SCHEDULING STATUS: S4

PROPRIETARY NAME (AND DOSAGE FORM):

CIPLA SIMVASTATIN 10 (Tablets)
CIPLA SIMVASTATIN 20 (Tablets)
CIPLA SIMVASTATIN 40 (Tablets)
CIPLA SIMVASTATIN 80 (Tablets)

COMPOSITION:

CIPLA SIMVASTATIN 10: Each film-coated tablet contains 10 mg simvastatin. Inactive ingredients include ascorbic acid, butylated hydroxy-anisole, citric acid monohydrate, hydroxypropyl cellulose, hypromellose, iron oxide black, iron oxide red, iron oxide yellow, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinised starch, talc and titanium dioxide.

CIPLA SIMVASTATIN 20: Each film-coated tablet contains 20 mg simvastatin. Inactive ingredients include ascorbic acid, butylated hydroxy-anisole, citric acid monohydrate, hydroxypropyl cellulose, hypromellose, iron oxide black, iron oxide red, iron oxide yellow, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinised starch, talc and titanium dioxide.

CIPLA SIMVASTATIN 40: Each film-coated tablet contains 40 mg simvastatin. Inactive ingredients include ascorbic acid, butylated hydroxyl-anisole, citric acid monohydrate, hydroxypropyl cellulose, hypromellose, iron oxide red, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinised starch, talc and titanium dioxide.

CIPLA SIMVASTATIN 80: Each film-coated tablet contains 80 mg simvastatin. Inactive ingredients include ascorbic acid, butylated hydroxyl-anisole, citric acid monohydrate, hydroxypropyl cellulose, hypromellose, iron oxide red, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinised starch, talc and titanium dioxide.

Contains lactose.

Sugar-free.

PHARMACOLOGICAL CLASSIFICATION:
A 7.5 Serum-cholesterol reducers.

PHARMACOLOGICAL ACTION:
Simvastatin, a cholesterol-lowering agent, is a synthetic derivative of a fermentation product of Aspergillus terreus. Simvastatin is an inactive lactone, and is hydrolysed to its active form, the corresponding beta-hydroxyacid, after oral ingestion. The beta-hydroxy acid, a principal metabolite, inhibits 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyses the conversion of HMG-CoA to mevalonate, which is an early and rate-limiting step in the biosynthesis of cholesterol. Simvastatin, due to the inhibition of this enzyme, therefore reduces total plasma cholesterol, low-density lipoprotein (LDL)- and very low-density lipoprotein (VLDL)-cholesterol concentrations. Simvastatin also reduces apolipoprotein B, variably reduces plasma triglycerides and moderately increases high-density lipoprotein (HDL)-cholesterol.

Pharmacokinetics:
There is extensive first-pass extraction by the liver, with oral bioavailability of the active medicine or metabolites being less than 5 %. More than 95 % of simvastatin and its beta-hydroxy metabolite are bound to plasma proteins. Following an oral dose, peak plasma concentrations of simvastatin are seen in 1 to 2 hours. Simvastatin is excreted primarily via the liver, and less than 13 % of its metabolites are excreted in the urine.

INDICATIONS:
HYPERCHOLESTEROLAEMIA:
CIPLA SIMVASTATIN is indicated, in combination with diet, to decrease elevated serum total cholesterol and LDL-cholesterol in patients with:
- Primary hypercholesterolaemia,
- Heterozygous familial hypercholesterolaemia, or
- Mixed hyperlipidaemia,

when response to diet or other nonpharmacological measures alone is not adequate.

CORONARY HEART DISEASE:
CIPLA SIMVASTATIN is indicated in patients with coronary heart disease and hypercholesterolaemia unresponsive to diet, to:
- Reduce the risk of non-fatal myocardial infarction,
- Reduce the risk of total mortality, by reducing coronary death,
- Slow the progression of coronary atherosclerosis, and
- Reduce the risk of undergoing myocardial revascularisation procedures (percutaneous transluminal coronary angioplasty and coronary artery bypass grafting).

