SCHEDULING STATUS S4

1 NAME OF THE MEDICINE
ROLTESIM 10 (Film-coated tablets)
ROLTESIM 20 (Film-coated tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film-coated **SIMVASTATIN 10** tablet contains 10 mg simvastatin.
Each film-coated **SIMVASTATIN 20** tablet contains 20 mg simvastatin.

Antioxidants: Ascorbic acid:	2,427 % m/m
Citric acid monohydrate:	1,213 % m/m
Butylated hydroxyanisole:	0,0485 % m/m
Contains sugar:	
ROLTESIM 10:	Lactose monohydrate 67,7 mg
ROLTESIM 20:	Lactose monohydrate 135,4 mg.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
ROLTESIM 10: Light pink coloured, oval, biconvex film coated tablets debossed with 'SVN 10' on one side and plain on the other side.
ROLTESIM 20: Tan coloured, oval, biconvex film coated tablets debossed with 'SVN 20' on one side and plain on the other side.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Hypercholesterolaemia:
ROLTESIM is indicated, in combination with diet, to decrease elevated serum total cholesterol and LDL-cholesterol in patients:
- Primary hypercholesterolaemia,
- Heterozygous familial hypercholesterolaemia, or
- Mixed hyperlipidaemia, when response to diet or other nonpharmacological measures alone is not adequate.

Coronary heart disease:
ROLTESIM 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).

4.2 Posology and method of administration
Posology
The patient must follow a cholesterol-lowering diet before initiation of, and while on **ROLTESIM** therapy.
Hypercholesterolaemia:
Adults: Initial dose: 10 mg daily as a single dose in the evening.
The dose of **ROLTESIM** 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 no less than 4 per week, up to a maximum of 80 mg daily as a single dose in the evening.

Special populations
Renal insufficiency:
ROLTESIM 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, **ROLTESIM** therapy should be closely monitored and doses above 10 mg/day should be implemented with caution.

Concomitant therapy:
ROLTESIM if effective on its own or in combination with bile acid sequestrants, but when these medicines are prescribed concomitantly, **ROLTESIM** should be administered 1 hour before or 4 hours after cholestyramine (see section 4.5). A maximum daily dose of 10 mg simvastatin is recommended in patients taking ciclosporin, fibrates or niacin concomitantly (see section 4.5).

Paediatric population
The safety and efficacy of **ROLTESIM** have not been established in paediatric patients (see section 4.4).

Method of administration
The tablet should be swallowed whole.
ROLTESIM can be taken with meals or on an empty stomach.

4.3 Contraindications
- Hypersensitivity to simvastatin, other HMG-CoA reductase inhibitors, or any of the ingredients (see section 6.1).
- Acute or chronic liver disease.
- Unexplained persistent elevations of serum transaminases.
- Pregnancy and lactation (see section 4.4).
- Porphyria: Safety has not been established.

4.4 Special warnings and precautions for use
ROLTESIM should not be used in female patients of child-bearing potential as the active metabolite is foetotoxic and teratogenic in rats.
ROLTESIM 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.

Hepatic effects:
Liver function tests, including serum transaminase determinations are recommended prior to initiation of **ROLTESIM** therapy and periodically until one year after the last elevation in dose. **ROLTESIM** 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 **ROLTESIM** 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, **ROLTESIM** should be discontinued.
2. *Measures to reduce the risk of myopathy caused by medicine interactions:* The benefits and risks of using **ROLTESIM** together with fibrates, lipid-lowering doses of niacin or immunosuppressants should be carefully considered, and in these instances the dose of **ROLTESIM** should generally not exceed 10 mg/day. Concomitant administration with ciclosporin, itraconazole, ketoconazole, erythromycin, clarithromycin, HIV-protease inhibitors and nefazodone, is not recommended.

ROLTESIM should be temporarily discontinued in patients who are also receiving ciclosporin if systemic azole derivative antifungal therapy is required.

Paediatric population
As the safety and efficacy of simvastatin has not been established in paediatric patients, it is not recommended in this population.

