PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

REMCEPT XL 8 mg (Prolonged release hard capsules)

REMCEPT XL 16 mg (Prolonged release hard capsules)

REMCEPT XL 24 mg (Prolonged release hard capsules)

COMPOSITION:

Active ingredient:

REMCEPT XL prolonged release capsules contain galantamine hydrobromide, equivalent to respectively 8 mg, 16 mg and 24 mg galantamine base.

Excipients:

Ethyl cellulose, erythrocin FD&C Red 3, gelatine, hypromellose, Indigo carmine FD&C Blue 2, magnesium stearate, microcrystalline cellulose, red iron oxide (E172), titanium dioxide (E171), yellow iron oxide (E172).

Sugar free.

PHARMACOLOGICAL CLASSIFICATION:

A 5.3 Cholinomimetics

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Galantamine, a tertiary alkaloid is a selective, competitive and reversible inhibitor of acetylcholinesterase. In addition, galantamine enhances the intrinsic action of acetylcholine on nicotinic receptors, probably through binding to an allosteric site of the receptor. As a consequence, an increased activity in the cholinergic system associated with improved cognitive function can be achieved in patients with dementia of the Alzheimer type.

Pharmacokinetic properties:

Absorption:

After oral intake of a single dose 8 mg galantamine (as tablets) , a peak plasma concentration of 43 ± 13 ng/ml, is reached after 1,2 hours, with a mean AUC_{∞} of 427 ± 102 ng.h/ml. The absolute oral bioavailability of galantamine is 88,5 %. Oral intake of galantamine with food slows down its rate of absorption (C_{max} reduced by about 25 %), but does not affect the extent to which it is absorbed (AUC). The prolonged release capsules are bioequivalent to the twice daily immediate release tablets with respect to AUC_{24h} and C_{min}. The C_{max} value is reached after 4,4 hours, was about 24 % lower than that of tablet. Food has no effect on AUC and C_{max} of the prolonged release capsules and slightly increases t_{max} by about 12 %.

Distribution:

The plasma protein binding of galantamine is low: 17,7 ± 0,8 %. In whole blood, galantamine is mainly distributed to blood cells (52,7 %) and plasma water (39,0 %), whereas the fraction of galantamine bound to plasma proteins is only 8,4 %. The blood-to-plasma concentration ratio of galantamine is 1,17.

Metabolism:

Major metabolic pathways were N-oxidation, N-demethylation, O-demethylation, glucuronidation and epimerisation. *In vitro* studies confirmed that cytochrome P450 2D6 and 3A4 were the major cytochrome P450 isoenzymes involved in the metabolism of galantamine. O-demethylation was far more important in extensive metabolisers of CYP2D6. The levels of excretion of total radioactivity in the urine and faeces were not different between poor and extensive metabolisers.

Norgalantamine was detectable in plasma from patients after multiple dosing, but did not represent more than 10 % of the galantamine levels.

Elimination:

The elimination of galantamine is bi-exponential, with a terminal half-life in the order of 7 – 8 h. Galantamine has a plasma clearance of approximately 200 ml/min with a volume of distribution (average Vd_{ss} of 175 l). Seven days after a single oral dose of 4 mg ^{3}H-galantamine, 90 – 97 % of the radioactivity was recovered in the urine and 2,2 – 6,3 % in the faeces. After I.V. and oral administration, 18 – 22 % of the dose was excreted as unchanged galantamine in the urine in 24 hours, with a renal clearance of about 65 ml/min, which represents 20 – 25 % of the total plasma clearance.

Dose-linearity:

After repeated oral dosing of 12 mg galantamine b.i.d. (as tablets), mean trough and peak plasma concentrations fluctuated between 30 and 90 ng/ml. The pharmacokinetics of galantamine is linear in the dose range 8 mg – 24 mg once daily

Special populations:

Elderly:

Data from clinical trials in patients indicate that the plasma concentrations of galantamine with Alzheimer's disease are 30 – 40 % higher than in healthy young subjects primarily due to the advanced age and reduced kidney function.

Hepatic impairment:

The pharmacokinetics of galantamine in subjects with mild hepatic impairment (Child Pugh score of 5 – 6) was comparable to those in healthy subjects. In patients with moderate hepatic impairment (Child Pugh score of 7 – 9), the AUC and half-life of galantamine were increased by about 30 %.

The disposition of galantamine was studied in young subjects with varying degrees of renal function.

Renal Impairment:

Elimination of galantamine decreased with decreasing creatinine clearance. Plasma concentrations of galantamine increased in subjects with impaired renal function by 38 % in moderate (Cl_{CR} = 52 – 104 ml/min) and by 67 % in severe impairment (Cl_{CR} = 9 – 51 ml/min), compared to age and weight-matched healthy subjects (Cl_{CR} > = 121 ml/min). A population pharmacokinetic analysis and simulations indicate that no dose-adjustments are needed in Alzheimer patients with renal impairment provided that the Cl_{CR} is at least 9 ml/min, as the galantamine renal clearance is lower in the Alzheimer population.

INDICATIONS:

REMCEPT XL is indicated for the symptomatic treatment of mild to moderately severe dementia of the Alzheimer type. Efficacy data beyond 6 months has not been established (see **WARNINGS AND SPECIAL PRECAUTIONS**).

CONTRAINDICATIONS:

- **REMCEPT XL** should not be administered to patients with a known hypersensitivity to galantamine hydrobromide or to any excipients used in the formulations.
- Severe impaired hepatic function (Child Pugh score > 9)
- Severe impaired renal function (Cl_{CR} = 9 – 51 ml/min)
- The use of **REMCEPT XL** is not recommended in patients with urinary outflow obstruction or recovering from bladder surgery.

WARNINGS AND SPECIAL PRECAUTIONS:

Types of dementia:

REMCEPT XL is indicated for a patient with mild to moderately severe dementia of the Alzheimer type. The benefit of **REMCEPT XL** in patients with other types of dementia or other types of memory impairment has not been demonstrated. A diagnosis of Alzheimer's dementia should be made according to current guidelines by an experienced medical practitioner. Therapy with **REMCEPT XL** should occur under the supervision of a medical practitioner and should only be initiated if a caregiver is available who will regularly monitor medicine intake by the patient.

Mild Cognitive Impairment (MCI):

REMCEPT XL is not indicated for individuals with mild cognitive impairment (MCI), i.e. those who demonstrate isolated memory impairment greater than expected for their age and education, but do not meet criteria for Alzheimer’s disease.

Serious skin reactions:

Serious skin reactions (Stevens Johnson syndrome and acute generalised exanthematous pustulosis) have been reported in patients receiving **REMCEPT XL** (see **SIDE EFFECTS**). It is recommended that patients be informed about the signs of serious skin reactions, and that use of **REMCEPT XL** be discontinued at the first appearance of skin rash.