CONTRA-INDICATIONS:
Hypersensitivity to simvastatin, other HMG-CoA reductase inhibitors, or any of the ingredients.
Acute or chronic liver disease.
Unexplained persistent elevations of serum transaminases.
Pregnancy and lactation (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).
Porphyria: Safety has not been established.

WARNINGS AND SPECIAL PRECAUTIONS:
CIPLA SIMVASTATIN should not be used in female patients of child-bearing potential as the active metabolite is foetotoxic and teratogenic in rats.
As the safety and efficacy of simvastatin has not been established in paediatric patients, it is not recommended in this population.

CIPLA SIMVASTATIN should be used with caution in patients who:
- Consume substantial amounts of alcohol and/or who have a history of liver disease.
- May be predisposed to developing renal failure secondary to rhabdomyolysis, such as in those with severe acute infection, hypotension, severe metabolic, endocrine or electrolyte disorders, uncontrolled seizures, major surgery or trauma. There is an increased risk of developing renal failure if rhabdomyolysis occurs.
- Have severe renal impairment.

Hepatic Effects:
Liver function tests, including serum transaminase determinations are recommended prior to initiation of **CIPLA SIMVASTATIN** therapy and periodically until one year after the last elevation in dose. **CIPLA SIMVASTATIN** should be discontinued if the rise in transaminase levels is persistent and/or increases to three times or more the upper limit of normal (ULN).

Myopathy:
Reducing the risk of myopathy:
1. General measures:
Patients starting therapy with **CIPLA SIMVASTATIN** should be advised of the risk of myopathy and should promptly report unexplained muscle pain, weakness or tenderness. Unexplained muscle symptoms in a patient and a creatine kinase (CK) level of more than 10 times the upper limit of normal (ULN), indicates myopathy. If myopathy is diagnosed or suspected, **CIPLA SIMVASTATIN** should be discontinued.

2. Measures to reduce the risk of myopathy caused by medicine interactions:
The benefits and risks of using **CIPLA SIMVASTATIN** together with fibrates, lipid-lowering doses of niacin or immunosuppressants should be carefully considered, and in these instances the dose of simvastatin should generally not exceed 10 mg/day. Concomitant administration with cyclosporin, itraconazole, ketoconazole, erythromycin, clarithromycin, HIV-protease inhibitors and nefazodone, is not recommended.
CIPLA SIMVASTATIN should be temporarily discontinued in patients who are also receiving cyclosporin, if systemic azole derivative antifungal therapy is required.
Lactose:
CIPLA SIMVASTATIN contains lactose. Patients with rare hereditary problems or a history of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take **CIPLA SIMVASTATIN**.

INTERACTIONS:
Myopathy caused by medicine interactions:
Concomitant administration of medicines that inhibit cytochrome P-450 isoenzyme CYP3A4 may result in high plasma levels of **CIPLA SIMVASTATIN**, thus increasing the risk of myopathy, and is not recommended. Medicines that inhibit cytochrome P-450 isoenzyme CYP3A4 include: cyclosporin, itraconazole, ketoconazole, erythromycin, clarithromycin, HIV-protease inhibitors and nefazodone.
The risk of myopathy is increased when other medicines that cause myopathy, such as fibrates and niacin, are given with **CIPLA SIMVASTATIN**. A maximum dose of 10 mg simvastatin daily is recommended in patients taking cyclosporin, fibrates or lipid-lowering doses of niacin (nicotinic acid).

Digoxin:
CIPLA SIMVASTATIN may cause increases in digoxin levels.