4.5 Interaction with other medicines and other forms of interaction
Myopathy caused by medicine interactions:
Concomitant administration of medicines that inhibit cytochrome P-450 isoenzyme CYP3A4 may result in high plasma levels of **ROLTESIM**, thus increasing the risk of myopathy, and is not recommended. Medicines that inhibit cytochrome P-450 isoenzyme CYP3A4, include ciclosporin, fibrates or lipid-lowering doses of niacin (nicotinic acid).

Digoxin:
ROLTESIM 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 **ROLTESIM** 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 **ROLTESIM,** this procedure should be repeated.

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

4.6 Fertility, pregnancy and lactation
Pregnancy
Safety in pregnancy and lactation has not been established.
ROLTESIM should not be used in female patients of child-bearing potential, as its active metabolite is foetotoxic and teratogenic in rats.

4.7 Effects on ability to drive and use machines
ROLTESIM can cause dizziness and fatigue that can influence their ability to drive and use machines. Patients should be advised to not drive or use machines until they know how **ROLTESIM** affects them (see section 4.8).

4.8 Undesirable effects
a. Summary of the safety profile
Not applicable.

b. Tabulated summary of adverse reactions

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Frequent	Anaemia, neutropenia.
Immune system disorders	Less frequent	Reactions may include angioedema, lupus-like syndrome, polymyalgia rheumatic, vasculitis, thrombocytopenia, increased erythrocyte sedimentation rate, eosinophilia, arthritis, arthralgia, urticarial, photosensitivity, fever, flushing, malaise and dyspnoea.
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 and subcutaneous tissue disorders	Frequent	Skin rash, alopecia.
Musculoskeletal and connective tissue disorders	Frequent	Myalgia, muscle cramps
	Less Frequent	Myopathy, myositis, rhabdomyolysis presenting as muscle pain with elevated creatine phosphokinase and myoglobinuria leading to renal failure.

c. Description of selected adverse reactions
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 section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8
The applicant can be reached at the following contact number: 010 045 2500.

4.9 Overdose
Liver function should be monitored, and general measures adopted. Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacological classification: A 7.5 Serum-cholesterol reducers.
Pharmacotherapeutic group: HMG CoA reductase inhibitors. ATC code: C10AA01
Mechanism of 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-hydoxyacid, a principal metabolite, inhibits 3-hydroxy-3methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyses the conversion of HMG-CoA to mevalonate, which is an early and rate-limiting step in 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.

5.2 Pharmacokinetic properties
Absorption
There is extensive first-pass extraction by the liver, with oral bioavailability of the active medicine or metabolites being less than 5 %.
Distribution
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.
Elimination
Simvastatin is excreted primarily via the liver, and less than 13 % of its metabolites are excreted in the urine.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Tablet core:
Ascorbic acid
Butylated hydroxy anisole
Citric acid monohydrate
Lactose monohydrate
Magnesium stearate
Microcrystalline cellulose
Pregelatinized starch
Film-coating:
SIMVASTATIN 10 STRIDES: Opadry® Pink 20A54692
SIMVASTATIN 20 STRIDES: Opadry® Brown 20A56767
Coating material contains hydroxypropyl cellulose, hypromellose, titanium dioxide, talc, iron oxide red, iron oxide black, iron oxide yellow.

6.2 Incompatibilities
Not applicable

6.3 Shelf life
ROLTESIM 10: 3 years
ROLTESIM 20: 2 years
Store at or below 25 °C.

6.4 Special precautions for storage
Protect from light. Keep the blisters in the outer carton until required for use. KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container
Blister pack comprises of clear, transparent, non-toxic, well thermoformable PVC/PVDC film with backing of aluminium foil with VMCH (Hard tempered, aluminium foil, coated with heat sealable lacquer against PVC). Suitable number of blister strips will be placed in an outer cardboard carton. Blister strips of 10's, 14's or 15's are packed into unit cartons for pack sizes of 28's or 30's. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Not applicable.