Weight monitoring:
Treatment with cholinesterase inhibitors, including **REMCEPT XL**, has been associated with weight loss in these patients. During therapy, patient's weight should be monitored.

Conditions requiring caution:
REMCEPT XL should be given with caution in the following conditions:

Cardiac disorders:
Cholinomimetics may have vagotonic effects on heart rate (e.g. bradycardia). The potential for this action may be particularly important to patients with ”sick sinus syndrome” or other supraventricular cardiac conduction disturbances or in those who use medicines that significantly reduce heart rate concomitantly, such as digoxin and beta-blockers or for patients with an uncorrected electrolyte disturbance (e.g. hyperkalaemia, hypokalaemia).
Caution should therefore be exercised when administering **REMCEPT XL** to patients with cardiovascular diseases, e.g. immediate post-myocardial infarction period, new-onset atrial fibrillation, second degree heart block or greater, unstable angina pectoris or congestive heart failure, especially NYHA group III – IV.

Gastrointestinal disorders:
Patients at increased risk of developing peptic ulcers, e.g. those with a history of ulcer disease or those predisposed to these conditions, including those receiving concurrent non-steroidal anti-inflammatory drugs (NSAIDS), should be monitored for symptoms. The use of **REMCEPT XL** is not recommended in patients with gastro-intestinal obstruction or recovering from gastro-intestinal surgery.

Nervous system disorders:
Seizures have been reported with **REMCEPT XL** (see section **SIDE EFFECTS**). Seizure activity may also be a manifestation of Alzheimer's disease. In some cases an increase in cholinergic tone may worsen Parkinsonian symptoms.

Respiratory, thoracic and mediastinal disorders:
Cholinomimetics should be prescribed with care for patients with a history of severe asthma or obstructive pulmonary disease or active pulmonary infections (e.g. pneumonia).

Renal and urinary disorders:

The use of **REMCEPT XL** is not recommended in patients with urinary outflow obstruction or recovering from bladder surgery (see **CONTRAINDICATIONS**).

Surgical and medical procedures:

REMCEPT XL, as a cholinomimetic, is likely to exaggerate succinylcholine-type muscle relaxation during anaesthesia, especially in cases of pseudocholinesterase deficiency.

Effects on ability to drive or use machinery:

Alzheimer's disease may cause gradual impairment of driving performance or compromise the ability to use machinery. **REMCEPT XL** may cause dizziness and somnolence, which could affect the ability to drive or use machines, especially during the first weeks after initiation of treatment.

INTERACTIONS:

Pharmacodynamic interactions:

Because of its mechanism of action, **REMCEPT XL** should not be given concomitantly with other cholinomimetics (such as ambenonium, donepezil, neostigmine, pyridostigmine, rivastigmine or systemically administered pilocarpine). **REMCEPT XL** has the potential to antagonise the effect of anticholinergic medicine. Should anticholinergic medicine such as atropine be abruptly stopped there is a potential risk that **REMCEPT XL** effects could be exacerbated. As expected with cholinomimetics, a pharmacodynamic interaction is possible with medicines that significantly reduce the heart rate such as digoxin, beta-blockers, certain calcium-channel blocking medicines and amiodarone (see **WARNINGS AND SPECIAL PRECAUTIONS**).

Caution should be taken with medicines that have potential to cause *torsade's de pointes*. In such cases an ECG should be considered.

REMCEPT XL, as a cholinomimetic, is likely to exaggerate succinylcholine-type muscle relaxation during anaesthesia, especially in cases of pseudocholinesterase deficiency.

Pharmacokinetic interactions:

Multiple metabolic pathways and renal excretion are involved in the elimination of **REMCEPT XL**. The occurrence of significant interactions may be clinically relevant in individual cases.

Concomitant administration with food slows the absorption rate of **REMCEPT XL** but does not affect the extent of absorption. It is recommended that **REMCEPT XL** be taken with food in order to minimise cholinergic side effects.

Other medicines affecting the metabolism of galantamine:

Formal interaction studies showed an increase in **REMCEPT XL** bioavailability of about 40 % during co-administration of paroxetine (a potent CYP2D6 inhibitor) and of 30 % and 12 % during co-treatment with ketoconazole and erythromycin (both CYP3A4 inhibitors). Therefore, during initiation of treatment with potent inhibitors of CYP2D6 (e.g. quinidine, paroxetine or fluoxetine) or CYP3A4 (e.g. ketoconazole or ritonavir) patients may experience an increased incidence of cholinergic adverse

reactions, predominantly nausea and vomiting. Under these circumstances, based on tolerability, a reduction of the **REMCEPT XL** maintenance dose can be considered (see **DOSAGE AND DIRECTIONS FOR USE**).

Memantine, an N-methyl-D-aspartate (NMDA) receptor antagonist, at a dose of 10 mg once a day for 2 days followed by 10 mg twice a day for 12 days, had no effect on the pharmacokinetics of galantamine at steady state.

Effect of REMCEPT XL on the metabolism of other medicines

Therapeutic doses of galantamine as in **REMCEPT XL** 24 mg/day had no effect on the kinetics of digoxin, although pharmacodynamic interactions may occur (see also **Pharmacodynamic interactions**).

Therapeutic doses of galantamine as in **REMCEPT XL** 24 mg/day had no effect on the kinetics and prothrombin time (INR) of warfarin.

PREGNANCY AND LACTATION:

No studies are available on the use of **REMCEPT XL** in pregnant women. **REMCEPT XL** should not be used during pregnancy.

Animal studies have shown reproductive toxicity.

It is not known whether galantamine is excreted in human breast milk and there are no studies in lactating women.

Women on **REMCEPT XL** should not breastfeed their infants.

DOSAGE AND DIRECTIONS FOR USE:

Adults:

Administration:

REMCEPT XL prolonged release capsules should be administered once daily in the morning, preferably with food.

Starting dose:

The recommended starting dose is 8 mg/day for 4 weeks.

Maintenance dose:

- The initial maintenance dose is 16 mg/day and patients should be maintained on 16 mg/day for at least 4 weeks.
- An increase to the maintenance dose of 24 mg/day should be considered after appropriate assessment including evaluation of clinical benefit and tolerability.
- In individual patients not showing an increased response or not tolerating 24 mg/day, a dose reduction to 16 mg/day should be considered.
- Maintenance treatment can be continued for as long as therapeutic benefit for the patient exists. Therefore, the clinical benefit of **REMCEPT XL** should be reassessed on a regular

basis. Discontinuation should be considered when evidence of a therapeutic effect is no longer present.

- There is no rebound effect after abrupt discontinuation of treatment (e.g. in preparation for surgery).
-

Children:

Use of **REMCEPT XL** in children is not recommended. No data on the use of **REMCEPT XL** in paediatric patients are available.

Hepatic and renal impairment:

REMCEPT XL plasma levels may be increased in patients with moderate to severe hepatic or renal impairment.