Coumarin derivatives (e.g. warfarin):
A possible increase in the anticoagulant effect of the coumarin anticoagulants may occur. Patients taking a coumarin anticoagulant should have their INR determined before starting **CIPLA SIMVASTATIN** therapy. The INR should be monitored frequently enough in the early stages of therapy until stabilised. Once the INR has been stabilised, it can then be monitored at the usual intervals recommended for patients on coumarin anticoagulants. When there is a dose adjustment of **CIPLA SIMVASTATIN**, this procedure should be repeated.

Bile acid sequestrants:
CIPLA SIMVASTATIN should be taken 1 hour before or 4 hours after cholestyramine. Concurrent use may decrease the bioavailability of **CIPLA SIMVASTATIN**.

PREGNANCY AND LACTATION:
Safety in pregnancy and lactation has not been established.
CIPLA SIMVASTATIN should not be used in female patients of child-bearing potential, as its active metabolite is foetotoxic and teratogenic in rats.

DOSAGE AND DIRECTIONS FOR USE:
The patient must follow a cholesterol-lowering diet before initiation of, and while on **CIPLA SIMVASTATIN** therapy.

HYPERCHOLESTEROLAEMIA:
Adults: Initial dose: 10 mg daily as a single dose in the evening.
The dose of **CIPLA SIMVASTATIN** should be reduced if LDL-cholesterol levels fall below 1,94 mmol/l, or total plasma cholesterol levels fall below 3,6 mmol/l.

CORONARY HEART DISEASE:
Adults: Initial dose: 20 mg/day as a single dose in the evening.

Dosage Adjustments:
If required, the dose should be adjusted at intervals of not less than 4 weeks, up to a maximum of 80 mg daily as a single dose in the evening.
CIPLA SIMVASTATIN can be taken with meals or on an empty stomach.

DOSAGE IN RENAL INSUFFICIENCY:
CIPLA SIMVASTATIN does not undergo significant renal excretion, therefore, modification of dose should not be necessary in patients with mild to moderate renal insufficiency. In patients with severe renal insufficiency, **CIPLA SIMVASTATIN** therapy should be closely monitored and doses above 10 mg/day should be implemented with caution.

CONCOMITANT THERAPY:
CIPLA SIMVASTATIN is effective on its own or in combination with bile acid sequestrants, but when these medicines are prescribed concomitantly, **CIPLA SIMVASTATIN** should be administered 1 hour before or 4 hours after cholestyramine (see **"INTERACTIONS"**). A maximum daily dose of 10 mg simvastatin is recommended in patients taking cyclosporin, fibrates or niacin concomitantly (see **"INTERACTIONS"**).

SIDE-EFFECTS:
Blood and lymphatic system disorders:
Frequent: Anaemia, neutropenia.

Metabolism and nutrition disorders:
Less frequent: Mass gain has been reported.

Nervous system disorders:
Less frequent: Headache, dizziness, fatigue, asthenia, paraesthesia, peripheral neuropathy.

Gastrointestinal disorders:
Frequent: Constipation, diarrhoea, nausea, vomiting, flatulence, dyspepsia, abdominal pain, cramps, and pancreatitis.

Skin, appendages and subcutaneous tissue disorders:
Frequent: Skin rash, alopecia.

Musculoskeletal disorders:
Frequent: Myalgia, muscle cramps.
Less frequent: Myopathy, myositis, rhabdomyolysis presenting as muscle pain with elevated creatine phosphokinase and myoglobinuria leading to renal failure.

Hypersensitivity reactions:
Less frequent: Reactions may include angioedema, lupus-like syndrome, polymyalgia rheumatica, vasculitis, thrombocytopenia, increased erythrocyte sedimentation rate, eosinophilia, arthritis, arthralgia, urticaria, photosensitivity, fever, flushing, malaise, and dyspnoea.

LABORATORY TEST FINDINGS
Marked and persistent increases of serum transaminases and elevated alkaline phosphatase and gamma-glutamyl transpeptidase have been reported. These liver function test abnormalities have generally been mild and have been of a transient nature. There have also been reports of increases in serum creatine kinase (CK) levels, derived from skeletal muscle (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
(See **"SIDE-EFFECTS** and **WARNINGS AND SPECIAL PRECAUTIONS"**).
Liver function should be monitored and general measures adopted.
Treatment is symptomatic and supportive.