7 HOLDER OF CERTIFICATE OF REGISTRATION
Strides Pharma SA (Pty) Ltd.
106 16th Road, Building 2, Midrand, 1685.

8 REGISTRATION NUMBER(S)
ROLTESIM 10: A40/7.5/0399
ROLTESIM 20: A40/7.5/0400

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
13 April 2007

10 DATE OF REVISION OF THE TEXT
14 May 2021

SKEDULERINGSTATUS S4

1 NAAM VAN DIE GENEESMIDDEL
ROLTESIM 10 (Filmbedekte tablette)
ROLTESIM 20 (Filmbedekte tablette)

2 KWALITATIEWE EN KWANTITATIEWE KOMPOSISIE
Elke filmbedekte **ROLTESIM 10** tablet bevat 10 mg simvastatien.
Elke filmbedekte **ROLTESIM 20** tablet bevat 20 mg simvastatien.

Antioksidante: Askorbiensuur:	2,427 % m/m
Sitroensuurmonohidraat:	1,213 % m/m
Butielhidroksianisool:	0,0485 % m/m
Bevat suiker:	
ROLTESIM 10:	Laktosemonohidraat 67,7 mg
ROLTESIM 20:	Laktosemonohidraat 135,4 mg.

Sien afdeling 6.1 vir 'n volledige lys hulpstowwe

3 FARMASEUTIESE VORM
ROLTESIM10: Ligte pienkgekleurde, ovaal, bikonvekse filmbedekte tablette met 'SVN 10' gegraveer aan die een kant en glad aan die ander kant.
ROLTESIM 20: Bruingekleurde, ovale, bikonvekse, filmbedekte tablette met 'SVN 20' gegraveer aan die een kant en glad aan die ander kant.

4 KLINIESE BESONDERHEDE
4.1 Terapeutiese indikasies
Hipercholesterolemie:
ROLTESIM 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:
ROLTESIM 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).

4.2 Posologie en metode van toediening
Posologie
Die pasiënt moet 'n cholesterolverlagende dieet volg voor aanvangs van, en tydens **ROLTESIM** behandeling.
Hipercholesterolemie:
Volwassenes: Aanvanklike dosis: 10 mg daagliks as 'n enkeldosis saans.
Die dosis van **ROLTESIM** 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: 10 mg daagliks 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.

Spesiale populasies
Nierinkorting:
ROLTESIM 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 **ROLTESIM** behandeling noukeurig gemonitor te word en dosisse bo 10 mg/dag moet met omsigtigheid aangewend word.

Gelyktydige terapie:
ROLTESIM is effektief op sy eie of in kombinasie met galsuursekwestreerders, maar indien hierdie middels saam voorgeskryf word, behoort **ROLTESIM** 1 uur voor of 4 uur na cholestiramien toegedien te word (sien afdeling 4.5). 'n Maksimum daaglikse dosis van 10 mg simvastatien word aanbeveel in pasiënte wat siklosporien, fibrate of niasien gelyktydig neem (sien afdeling 4.5).

Pediatriese populasie
Die veiligheid en effektiwiteit van **ROLTESIM** is nie by pediatriese pasiënte vasgestel nie (sien afdeling 4.4).

Metode van toediening
Die tablet moet heel geneem word.
ROLTESIM kan met maaltye of op 'n leë maag geneem word.

4.3 Kontraindikasies
- Hipersensitiwiteit vir simvastatien, ander HMG-CoA reduktase inhibeerders, of enige van die bestanddele (sien afdeling 6.1).
- Akute of chroniese lewersiekte.
- Onverklaarbare volgehoue stygings van serumtransaminases.
- Swangerskap en laktasie (sien afdeling 4.4).
- Porfirie: Veiligheid is nog nie vasgestel nie.

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik
ROLTESIM behoort nie gebruik te word in vroulike pasiënte wat swanger kan raak nie, aangesien die aktiewe metaboliet fetotoksies en teratogenies in rotte is.
ROLTESIM 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, ernstige chirurgie of trauma. Daar is 'n verhoogde risiko om nierversaking te ontwikkel indien rabdomiolise voorkom.