In patients with moderately impaired hepatic function, based on pharmacokinetic modelling, dosing should begin with 8 mg every other day for at least one week, preferably taken in the morning. Thereafter, patients should proceed with 8 mg once daily for at least four weeks. In these patients total daily doses should not exceed 16 mg.

In patients with severe hepatic impairment (Child Pugh score greater than 9), the use of **REMCEPT XL** is contraindicated.

For patients with a creatinine clearance greater than 9 ml/min, no dosage adjustment is required.

In patients, with severe renal impairment (creatinine clearance less than 9 ml/min), the use of **REMCEPT XL** is contraindicated.

Concomitant treatment:

In patients treated with potent CYP2D6 or CYP3A4 inhibitors, dose reductions can be considered. (see **INTERACTIONS**).

Patients currently being treated with **REMCEPT XL** immediate release tablets can convert to **REMCEPT XL** prolonged release capsules by taking their last dose of **REMCEPT XL** immediate release tablets in the evening and starting **REMCEPT XL** prolonged release capsules once daily treatment the next morning. When converting from **REMCEPT XL** twice daily immediate release tablets to **REMCEPT XL** once daily prolonged release capsules, the same total daily dose should be administered.

SIDE EFFECTS:

System Organ Class	Frequency	Undesirable effects
Blood and the lymphatic system disorders	*Frequent* *Less frequent*	Anaemia Thrombocytopenia
Immune system disorders	*Less frequent*	Hypersensitivity
Metabolism and nutrition disorders	*Frequent* *Less frequent*	Decreased appetite, weight decrease Dehydration, hyperglycaemia, increased

		alkaline phosphate
Psychiatric disorders	*Frequent* *Less frequent*	Hallucination, depression, insomnia, anorexia, somnolence, agitation, confusion, anxiety Hallucination visual, hallucination auditory, paranoid reaction, increased libido, delirium, suicidal ideation, suicide
Nervous system disorder	*Frequent* *Less frequent*	Headache, somnolence, lethargy, tremor, dizziness, syncope Paraesthesia, dysgeusia, hypersomnia, seizures, vertigo, hypertonia, convulsions, involuntary muscle contractions, ataxia, hyperkinesia, apraxia, aphasia, leg cramps
Eye disorders	*Less frequent*	Blurred vision
Ear and labyrinth disorders	*Less frequent*	Tinnitus
Cardiac disorders	*Frequent* *Less frequent*	Bradycardia Supraventricular extrasystoles, first degree atrioventricular block, sinus bradycardia, palpitations, cardiac failure, myocardial ischaemia or infarction, atrial dysrhythmias, atrial fibrillation, supraventricular tachycardia's, QT prolonged, bundle branch block, T-wave inversion, ventricular tachycardia
Vascular disorders	*Frequent* *Less frequent*	Hypertension, peripheral oedema Hypotension, flushing, postural hypotension, dependent oedema, purpura, epistaxis
Gastrointestinal disorders	*Frequent* *Less frequent*	Nausea, vomiting, constipation, flatulence, abdominal pain, upper abdominal pain, diarrhoea, dyspepsia, abdominal discomfort Retching, gastritis, melaena, dysphagia, rectal haemorrhage, dry mouth, increased saliva, diverticulitis, gastroenteritis, hiccup, oesophageal perforation,
Hepatobiliary disorders	*Less frequent*	Hepatitis, elevated liver enzymes
Skin and subcutaneous	*Frequent*	Hyperhidrosis

tissue disorders	*Less frequent*	Stevens Johnson syndrome, acute generalised exanthematous pustulosis, erythema multiforme
Musculoskeletal, Connective tissue and bone disorders	*Frequent* *Less frequent*	Muscle spasms Muscle weakness
Renal and urinary disorders	*Frequent* *Less frequent*	Urinary tract infection, haematuria, urinary incontinence Micturition frequency, cystitis, urinary retention, nocturia, renal calculi
Respiratory, thoracic and mediastinal disorders	*Frequent*	Rhinitis, upper respiratory tract infection, bronchitis, coughing
General disorders and administrative site conditions	*Frequent*	Fatigue, syncope, asthenia, malaise, fall, injury, back pain, chest pain, fever
Investigations	*Frequent*	Hepatic enzyme increase

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms:

Signs and symptoms of significant overdosing of **REMCEPT XL** are predicted to be similar to those of overdosing of other cholinomimetics. These effects generally involve the central nervous system, the parasympathetic nervous system, and the neuromuscular junction. In addition to muscle weakness or fasciculation's, some or all of the signs of a cholinergic crisis may develop: severe nausea, vomiting, gastro-intestinal cramping, salivation, lacrimation, urination, defaecation, sweating, bradycardia, hypotension, collapse and convulsions. Increasing muscle weakness together with tracheal hypersecretions and bronchospasms, may lead to vital airway compromise.

There have been post-marketing reports of Torsade de Pointes, QT prolongation, bradycardia, ventricular tachycardia and loss of consciousness in association with inadvertent overdoses of **REMCEPT XL**.

Treatment:

General supportive measures should be used. In severe cases, anticholinergics such as atropine can be used as a general antidote for cholinomimetics. An initial dose of 0,5 to 1,0 mg I.V. is recommended, with subsequent doses based on the clinical response. Because strategies for the management of overdose are continually evolving, it is advisable to contact a poison control centre to determine the latest recommendations for the management of an overdose.

IDENTIFICATION:

REMCEPT XL 8 mg: Opaque white-white size 2 hard gelatine capsules containing one round biconvex tablet of 8 mg

REMCEPT XL 16 mg: Opaque, flesh-flesh size 2 hard gelatine capsules containing two round biconvex tablets of 8 mg

REMCEPT XL 24 mg: Opaque orange-orange size 2 hard gelatine capsules containing three round biconvex tablets of 8 mg

PRESENTATION:

Packs of 28's or 30's prolonged release hard capsules packed in glossy, transparent , PVC/PE/PVDC film and aluminium foil, shiny on the inside and dull (matte) on the outside blisters in a cardboard carton.

White opaque, round HDPE bottles with a white plastic child-resistant tamper-evident screw cap and an aperture for desiccant in packs of 100's prolonged release hard capsules in a cardboard carton.

STORAGE INSTRUCTIONS:

Store at or below 25 °C. Store in the original packaging. Keep blisters in the carton and capsules in the bottle until required for use. Keep the HDPE container tightly closed.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBERS:

REMCEPT XL 8 mg: 46/5.3/0998

REMCEPT Xl. 16 mg: 46/5.3/0999

REMCEPT XL 24 mg: 46/5.3/1000

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

Actavis Pharma (Pty) Ltd
Maxwell Office Park
Magwa Crescent West
Waterfall City
Midrand
2090

DATE OF PUBLICATION OF THE PACKAGE INSERT:

Date of registration: 29 September 2017

VOUBILJET

SKEDULERINGSTATUS:

S4

EIENDOMSNAAM EN DOSEERVORM:

REMCEPT XL 8 mg (Verlengde-vrystelling harde kapsules)

REMCEPT XL 16 mg (Verlengde-vrystelling harde kapsules)

REMCEPT XL 24 mg (Verlengde-vrystelling harde kapsules)

SAMESTELLING:

Aktiewe bestanddeel:

REMCEPT XL verlengde-vrystellingkapsules bevat galantamienhidrobromied, ekwivalent onderskeidelik aan 8 mg, 16 mg en 24 mg galantamienbasis.

