknown*	Rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, bullous rashes Alopecia, pruritus, urticaria, cheilitis, contact dermatitis, dry skin, ecchymosis, eczema, petechiae,

		seborrhea, angioneurotic oedema, acne, photosensitivity
Musculoskeletal, connective tissue and bone disorders	*Less frequent* *Frequency Unknown*	Myalgia, myopathy, rhabdomyolysis, arthralgia, back pain, pain in extremity, muscle spasms, joint swelling tendonopathy, sometimes complicated by rupture, neck pain, muscle fatigue Increase in creatine phosphokinase, tendinous contracture, bursitis, gout, hypertonia, leg cramps, myasthenia, myositis, neck rigidity, tenosynovitis, hyperkinesia, immune-mediated necrotising myopathy, arthritis

Renal and urinary disorders	*Frequency Unknown*	Albuminuria, cystitis, dysuria, haematuria, kidney calculus, nephritis, nocturia, urinary incontinence, urinary retention, urinary urgency
Reproductive system and breast disorders	*Less frequent* *Frequency Unknown*	Gynecomastia Impotence, breast enlargement, epididymitis, fibrocystic breasts, metrorrhagia
General disorders and administrative site conditions	*Less frequent* *Frequency Unknown*	Asthenia, flu syndrome, fatigue Peripheral oedema, malaise, fever, taste loss, taste perversion
Investigations	*Less frequent*	White blood cells urine positive, flu syndrome
Injury and poisoning	*Frequency Unknown*	Tendon rupture, accidental injury

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

There is no specific treatment for **DYNATOR** overdosage. The patient should be treated symptomatically, and supportive measures instituted as required, in the event of an overdose. Haemodialysis is not expected to significantly enhance **DYNATOR** clearance due to extensive

medicine binding to plasma proteins.

IDENTIFICATION:

DYNATOR 10 mg: Cylindrical, biconvex, coated white tablet, scored on one side and with the code, AT1 on the other side.

DYNATOR 20 mg: Cylindrical, biconvex, coated white tablet, scored on one side and with the code, AT2 on the other side.

DYNATOR 40 mg: Cylindrical, biconvex, coated white tablet, scored on one side and with the code, AT4 on the other side.

DYNATOR 80 mg: Oblong, biconvex, coated white tablets, scored on one side and with the code, AT 8 on the other.

PRESENTATION:

DYNATOR tablets are packed into silver, hard aluminium / aluminium blister strips of 3 x 10 tablets inside an outer cardboard box.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from light and moisture.

Keep the blisters in the outer container until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

DYNATOR 10 mg: A43/7.5/0167

DYNATOR 20 mg: A43/7.5/0168

DYNATOR 40 mg: A43/7.5/0169

DYNATOR 80 mg: A43/7.5/0170

Namibia

DYNATOR 10 mg: NAM NS2 13/7.5/0111

DYNATOR 20 mg: NAM NS2 13/7.5/0112

DYNATOR 40 mg: NAM NS2 13/7.5/0113

DYNATOR 80 mg: NAM NS2 13/7.5/0114

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pharma Dynamics (Pty) Ltd

1st Floor Grapevine House, Steenberg Office Park

Silverwood Close

Westlake

Cape Town

7945

South Africa

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION:

Date of registration: 07 December 2012

Date of latest approval by MCC: 02 June 2017