Hepatiese effekte:
Lewerfunksietoetse, insluitende serumtransaminase bepalings word aanbeveel voor die aanvang van **ROLTESIM** behandeling en periodiek daarna tot een jaar na die laaste toename in dosis. **ROLTESIM** 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 **ROLTESIM** 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 **ROLTESIM** gestaak te word.
2. *Maatreëls om die risiko vir miopatie veroorsaak deur middelinteraksies te verminder*: Die voordele en risiko deur **ROLTESIM** 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 **ROLTESIM** 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.

ROLTESIM behoort tydelik gestaak te word in pasiënte wat ook siklosporien ontvang, indien sistemiese asoolderivaat anti-swam behandeling benodig word.

Pediatriese populasie
Omdat die veiligheid en effektiwiteit van simvastatien nie by pediatriese pasiënte vasgestel is nie, is dit nie vir die populasie aanbeveel nie.

4.5 Interaksie met ander medisyne en ander vorme van interaksie
Miopatie wat deur medisyne interaksies veroorsaak word:
Gesamentlike toediening van middels wat sitochroom P-450 isoensiem CYP3A4 inhibeer kan hoë plasmavlakke van **ROLTESIM** tot gevolg hê, dus die risiko van miopatie verhoog, en word nie aanbeveel nie. Middels van sitochroom P-450 isoensiem CYP3A4 inhibeer, sluit in: siklosporien, fibrate of lipied-verlangende dosisse van niasien (nikotiensuur) neem.

Digoksien:
ROLTESIM kan stygings in digoksienvlakke veroorsaak.

Kumariënderivate (bv. warfarien):
'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 **ROLTESIM** 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.
As daar 'n dosisaanpassing van **ROLTESIM** is, moet hierdie prosedure herhaal word.

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

4.6 Vrugbaarheid, swangerskap en laktasie
Swangerskap
Die veiligheid in swangerskap en laktasie is nog nie vasgestel nie.
ROLTESIM behoort nie gebruik te word in vroulike pasiënte wat swanger kan raak nie, aangesien die aktiewe metaboliet fetotoksies en teratogenies in rotte is.

4.7 Effekte op die vermoë om te bestuur en masjiene te gebruik
ROLTESIM kan duiseligheid en moegheid veroorsaak wat die vermoë om te bestuur en masjiene te gebruik kan beïnvloed. Pasiënte moet aangeraai word om nie te bestuur of masjiene te gebruik voordat hulle weet hoe **ROLTESIM** hulle beïnvloed nie (sien afdeling 4.8).

4.8 Ongewenste effekte
a. Opsomming van die veiligheidsprofiel
Nie van toepassing nie.

b. Getabelleerde opsomming van nadelige reaksies

MedDRA-stelsel orgaanklas	Frekwensie	Nadelige reaksies
Bloed en limfatiese sisteem afwykings	Dikwels	Anemie, neutropenie.
Immuunstelselafwykings	Minder dikwels	Reaksies kan angioedeem, lupus-agtige sindroom, polimialgie rumatiek, vaskulitis, trombositopenie, verhoogde bloedbeskinking tempo, eosinofilie, artritis, artralgie, urtikarieë, fotosensitiwiteit, koors, gloede, malaise en dispnee insluit.
Metabolisme en voedingsafwykings	Minder dikwels	Gewigstoename is gemeld.
Senustelsel afwykings	Minder dikwels	Hoofpyn, duiseligheid, moegheid, 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.

c. Beskrywing van geselekteerde nadelige reaksies
Laboratoriumtoetsbevindings:
Uitgesproke en volgehoue stygings van serumtransaminases en verhoogde alkaliese fosfatase en gamma-glutamieltranspeptidase is gemeld. Hierdie lewerfunksie fetusabnormaliteite was oor die algemeen gering en van 'n verbygaande aard. Toenames in serum kreatienkinase (KK) vlakke, afkomstig van skeletspiere, is ook gemeld (sien afdeling 4.4).