Onaktiewe bestanddele:

Etielsellulose, eritrosien FD&C Rooi 3, gelatien, hipromellose, Indigo-karmosyn FD&C Blou 2, magnesiumstearaat, mikrokristallyne sellulose, rooi ysteroksied (E172), titaandioksied (E172), geel ysteroksied (E172).

Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:

A 5.3 Cholinomimetika

FARMAKOLOGIESE WERKING:

Farmakodinamiese eienskappe:

Galantamien, ‘n tersiêre alkaloïed, is ‘n selektiewe, mededingende en omkeerbare inhibeerder van asetielcholienesterase. Daarbenewens versterk galantamien die intrinsieke werking van asetielcholien op nikotieniese reseptore, waarskynlik deur binding aan ‘n allosteriese setel van die reseptor. Gevolglik kan ‘n verhoogde aktiwiteit in die cholinergiese sisteem geassosieer met verbeterde kognitiewe funksie bereik word by pasiënte met demensie van die Alzheimer-tipe.

Farmakokinetiese eienskappe:

***Absorpsie*:**

Na orale inname van ‘n enkele dosis 8 mg galantamien (as tablette), word ‘n piek plasmakonsentrasie van 43 ± 13 ng/ml na 1,2 uur bereik, met ‘n gemiddelde AOK_{∞} van 427 ± 102 ng.uur/ml. Die absolute orale biobeskikbaarheid van galantamien is 88,5 %. Orale inname van galantamien saam met voedsel vertraag die tempo van absorpsie daarvan (K_{maks} word met ongeveer 25 % verlaag), maar affekteer nie die mate waartoe dit geabsorbeer word nie (AOK). Die verlengde-vrystellingkapsules is bio-ekwivalent aan die twee-keer-daaglikse onmiddellike-vrystellingstablette met betrekking tot

AOK_{24uur} en K_{min}. Die K_{maks}-waarde word na 4,4 uur bereik, en is ongeveer 24 % laer as dié van die tablet. Voedsel het geen effek op AOK en K_{maks} van die verlengde-vrystellingkapsules nie en verhoog die t_{maks} effens met omtrent 12 %.

***Distribusie*:**
Die plasmaproteïenbinding van galantamien is laag: 17,7 ±0,8 %. In heel bloed word galantamien hoofsaaklik na die bloedselle (52,7 %) en plasmawater (39,0 %) versprei, terwyl die fraksie van galantamien wat aan plasmaproteïene gebind is slegs 8,4 % bedra. Die bloed-tot-plasmakonsentrasie-verhouding van galantamien is 1,17.

***Metabolisme*:**
Die hoof metaboliese kringlope was N-oksidasie, N-demetilering, O-demetilering, glukuronidasie en epimerisasie. *In vitro* studies het bevestig dat sitochroom P450 2D6 en 3A4, die hoof sitochroom P450-isoënsieme is wat by die metabolisme van galantamien betrokke is. O-demetilering was baie meer belangrik in ekstensiewe metaboliseerders van CYP2D6. Die vlak van uitskeiding van totale radioaktiwiteit in die urine en faeces was nie verskillend by swak of ekstensiewe metaboliseerders nie.
Norgalantamien was waarneembaar in plasma van pasiënte na veelvoudige dosering, maar dit het nie meer as 10 % van die galantamienvlakke verteenwoordig nie.

***Eliminasie*:**
Die eliminasie van galantamien is bi-eksponensiaal, met ‘n terminale halfleeftyd in die orde van 7-8 uur. Galantamien het ‘n plasmaopruiming van ongeveer 200 ml/min met ‘n volume van distribusie (gemiddeld Vd_{ss} van 175ℓ). Sewe dae na ‘n enkele orale dosis van 4 mg ^{3}H-galantamien, is 90-97 % van die radioaktiwiteit in die urine herwin en 2,2-6,3 % in die faeces.
Na I.V. en orale toediening, is 18-22 % van die dosis as onveranderde galantamien in die urine in 24 uur uitgeskei, met ‘n renale opruiming van ongeveer 65 ml/min, wat 20-25 % van die totale plasmaopruiming verteenwoordig.

***Dosis-lineariteit*:**
Na herhaalde orale dosering van 12 mg galantamien b.i.d. (as tablette), het gemiddelde trog- en piek-plasmakonsentrasies tussen 30 en 90 ng/ml gefluktueer.
Die farmakokinetika van galantamien is liniêre in die dosisreikwydte van 8 mg - 24 mg een keer daagliks.

***Spesiale bevolkings*:**
***Bejaardes*:**
Data van kliniese studies het aangedui dat by pasiënte met Alzheimer se siekte, die plasmakonsentrasies van galantamien 30-40 % hoër is as in gesonde jong proefpersone primêr as gevolg van die gevorderde ouderdom en verminderde nierfunksie.

***Hepatiese inkorting*:**
Die farmakokinetika van galantamien in proefpersone met ligte hepatiese inkorting (Child Pugh-telling van 5-6), was vergelykbaar aan dié in gesonde proefpersone. In pasiënte met matige hepatiese inkorting (Child Pugh-telling van 7-9), was die AOK en halfleeftyd van galantamien met ongeveer 30 % verhoog.

Die disposisie van galantamien is in jong proefpersone met wisselende grade van renale funksie bestudeer.

***Renale Inkorting*:**
Die eliminasie van galantamien het verminder met afnemende kreatinienopruiming. Plasmakonsentrasies van galantamien het toegeneem in proefpersone met ingekorte renale funksie met 38 % in matige (Cl_{CR} = 52 - 104 ml/min) en met 67 % in ernstige inkorting (Cl_{CR} = 9 - 51 ml/min), in vergelyking met ouderdom- en gewig-gepaarde, gesonde proefpersone (Cl_{CR} > 121 ml/min). ‘n Farmakokinetiese bevolkingsanalise en s.imulasies het aangedui dat geen dosisaanpassings by Alzheimer pasiënte met renale inkorting nodig is nie, mits die Cl_{CR} ten minste gelyk is aan 9 ml/min, omdat die renale opruiming van galantamien in die Alzheimer bevolking laer is.

INDIKASIES:
REMCEPT XL word aangedui vir die simptomatiese behandeling van ligte tot matig ernstige demensie van die Alzheimer-tipe. Doeltreffendheidsdata vir langer as 6 maande is nie vasgestel nie (sien **WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS**).