IDENTIFICATION:
CIPLA SIMVASTATIN 10: Light pink coloured, oval, biconvex, intact film-coated tablets debossed with 'SVN 10' on one side and plain on the other side.
CIPLA SIMVASTATIN 20: Tan coloured, oval, biconvex, intact film-coated tablets debossed with 'SVN 20' on one side and plain on the other side.
CIPLA SIMVASTATIN 40: Pink coloured, oval, biconvex, intact film-coated tablets debossed with 'SVN 40' on one side and scored on the other.
CIPLA SIMVASTATIN 80: Pink coloured, capsule shaped, biconvex, intact film-coated tablets debossed with 'SVN 80' on one side and scored on the other.

PRESENTATION:
White, opaque PVC and aluminium foil blister strips of 10 tablets packed in 30's or blister strips of 14 tablets packed in 28's.

STORAGE INSTRUCTIONS:
Store in a dry place at or below 25°C. Protect from light. Keep the blisters in the outer carton until required for use.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:
CIPLA SIMVASTATIN 10 : A40/7.5/0397
CIPLA SIMVASTATIN 20 : A40/7.5/0398
CIPLA SIMVASTATIN 40 : A38/7.5/0370
CIPLA SIMVASTATIN 80 : A38/7.5/0371

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:
CIPLA MEDPRO (PTY) LTD.
Building 9, Parc du Cap,
Mispel Street, Bellville, 7530, RSA.

DATE OF PUBLICATION OF THIS PACKAGE INSERT:
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Namibia: NS2

Cipla Simvastatin 10 :	10/7.5/0195
Cipla Simvastatin 20 :	10/7.5/0194
Cipla Simvastatin 40 :	06/7.5/0295
Cipla Simvastatin 80 :	06/7.5/0296

SKEDULERINGSTATUS: S4

EIENDOMSNAAM (EN DOSEERVORM):

CIPLA SIMVASTATIN 10 (Tablette)
CIPLA SIMVASTATIN 20 (Tablette)
CIPLA SIMVASTATIN 40 (Tablette)
CIPLA SIMVASTATIN 80 (Tablette)

SAMESTELLING:

CIPLA SIMVASTATIN 10: Elke filmbedekte tablet bevat 10 mg simvastatien. Onaktiewe bestanddele sluit askorbiensuur, butielhidroksie-anisool, sitroensuurmonohidraat, hidroksipropielsellulose, hipromellose, swart ysteroksied, rooi ysteroksied, geel ysteroksied, laktosemonohidraat, magnesiumstearaat, mikrokristallyne sellulose, pregelatiniseerde stysel, talk en titaandioksied in.

CIPLA SIMVASTATIN 20: Elke filmbedekte tablet bevat 20 mg simvastatien. Onaktiewe bestanddele sluit askorbiensuur, butielhidroksie-anisool, sitroensuurmonohidraat, hidroksipropielsellulose, hipromellose, swart ysteroksied, rooi ysteroksied, geel ysteroksied, laktosemonohidraat, magnesiumstearaat, mikrokristallyne sellulose, pregelatiniseerde stysel, talk en titaandioksied in.

CIPLA SIMVASTATIN 40: Elke filmbedekte tablet bevat 40 mg simvastatien. Onaktiewe bestanddele sluit askorbiensuur, butielhidroksie-anisool, sitroensuurmonohidraat, hidroksipropielsellulose, hipromellose, rooi ysteroksied, laktosemonohidraat, magnesiumstearaat, mikrokristallyne sellulose, pregelatiniseerde stysel, talk en titaandioksied in.