Aanmelding van vermoedelike nadelige reaksies
Dit is belangrik om newe-effekte wat vermoed word na die medisyne gemagtig is, te rapporteer. Dit laat die voortgesette monitering van die voordeel/risiko-balans van die medisyne toe. Gesondheidsverskaffers word gevra om enige vermoedens van newe-effekte aan te meld by SAHPRA deur die "6.04 Adverse Drug Reaction Reporting Form", wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8 Die applikant kan bereik word by die volgende kontaknommer: 010 045 2500.

4.9 Oordosering
Lewerfunksie behoort gemonitor te word en algemene maatreëls toegepas te word. Behandeling is simptomaties en ondersteunend.

5 FARMAKOLOGIESE EIENSKAPPE
5.1 Farmakodinamiese eienskappe
Farmakologiese klassifikasie: A 7.5 Serumcholesterol verlagers.
Farmakoterapeutiese groep: HMG CoA reduktase inhibeerders. ATC kode: C10AA01
Meganisme van aksie
Simvastatien, 'n cholesterol-verlagende middel, is 'n sintetiese derivaat van 'n fermentasieproduk van *Aspergillus terreus.* Simvastatien is 'n inaktiewe 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-beperkte 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.

5.2 Farmakokinetiese eienskappe
Absorpsie
Daar is ekstensiewe eerstedeurgangs verwydering deur die lewer, met orale biobeskikbaarheid van die aktiewe middel of metaboliete minder as 5 %.
Verspreiding
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.
Eliminasie
Simvastatien word primêr uitgeskei deur die lewer, en minder as 13 % van die metaboliete word uitgeskei in die uriene.

6 FARMASEUTIESE BESONDERHEDE
6.1 Lys van hulpstowwe
Tabletkern:
Askorbiensuur
Butielhidroksianisool
Sitroensuurmonohidraat
Laktosemonohidraat
Magnesiumstearaat
Mikrokristallyne sellulose
Voorafgelatiniseerde stysel
Filmbedekking:
SIMVASTATIN 10 STRIDES: Opadry® Pienk 20A54692
SIMVASTATIN 20 STRIDES Opadry® Bruin 20A56767
Bedekkingsmateriaal bevat hidroksipropielsellulose, hipromellose, titaandioksied, talk, ysteroksied rooi, ysteroksied swart, ysteroksied geel.

6.2 Onverenigbaarhede
Nie van toepassing

6.3 Raklewe
ROLTESIM 10: 3 Jaar.
ROLTESIM 20: 2 Jaar
Bêre by of onder 25 ° C.

6.4 Spesiale voorsorgmaatreëls vir berging
Beskerm teen lig. Behou die stulpverpakte stroke in die buitekarton totdat dit benodig word. HOU BUITE DIE BEREIK VAN KINDERS.

6.5 Aard en inhoud van die houer
Stulpverpakking bestaan uit deursigtige, nie-giftige, goed termo-vormbare PVC/PVDC film met aluminiumfolie rugkant met VMCH (Hard getemper, aluminiumfolie, bedek met hitte seëlbare lak teen PVC). Geskikte aantal stulpstroke sal in 'n buitekarton geplaas word. Stulpstroke van 10's, 14's of 15's word in verpakkingseenhede verpak van verpakkingsgroottes van 28's of 30's. Nie alle verpakkingsgroottes word moontlik bemark nie.

6.6 Spesiale voorsorgmaatreëls vir wegdoening
Nie van toepassing nie.

7 HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE
Strides Pharma SA (Edms) Bpk
16de Weg 106, Gebou 2, Midrand, 1685

8 REGISTRASIE NOMMER(S)
ROLTESIM 10: A40/7.5/0399
ROLTESIM 20: A40/7.5/0400

9 DATUM VAN EERSTE MAGTIGING/HERNUWING VAN DIE MAGTIGING
13 April 2007

10 DATUM VAN HERSIENING VAN DIE TEKS
14 May 2021

Strides

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