KONTRA-INDIKASIES:
REMCEPT XL behoort nie aan pasiënte met ‘n bekende hipersensitiwiteit teenoor galantamienhidrobromied of enige ander onaktiewe bestanddele wat in die formulerings gebruik word, toegedien te word nie.

- Ernstig ingekorte hepatiese funksie (Child Pugh-telling > 9)
- Ernstig ingekorte renale funksie (Cl_{CR} = 9 - 51 ml/min)
- Die gebruik van **REMCEPT XL** word nie by pasiënte met urinêre uitvloei-obstruksie of wat van blaaschirurgie herstel, aanbeveel nie.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
Tipes demensie:
REMCEPT XL word aangedui vir ‘n pasiënt met ligte tot matig ernstige demensie van die Alzheimer-tipe. Die voordeel van **REMCEPT XL** in pasiënte met ander soorte demensie of ander soorte geheue-inkorting is nie gedemonstreer nie. ‘n Diagnose van Alzheimer se demensie behoort volgens teenswoordige riglyne deur ‘n ervare medisyne praktisyn gemaak te word. Terapie met **REMCEPT XL**

behoort plaas te vind onder die toesig van ‘n mediese praktisyn en behoort alleenlik begin te word indien ‘n versorger beskikbaar is wat die inname van die medisyne deur die pasiënt gereeld sal moniteer.

Ligte Kognitiewe Inkorting (MCI):
REMCEPT XL word nie aangedui vir persone met ligte kognitiewe inkorting (MCI), d.i. dié wat geïsoleerde geheue-inkorting demonstreer wat die verwagte inkorting vir hul ouderdom en opvoeding oortref, maar nie aan die kriteria vir Alzheimer se siekte voldoen nie.

Ernstige velreaksies:
Ernstige velreaksies (Stevens-Johnson-sindroom en akute veralgemeende eksantemateuse pustulose) is aangemeld by pasiënte wat **REMCEPT XL** ontvang (sien **NEWE-EFFEKTE**). Daar word aanbeveel dat pasiënte ingelig word oor die tekens van ernstige velreaksies, en dat die gebruik van **REMCEPT XL** met die eerste verskyning van veluitslag gestaak moet word.

Monitering van gewig:
Behandeling met cholienesterase-inhibeerders, insluitend **REMCEPT XL**, is geassosieer met gewigsverlies in hierdie pasiënte. Gedurende terapie behoort die pasiënte se gewig gemoniteer te word.

Toestande wat omsigtigheid verg:
REMCEPT XL behoort met omsigtigheid gegee te word in die volgende toestande:

Kardiale versteurings:
Cholinomimetika mag vagotoniese effekte op die harttempo uitoefen (bv. bradikardie). Die potensiaal vir hierdie effek mag veral belangrik wees vir pasiënte met “sieksinussindroom” of ander supraventrikulêre kardiale geleidingsversteurings, of by dié wat medisyne gelyktydig gebruik wat die harttempo beduidend verminder, soos digoksien en betablokkeerders of vir pasiënte met ‘n ongekorrigeerde elektrolietversteuring (bv. hiperkalemie, hipokalemie). Omsigtigheid behoort dus uitgeoefen te word wanneer **REMCEPT XL** toegedien word aan pasiënte met kardiovaskulêre siektes, bv. onmiddellike post-miokardiale infarksie periode, nuwe-aanvang atriale fibrillasie, twee-graad hartblok of groter, onstabiele angina pectoris of kongestiewe hartversaking, veral NYHA groep III-IV.

Gastroïntestinale versteurings:
Pasiënte wat blootgestel is aan verhoogde risiko om peptiese ulkusse te ontwikkel, bv. dié met ‘n geskiedenis van ulkussiekte of dié wat gepredisponeer is tot hierdie toestande, insluitend dié wat gelyktydige nie-steroïedale anti-inflammatoriese middels (NSAIMs) ontvang, behoort vir simptome gemoniteer te word. Die gebruik van **REMCEPT XL** word nie by pasiënte met gastroïntestinale obstruksie of wat van gastroïntestinale chirurgie herstel, aanbeveel nie.

Senusisteemversteurings:
Aanvalle is met **REMCEPT XL** gerapporteer (sien afdeling oor **NEWE-EFFEKTE**). Aanvalaktiwiteit mag ook ‘n manifestasie van Alzheimer se siekte wees. In sommige gevalle mag ‘n verhoging in cholinergiese tonus Parkinsoniese simptome vererger.

Respiratoriese, torakale en mediastinale versteurings:

Cholinomimetika behoort met omsigtigheid voorgeskryf te word vir pasiënte met ‘n geskiedenis van ernstige asma of obstruktiewe pulmonale siekte of aktiewe pulmonale infeksies (bv. pneumonie).

Renale en urinêre versteurings:
Die gebruik van **REMCEPT XL** word nie by pasiënte met urinêre uitvloei-obstruksie of wat van blaaschirurgie herstel, aanbeveel nie (sien **KONTRA-INDIKASIES**).

Chirurgiese en mediese prosedures:
REMCEPT XL, as ‘n cholinomimetikum, sal waarskynlik suksinielcholien-tipe spierverslapping tydens narkose vererger, veral in gevalle van ‘n gebrek aan pseudocholienesterase.
Effekte op die vermoë om te bestuur of masjiene te gebruik:
Alzheimer se siekte mag geleidelike agteruitgang veroorsaak van bestuur-vaardigheid of die vermoë om masjiene te gebruik. **REMCEPT XL** mag duiseligheid en lomerigheid veroorsaak wat die vermoë om te bestuur of masjiene te gebruik kan affekteer, veral gedurende die eerste weke na instelling van behandeling.

INTERAKSIES:
Farmakodinamiese interaksies:
As gevolg van sy meganisme van werking, behoort **REMCEPT XL** nie saam met ander cholinomimetika (soos ambenonium, donepesiel, neostigmien, piridostigmien, rivastigmien of sistemies toegediende pilokarpien) gegee te word nie. **REMCEPT XL** het die potensiaal om die effekte van anticholinergiese medisyne te antagoniseer. Indien anticholinergiese medisyne soos atropien skielik gestaak sou word, is daar ‘n potensiële risiko dat die effekte van **REMCEPT XL** versterk kan word. Soos verwag met cholinomimetika, is farmakodinamiese interaksie met medisyne wat die harttempo beduidend verlaag soos digoksien, betablokkeerders, sekere kalsiumkanaal-blokkerende medisyne en amiodaroon, moontlik (sien **WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS**).

Omsigtigheid moet gebruik word met medisyne wat die potensiaal besit om *torsades de pointes* te veroorsaak. In sulke gevalle behoort ‘n EKG oorweeg te word.

REMCEPT XL, as ‘n cholinomimetikum, sal waarskynlik suksinielcholien-tipe spierverslapping tydens narkose vererger, veral in gevalle van ‘n gebrek aan pseudocholienesterase.