CIPLA SIMVASTATIN 80: Elke filmbedekte tablet bevat 80 mg simvastatien. Onaktiewe bestanddele sluit askorbiensuur, butielhidroksie-anisool, sitroensuurmonohidraat, hidroksipropielsellulose, hipromellose, rooi ysteroksied, laktosemonohidraat, magnesiumstearaat, mikrokristallyne sellulose, pregelatiniseerde stysel, talk en titaandioksied in.

Bevat laktose.

Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:
A 7.5 Anti-serumcholesterolmiddels.

FARMAKOLOGIESE WERKING:
Simvastatien, 'n cholesterol-verlagende middel, is 'n sintetiese derivaat van 'n fermentasieproduk van Aspergillus terreus. Simvastatien is 'n onaktiewe laktoon, en word gehidroliseer na sy aktiewe vorm, die ooreenstemmende beta-hidroksiesuur, na orale inname. Die beta-hidroksiesuur, 'n hoofmetaboliet, inhibeer 3-hidroksie-3-metielglutariel-koënsiem A (HMG-CoA) reduktase. Hierdie ensiem kataliseer die omsetting van HMG-CoA na mevalonaat, wat 'n vroeë en tempo-beperkende stap in die biosintese van cholesterol is. Simvastatien, weens die inhibering van hierdie ensiem, verlaag dus totale plasma cholesterol, lae-digtheid lipoproteïen (LDL)- en baie lae-digtheid lipoproteïen (VLDL)-cholesterol konsentrasies. Simvastatien verlaag ook apolipoproteïen B, verminder plasma-trigliseriede tot 'n mindere of 'n meerdere mate en veroorsaak matige verhogings in hoë-digtheid lipoproteïen (HDL)-cholesterol.

Farmakokinetika:
Daar is ekstensiewe eerstedeurgangs verwydering deur die lewer, met orale biobeskikbaarheid van die aktiewe middel of metaboliete minder as 5 %. Meer as 95 % van simvastatien en die beta-hidroksiemetaboliet is gebonde aan plasmaproteïene. Na 'n orale dosis word piek plasmakonsentrasies van simvastatien gesien binne 1 tot 2 uur. Simvastatien word primêr uitgeskei deur die lewer, en minder as 13 % van die metaboliete word uitgeskei in die uriene.

INDIKASIES:
HIPERCHOLESTEROLEMIE:
CIPLA SIMVASTATIN word aangedui, in kombinasie met dieet, om verhoogde serum totale cholesterol en LDL-cholesterol te verlaag in pasiënte met:
- Primêre hipercholesterolemie,
- Heterosigotiese familiële hipercholesterolemie, of
- Gemengde hiperlipidemie, wanneer die respons op 'n dieet of ander nie-farmakologiese maatreëls alleen nie voldoende is nie.

KORONÊRE HARTSIEKTE:
CIPLA SIMVASTATIN word aangedui vir pasiënte met koronêre hartsiekte en hipercholesterolemie wat nie op dieet reageer nie, om:
- Die risiko vir nie-noodlottige miokardiale infarksie te verminder,
- Die risiko van totale mortaliteit te verlaag deur koronêre sterftes te verminder,
- Die progressie van koronêre vat aterosklerose te vertraag, en
- Die risiko om miokardiale revaskularisasie prosedures te ondergaan, te verminder (perkutane transluminale koronêre angioplastie en koronêre vat omleidingsoorplanting).