Farmakokinetiese interaksies:
Veelvoudige metaboliese kringlope en renale uitskeiding is betrokke by die eliminasie van **REMCEPT XL**. Die voorkoms van beduidende interaksies mag klinies relevant wees in individuele gevalle. Gelyktydige toediening saam met voedsel vertraag die absorpsietempo van **REMCEPT XL**, maar affekteer nie die mate van absorpsie nie. Dit word aanbeveel dat **REMCEPT XL** saam met voedsel geneem moet word om die cholinergiese newe-effekte tot ‘n minimum te beperk.

Ander medisyne wat die metabolisme van galantamien affekteer:
Formele interaksiestudies het aangedui dat daar ‘n verhoging in **REMCEPT XL-** biobeskikbaarheid voorkom van ongeveer 40% tydens gelyktydige toediening van paroksetien (‘n potente CYP2D6-inhibeerder) en van 30% en 12% tydens gelyktydige behandeling met ketokonasool en eritromisien (beide CYP3A4-inhibeerders). Gedurende die begin van behandeling met potente inhibeerders van CYP2D6 (bv, kinidien, paroksetien of fluoksetien) of CYP3A4 (bv. ketokonasool of ritonavir), mag pasiënte ‘n verhoogde voorkoms van nadelige cholinergiese reaksies ondervind, veral naarheid en braking. Onder hierdie omstandighede, gegrond op verdraagsaamheid, kan ‘n vermindering van die instandhoudingsdosis van **REMCEPT XL** oorweeg word (sien **DOSIS EN GEBRUIKSAANWYSINGS**).

Memantien, ‘n N-metiel-D-aspartaat (NMDA) reseptor-antagonis, teen ‘n dosis van 10 mg een keer per dag vir 2 dae gevolg deur 10 mg twee keer per dag vir 12 dae, het geen effek op die farmakokinetika van galantamien in die ewewigstoestand gehad nie.

Effek van REMCEPT XL op die metabolisme van ander medisyne:
Terapeutiese dosisse van galantamien soos in **REMCEPT XL** 24 mg/dag het geen effek op die kinetika van digoksien, alhoewel farmakodinamiese interaksies mag voorkom (sien ook **Farmakodinamiese interaksies**).

Terapeutiese dosisse van galantamien soos in **REMCEPT XL** 24 mg/dag het geen effek op die kinetika en protrombientyd (INR) van warfarien nie.

SWANGERSKAP EN LAKTASIE:
Geen studies is beskikbaar oor die gebruik van **REMCEPT XL** in swanger vrouens nie. **REMCEPT XL** behoort nie tydens swangerskap gebruik te word nie.
Dierestudies het voortplantingstoksisiteit aangedui.
Dit is nie bekend of galantamien in menslike borsmelk uitgeskei word nie en daar is geen studies in lakterende vrouens nie.
Vrouens op **REMCEPT XL** behoort nie hul suigelinge te borsvoed nie.

DOSIS EN GEBRUIKSAANWYSINGS:

Volwassenes:

***Toediening*:**

REMCEPT XL verlengde-vrystellingkapsules behoort een keer daagliks in die oggend, verkieslik saam met voedsel, toegedien te word.

***Aanvangsdosis*:**

Die aanbevole aanvangsdosis is 8 mg/dag vir 4 weke.

***Instandhoudingsdosis*:**

Die aanvanklike instandhoudingsdosis is 16 mg/dag en pasiënte behoort op 16 mg/dag vir ten minste 4 weke onderhou te word.

'n Verhoging in die instandhoudingsdosis van 24 mg/dag behoort oorweeg te word na toepaslike evaluering insluitend evaluering van kliniese voordeel en verdraagsaamheid.

In individuele pasiënte wat nie 'n verhoogde reaksie toon of wat nie 24 mg/dag kan verdra nie, behoort 'n dosisverlaging na 16 mg/dag oorweeg te word.

Onderhoudsbehandeling kan voortgesit word vir so lank as daar terapeutiese voordeel vir die pasiënt bestaan. Die kliniese voordeel van **REMCEPT XL** behoort dus op 'n gereelde basis weer geëvalueer te word. Staking behoort oorweeg te word wanneer bewyse van 'n terapeutiese effek nie langer teenwoordig is nie.

Daar is geen terugslageffek na skielike staking van behandeling nie (bv. in voorbereiding vir chirurgie).

Kinders:

Die gebruik van **REMCEPT XL** by kinders word nie aanbeveel nie. Geen data oor die gebruik van **REMCEPT XL** in pediatriese pasiënte is beskikbaar nie.

Hepatiese en renale inkorting:

Die plasmavlakke van **REMCEPT XL** mag verhoog wees in pasiënte met matige tot ernstige hepatiese of renale inkorting.

In pasiënte met matig ingekorte hepatiese funksie, gegrond op farmakokinetiese modellering, behoort dosering met 8 mg elke tweede dag te begin vir ten minste een week, wat verkieslik in die oggend geneem word. Daarna behoort pasiënte met 8 mg een keer daagliks vir ten minste 4 weke voort te gaan. By hierdie pasiënte behoort die totale daaglikse dosisse 16 mg nie te oorskry nie.

In pasiënte met ernstige hepatiese inkorting (Child Pugh-telling groter as 9), is die gebruik van **REMCEPT XL** teenaangedui.

Vir pasiënte met 'n kreatinienopruiming wat 9 ml/min oorskry, is geen dosisaanpassing nodig nie.

In pasiënte met ernstige renale inkorting (kreatinienopruiming minder as 9 ml/min), is die gebruik van **REMCEPT XL** teenaangedui.

Gelyktydige behandeling:
In pasiënte wat met potente CYP2D6- of CYP3A4-inhibeerders behandel word, kan dosisverminderings oorweeg word. (Sien **INTERAKSIES**).

Pasiënte wat teenswoordig met **REMCEPT XL** onmiddellike-vrystellingstablette behandel word, kan oorskakel na **REMCEPT XL** verlengde-vrystellingkapsules deur hulle laaste dosis **REMCEPT XL** onmiddellike-vrystellingstablette in die aand te neem en dan **REMCEPT XL** verlengde-vrystellingkapsules een keer daagliks die volgende oggend te neem. Wanneer daar oorgeskakel word van **REMCEPT XL** twee-keer-daaglikse onmiddellike-vrystellingstablette na een-keer-daaglikse **REMCEPT XL** verlengde-vrystellingkapsules, behoort dieselfde totale daaglikse dosis toegedien te word.