KONTRA-INDIKASIES:
Hipersensitiwiteit vir simvastatien, ander HMG-CoA reduktase inhibeerders, of enige van die bestanddele.
Akute of chroniese lewersiekte.
Onverklaarbare volgehoue stygings van serumtransaminases.
Swangerskap en laktasie (sien **"WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS"**).
Porfirie: Veiligheid is nog nie vasgestel nie.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
CIPLA SIMVASTATIN behoort nie gebruik te word in vroulike pasiënte wat swanger kan raak nie, aangesien die aktiewe metaboliet fetotoksies en teratogenies in rotte is.
Aangesien die veiligheid en effektiwiteit van simvastatien nog nie vasgestel is in pediatriese pasiënte nie, word dit nie aanbeveel in hierdie bevolking nie.
CIPLA SIMVASTATIN behoort met omsigtigheid gebruik te word in pasiënte wat:
- Groot hoeveelhede alkohol gebruik en/of wat 'n geskiedenis van lewersiekte het.
- Kan predisponeer tot die ontwikkeling van nierversaking sekondêr tot rabdomiolise, soos dié met 'n erge akute infeksie, hipotensie, erge metaboliese, endokriene of elektrolietstoornisse, ongekontroleerde konvulsies, groot chirurgie of trauma. Daar is 'n verhoogde risiko om nierversaking te ontwikkel indien rabdomiolise voorkom.
- Erge nierinkorting het.

Hepatiese Effekte:
Lewerfunksietoetse, insluitende serumtransaminase bepalings word aanbeveel voor die aanvang van **CIPLA SIMVASTATIN** behandeling en periodiek daarna tot een jaar na die laaste toename in dosis. **CIPLA SIMVASTATIN** behoort gestaak te word indien die styging in transaminasevlakke volgehoue is en/of styg tot drie maal of meer die boonste grens van normaal (BGN).

Miopatie:
Vermindering van die risiko vir miopatie:
1. Algemene maatreëls:
Pasiënte wat behandeling met **CIPLA SIMVASTATIN** begin behoort ingelig te word van die risiko vir miopatie en behoort dadelik onverklaarbare spierpyne, -swakheid of -teerheid aan te meld. Onverklaarbare spiersimptome in 'n pasiënt en 'n kreatienkinase (KK) vlak van meer as 10 maal die boonste grens van normaal (BGN), dui op miopatie. Indien miopatie gediagnoseer word of vermoed word, behoort **CIPLA SIMVASTATIN** gestaak te word.

2. Maatreëls om die risiko vir miopatie veroorsaak deur middelinteraksies te verminder:
Die voordele en risiko deur **CIPLA SIMVASTATIN** te gebruik saam met fibrate, lipied-verlagende dosisse van niasien of immuunonderdrukkende middels behoort versigtig oorweeg te word, en in hierdie gevalle behoort die dosis van simvastatin oor die algemeen nie 10 mg/dag te oorskry nie. Gesamentlike toediening met siklosporien, itrakonasool, ketokonasool, eritromisien, klaritromisien, HIV-protease-inhibeerders en nefasodoon, word nie aanbeveel nie.
CIPLA SIMVASTATIN behoort tydelik gestaak te word in pasiënte wat ook siklosporien ontvang, as sistemiese asooldervaat antiswam behandeling benodig word.
Laktose:
CIPLA SIMVASTATIN bevat laktose. Die gebruik daarvan is nie aanbeveel in pasiënte met galaktose onverdraagsaamheid, die Lapp laktase tekort of glukose of galaktose wanabsorpsiesindroom nie.

INTERAKSIES:
Miopatie veroorsaak deur middelinteraksies:
Gesamentlike toediening van middels wat sitochroom P-450 isoensiem CYP3A4 inhibeer kan hoë plasmavlakke van **CIPLA SIMVASTATIN** tot gevolg hê, dus die risiko van miopatie verhoog, en word nie aanbeveel nie. Middels wat sitochroom P-450 isoensiem CYP3A4 inhibeer, sluit in: siklosporien, itrakonasool, ketokonasool, eritromisien, klaritromisien, HIV-protease- inhibeerders en nefasodoon.
Die risiko vir miopatie is verhoog wanneer ander middels wat miopatie veroorsaak, soos fibrate en niasien, saam met **CIPLA SIMVASTATIN** gegee word. 'n Maksimum dosis van 10 mg simvastatien daagliks word aanbeveel in pasiënte wat siklosporien, fibrate of lipied-verlagende dosisse van niasien (nikotiensuur) neem.