NEWE-EFFEKTE:

Sisteem-Orgaanklas	**Frekwensie**	**Ongewenste effekte**
Bloed- en limfatiese sisteemversteurings	*Dikwels:* *Minder dikwels*:	Anemie Trombositopenie
Immuunsisteem-versteurings	*Minder dikwels:*	Hipersensitiwiteit
Metabolisme en voedingversteurings	*Dikwels:* *Minder dikwels:*	Verminderde aptyt, gewigsverlies Dehidrasie, hiperglisemie, verhoogde alkaliese fosfatase
Psigiatriese versteurings	*Dikwels:* *Minder dikwels:*	Hallusinasie, depressie, slaaploosheid, anoreksie, lomerigheid, agitasie, verwarring, angs Hallusinasie visueel, hallusinasie gehoor, paranoïede reaksie, verhoogde libido, delirium, selfmoordgedagtes, selfmoord
Senusisteem-versteurings	*Dikwels:* *Minder dikwels:*	Hoofpyn, lomerigheid, lusteloosheid, tremor, duiseligheid, sinkopee Parestesie, disgeusie, hipersomnie, aanvalle, vertigo, hipertonie, konvulsies, onwillekeurige spiersametrekkings, ataksie, hiperkinesie, apraksie, afasie, beenkrampe

Oogversteurings	*Minder dikwels:*	Versteurde visie
Oor- en doolhofversteurings	*Minder dikwels:*	Tinnitus
Kardiale versteurings	*Dikwels:* *Minder dikwels:*	Bradikardie Supraventrikulêr ekstrasistole, eerste-graad atrioventrikulêre blok, sinus bradikardie, hartkloppings, hartversaking, miokardiale iskemie of infarksie, atriale disritmieë, atriale fibrillasie, supraventrikulêre tagikardieë, QT-verleng, bundeltakblok, T-golf-inversie, ventrikulêre tagikardie
Vaskulêre versteurings	*Dikwels:* *Minder dikwels:*	Hipertensie, perifere edeem Hipotensie, blosing, posturale hipotensie, afhanklike edeem, purpura, neusbloeding
Gastroïntestinale versteurings	*Dikwels:* *Minder dikwels:*	Naarheid, braking, hardlywigheid, winderigheid, abdominale pyn, boonste abdominale pyn, diarree, dispepsie, abdominale ongemak Braakbewegings, gastritis, melena, disfagie, rektale bloeding, droë mond, toename in speeksel, divertikulitis, gastroënteritis, hik, esofageale perforasie
Hepatobiliêre versteurings	*Minder dikwels:*	Hepatitis, verhoogde lewerensieme
Vel- en onderhuidse weefselversteurings	*Dikwels:* *Minder dikwels:*	Hiperhidrose Stevens-Johnson-sindroom, akute veralgemeende eksantemateuse pustulose, erythema multiforme
Muskuloskeletale, Bindweefsel- en beenversteurings	*Dikwels:* *Minder dikwels:*	Spierspasmas Spierswakheid

Renale en urinêre versteurings	*Dikwels:* *Minder dikwels:*	Urienweginfeksie, hematurie, urinêre inkontinensie Mikturisie frekwensie, sistitis, urinêre retensie, nokturie, nierstene
Respiratoriese, torakale en mediastinale versteurings	*Dikwels:*	Rinitis, infeksie van die boonste lugweg, brongitis, hoes
Algemene versteurings en toestande by die toedieningsplek	*Dikwels:*	Moegheid, sinkopee, astenie, malaise, val, besering, rugpyn, borspyn, koors
Ondersoeke	*Dikwels:*	Verhoging van hepatiese ensieme

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:

Simptome:

Daar word voorspel dat tekens en simptome van beduidende oordosering van **REMCEPT XL** soortgelyk sal wees aan dié van oordosering met ander cholinomimetika. Hierdie effekte betrek gewoonlik die sentrale senusisteem, die parasimpatiese senusisteem, en die neuromuskulêre aansluiting. Benewens spierswakheid of fassikulasies, mag sommige of al die tekens van ‘n cholinergiese krisis ontwikkel: ernstige naarheid, braking, gastroïntestinale krampe, speekselafskeiding, traanafskeiding, urinering, ontlasting, sweet, bradikardie, hipotensie, ineenstorting en konvulsies. Toenemende spierswakheid saam met trageale hipersekresies en brongospasmas mag lei tot vitale lugweg kompromie.

Nabemarkingberigte van Torsades de Pointes, QT-verlenging, bradikardie, ventrikulêre tagikardie en verlies aan bewussyn in assosiasie met toevallige oordosisse van **REMCEPT XL**, is ontvang.

Behandeling:

Algemene ondersteunende maatreëls behoort gebruik te word. In ernstige gevalle, kan anticholinergiese middels soos atropien gebruik word as ‘n algemene teenmiddel vir cholinomimetika. ‘n Aanvanklike dosis van 0,5 tot 1,0 mg I.V. word aanbeveel, met daaropvolgende dosisse gebaseer op die kliniese reaksie. Omdat strategieë vir die hantering van oordosis gedurig ontwikkel, is dit raadsaam om ‘n gifbeheersentrum te kontak om die jongste aanbeveling vir die hantering van ‘n oordosis, te bepaal.

IDENTIFIKASIE:

REMCEPT XL 8 mg: Ondeurskynende wit-wit, grootte 2, harde gelatienkapsules wat een ronde bikonvekse tablet van 8 mg bevat.

REMCEPT XL 16 mg: Ondeurskynende vleeskleurige-vleeskleurige, grootte 2, harde gelatienkapsules wat twee ronde bikonvekse tablette van 8 mg bevat.

REMCEPT XL 24 mg: Ondeurskynende oranje-oranje, grootte 2, harde gelatienkapsules wat drie ronde bikonvekse tablette van 8 mg bevat.

AANBIEDING:
Verpakkings van 28 of 30 verlengde-vrystelling, harde kapsules verpak in glansende, deurskynende PVC/PE/PVDC-film en aluminiumfoelie, glansend aan die binnekant en dof (mat) aan die buitekant, stulpverpakkings in ‘n kartondoos.

Wit ondeurskynende, ronde HDPE-bottels met ‘n wit plastiek kinderbestande, peuterbestande skroefdop en ‘n opening vir ‘n droogmiddel in verpakkings van 100 verlengde-vrystelling harde kapsules in ‘n kartondoos.

BEWARINGSINSTRUKSIES:
Bewaar by of benede 25 ^{o}C. Bewaar in die oorspronklike verpakking. Hou stulpverpakkings in die kartondoos en kapsules in die bottel totdat dit benodig word vir gebruik.
Hou die HDPE-houer dig gesluit.
HOU BUITE DIE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:
REMCEPT XL 8 mg: 46/5.3/0998
REMCEPT Xl. 16 mg: 46/5.3/0999
REMCEPT XL 24 mg: 46/5.3/1000

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:
Actavis Pharma (Edms) Bpk
Maxwell Kantoorpark
Magwa singel Wes
Waterfall City
Midrand
2090

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET:
Datum van registrasie: 29 September 2017

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:

REMCEPT XL 8 mg (Prolonged release hard capsules)

REMCEPT XL 16 mg (Prolonged release hard capsules)

REMCEPT XL 24 mg (Prolonged release hard capsules)

Read this entire leaflet carefully before you start taking REMCEPT XL.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **REMCEPT XL** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

1. WHAT REMCEPT XL CONTAINS:

The active ingredient is:

REMCEPT XL prolonged release capsules contain galantamine hydrobromide, equivalent to respectively 8 mg, 16 mg and 24 mg galantamine base.