Digoksien:
CIPLA SIMVASTATIN kan stygings in digoksienvlakke veroorsaak.

Kumarienderivate (bv. warfarin):
'n Moontlike verhoging in die antistoleffek van die kumarien antistolmiddels kan voorkom. Pasiënte wat 'n kumarien antistolmiddel neem behoort hulle INR te laat vasstel alvorens daar met **CIPLA SIMVASTATIN** behandeling begin word. Die INR behoort gereeld genoeg gemonitor te word in die vroeë stadiums van behandeling totdat dit stabiliseer. Sodra die INR gestabiliseer is, kan dit gemonitor word met die gewone tussenposes soos aanbeveel vir pasiënte op kumarien antistolmiddels. Wanneer daar 'n dosisaanpassing van **CIPLA SIMVASTATIN** is, moet hierdie prosedure herhaal word.

Galsuursekwestreerders:
CIPLA SIMVASTATIN behoort 1 uur voor of 4 uur na cholestiramien geneem te word. Gelyktydige gebruik kan die biobeskikbaarheid van **CIPLA SIMVASTATIN** verminder.

SWANGERSKAP EN LAKTASIE:
Die veiligheid in swangerskap en laktasie is nog nie vasgestel nie.
CIPLA SIMVASTATIN behoort nie gebruik te word in vroulike pasiënte wat swanger kan raak nie, aangesien die aktiewe metaboliet fetotoksies en teratogenies in rotte is.

DOSIS EN GEBRUIKSAANWYSINGS:
Die pasiënt moet 'n cholesterolverlagende dieet volg voor daar begin word met **CIPLA SIMVASTATIN** behandeling en moet hierdie dieet volhou tydens behandeling.

HIPERCHOLESTEROLEMIE:
Volwassenes: Aanvanklike dosis: 10 mg daagliks as 'n enkeldosis saans.
Die dosis van **CIPLA SIMVASTATIN** moet verminder word indien LDL-cholesterolvlakke daal benede 1,94 mmol/l, of totale plasma cholesterolvlakke daal onder 3,6 mmol/l.

KORONÊRE HARTSIEKTE:
Volwassenes: Aanvanklike dosis: 20 mg/dag as 'n enkeldosis saans.

Dosisaanpassings:
Indien nodig, behoort die dosis aangepas te word met tussenposes van nie minder as 4 weke nie, tot 'n maksimum van 80 mg daagliks as 'n enkeldosis saans.
CIPLA SIMVASTATIN kan met maaltye of op 'n leë maag geneem word.

DOSIS IN NIERINKORTING:
CIPLA SIMVASTATIN ondergaan nie betekenisvolle nieruitskeiding nie, aanpassing van die dosis behoort dus nie nodig te wees in pasiënte met geringe tot matige nierinkorting nie. In pasiënte met erge nierinkorting behoort **CIPLA SIMVASTATIN** behandeling noukeurig gemonitor te word en dosisse bo 10 mg/dag moet met omsigtigheid aangewend word.

GELYKTYDIGE TERAPIE:
CIPLA SIMVASTATIN is effektief op sy eie of in kombinasie met galsuursekwestreerders, maar indien hierdie middels saam voorgeskryf word, behoort **CIPLA SIMVASTATIN** 1 uur voor of 4 uur na cholestiramien toegedien te word (sien **"INTERAKSIES"**). 'n Maksimum daaglikse dosis van 10 mg simvastatien word aanbeveel in pasiënte wat siklosporien, fibrate of niasien gelyktydig neem (sien **"INTERAKSIES"**).

NEWE-EFFEKTE:
Bloed en limfatiese sisteem afwykings:
Dikwels: Anemie, neutropenie.

Metabolisme en voedingsafwykings:
Minder dikwels: Gewigstoename is gemeld.

Senustelsel afwykings:
Minder dikwels: Hoofpyn, duiseligheid, moegheid, swakheid, parastesieë, perifere neuropatie.

Gastro-intestinale afwykings:
Dikwels: Hardlywigheid, diarree, naarheid, braking, winderigheid, dispepsie, buikpyn, krampe, en pankreatitis.

Vel, velaanhangsel en subkutane weefsel afwykings:
Dikwels: Veluitslag, haarverlies.

Muskuloskeletale afwykings:
Dikwels: Mialgie, spierkrampe.
Minder dikwels: Miopatie, miositis, rabdomiolise wat voordoen as spierpyn met 'n styging in kreatienfosfokinase en mioglobinurie wat nierversaking tot gevolg kan hê.

Hipersensitiwiteitsreaksies:
Minder dikwels: Reaksies kan angioedeem, lupus-agtige sindroom, polimialgie reumatika, vaskulitis, trombositopenie, verhoogde bloedbesinking tempo, eosinofilie, artritis, artralgie, urtikarieë, fotosensitiwiteit, koors, gloede, malaise, en dispnee insluit.

LABORATORIUMTOETSBEVINDINGS:
Uitgesproke en volgehoue stygings van serumtransaminases en verhoogde alkaliese fosfatase en gamma-glutamieltranspeptidase is gemeld. Hierdie lewerfunksie toetsabnormaliteite was oor die algemeen gering en van 'n verbygaande aard. Toenames in serum kreatienkinase (KK) vlakke, afkomstig van skeletale spier, is ook gemeld (sien **"WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS"**).

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
(Sien **"NEWE-EFFEKTE** en **WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS"**).
Lewerfunksie behoort gemonitor te word en algemene maatreëls toegepas te word.
Behandeling is simptomaties en ondersteunend.

IDENTIFIKASIE:
CIPLA SIMVASTATIN 10: Ligte pienkgekleurde, ovaal, bikonvekse, intakte filmbedekte tablette met 'SVN 10' gegraveer aan die een kant en glad aan die ander kant.
CIPLA SIMVASTATIN 20: Taangekleurde, ovaal, bikonvekse, intakte filmbedekte tablette met 'SVN 20' gegraveer aan die een kant en glad aan die ander kant.
CIPLA SIMVASTATIN 40: Pienkgekleurde, ovaal, bikonvekse, intakte filmbedekte tablette met 'SVN 40' gegraveer aan die een kant en gekeep aan die ander kant.
CIPLA SIMVASTATIN 80: Pienkgekleurde, kapsulevormige, bikonvekse, intakte filmbedekte tablette met 'SVN 80' gegraveer aan die een kant en gekeep aan die ander kant.

AANBIEDING:
Wit, ondeursigtige PVC en aluminiumfoelie stulpverpakte stroke van 10 tablette verpak in 30's of stulpverpakte stroke van 14 tablette verpak in 28's.

BERGINGSINSTRUKSIES:
Berg in 'n droë plek teen of benede 25 °C. Beskerm teen lig. Behou die stulpverpakte stroke in die kartonhouer totdat dit benodig word vir gebruik.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:
CIPLA SIMVASTATIN 10 : A40/7.5/0397
CIPLA SIMVASTATIN 20 : A40/7.5/0398
CIPLA SIMVASTATIN 40 : A38/7.5/0370
CIPLA SIMVASTATIN 80 : A38/7.5/0371

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKATE VAN REGISTRASIE:
CIPLA MEDPRO (EDMS) BPK.
Gebou 9, Parc du Cap,
Mispelstraat, Bellville, 7530, RSA.

DATUM VAN PUBLIKASIE VAN DIE VOUBILJET:
Januarie 2008

Namibia: NS2
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Cipla Simvastatin 20 : 10/7.5/0194
Cipla Simvastatin 40 : 06/7.5/0295
Cipla Simvastatin 80 : 06/7.5/0296