The other ingredients are:

Ethyl cellulose, erythrocin FD&C Red 3, gelatine, hypromellose, Indigo carmine FD&C Blue 2, magnesium stearate, microcrystalline cellulose, red iron oxide (E172), titanium dioxide (E171), yellow iron oxide (E172).

Sugar free.

2. WHAT REMCEPT XL IS USED FOR:

REMCEPT XL is used for:

- the treatment of symptoms of dementia related to Alzheimer's disease.

3. BEFORE YOU TAKE REMCEPT XL:

Do not take **REMCEPT XL**:

- if you are hypersensitive (allergic) to galantamine or to any of the other ingredients of **REMCEPT XL** (see **WHAT REMCEPT XL CONTAINS**).
- If you have serious liver or kidney disease
- If you have problems with urinary flow or recovering from bladder surgery.

Take special care with REMCEPT XL:

- **REMCEPT XL** must only be taken under the supervision of your doctor, who will regularly monitor you, after he has diagnosed your condition
- Inform your doctor immediately if you notice a skin rash as **REMCEPT XL** may cause serious skin reactions including a potential life threatening reaction called Stevens Johnson syndrome (purplish rash) or blisters containing pus (see **POSSIBLE SIDE EFFECTS**).
- you may experience weight loss, which will be monitored by your doctor during your treatment
- If you have any heart condition, or are taking any medication such as digoxin or beta-blockers, inform your doctor before taking **REMCEPT XL**, as your heart rate will need to be monitored
- If you have an ulcer, history of ulcers or are taking anti-inflammatory medicine
- If you have any obstruction in your stomach or recovering from surgery
- If you suffer from seizures or Parkinson's disease
- If you have a history of severe asthma or lung infection
- If you suffer from urinary flow problems or are recovering from bladder surgery.

Taking REMCEPT XL with food and drink:
It is recommended that **REMCEPT XL** be taken with food, to reduce any side effects that may occur without food.

Pregnancy and breastfeeding:
If you are pregnant or breastfeeding your baby, please contact your doctor, pharmacist or other healthcare professional for advice before taking **REMCEPT XL**.
You should not take **REMCEPT XL:**

- if you are pregnant, planning to become pregnant or if you suspect you are pregnant;
- if you are breastfeeding your baby.

If you become pregnant whilst taking **REMCEPT XL**, please consult your doctor immediately (see **Do not take REMCEPT XL**).

Driving and using machines:
You may experience dizziness or blurred vision while taking **REMCEPT XL.** Do not drive, operate machinery, or do anything else that could be dangerous until you know how you react on **REMCEPT XL**, especially during the first weeks of your treatment.

Taking other medicines with REMCEPT XL:
Always tell your healthcare professional if you are taking any other medicine.
(This includes complementary or traditional medicines.)
Please tell your doctor if you are taking any of the following medicines:

- Ambenomium, donepezil, neostigmine, pyridostigmine, rivastigmine (to treat muscle weakness), pilocarpine (to treat glaucoma).

- Heart medication such as digoxin, beta-blockers and amiodarone (see **Take special care with REMCEPT XL**).
- Food slows the absorption of **REMCEPT XL**, but to reduce side effects, it should be taken with food.
- Paroxetine or fluoxetine (to treat depression) ketoconazole (to treat fungal infections), erythromycin (antibiotic) as this may increase the levels of **REMCEPT XL** in your blood and increase side effects such as nausea and vomiting.
- Before surgery, tell your doctor if you are taking **REMCEPT XL.**

4. HOW TO TAKE REMCEPT XL:

Do not share medicines prescribed for you with any other person.

Always take **REMCEPT XL** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

REMCEPT XL capsules should be taken once daily in the morning, preferably with food.

The recommended starting dose is 8 mg/day.

Your doctor may adjust your dose depending on your condition and your reaction to the medicine.

Children:

Use of **REMCEPT XL** in children is not recommended.

If you take more REMCEPT XL than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

In the event of overdose, you may experience nausea, vomiting, stomach cramps, muscle weakness or dizziness.

If you forget to take REMCEPT XL:

It is important to take your medicine every day. However, if you forget to take one or more doses, take another as soon as you remember and then go on as prescribed on a normal daily dose.

Do not take a double dose to make up for forgotten individual doses.

Effects when treatment with REMCEPT XL is stopped:

It is important that you continue the course of treatment. Do not stop taking **REMCEPT XL** unless your doctor instructs you to.

5. POSSIBLE SIDE EFFECTS:

REMCEPT XL can have side effects. Not all side effects reported for **REMCEPT XL** are included in this leaflet.

Should your general health worsen while taking **REMCEPT XL**, please consult your doctor, pharmacist or other health care professional for advice.

If any of the following happens, stop taking **REMCEPT XL** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, lips, mouth or throat which may cause difficulty in breathing,
- Rash or itching.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to **REMCEPT XL**. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go the casualty department at your nearest hospital if you notice any of the following:

- Very slow heartbeat making you feel dizzy, rapid heartbeat, irregular heartbeat, heart attack (with symptoms such as chest pain, sweating and shortness of breath)
- High or low blood pressure, feeling dizzy when you stand up, swelling of hands and feet, flushing, nose bleed
- Stevens Johnson syndrome (a serious skin disorder, with purple rash) or blisters on the skin containing pus
- Suicidal thoughts and tendencies, depression, seeing or hearing things that aren't there, confusion and anxiety
- Seizures (fits), blurred vision
- Mouth or throat infection
- Liver problems
- Urinary tract infection, difficulty in urination, blood in the urine, urinating more often than usual, inability to urinate or feeling the need to urinate at night.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

- Decreased appetite *(frequent),* decreased weight *(frequent),* dehydration *(less frequent),* high blood sugar *(less frequent),* feeling sleepy *(frequent)*
- Nausea *(frequent),* vomiting *(frequent),* constipation *(frequent),* feeling bloated *(frequent),* stomach pain and discomfort *(frequent),* diarrhoea *(frequent),* indigestion *(frequent)*
- Dry mouth *(less frequent),* hiccups *(less frequent),* increased saliva *(less frequent),* rectal bleeding *(less frequent),* dark faeces *(less frequent),* retching *(less frequent),* difficulty in swallowing *(less frequent)*
- Increased sweating *(frequent)*
- Headache *(frequent),* tremor *(frequent),* dizziness *(frequent),* "pins and needles" *(less frequent),* involuntary muscle contractions *(less frequent),* loss of movement *(less frequent),* leg cramps *(less frequent)*

- Metallic taste in the mouth *(less frequent)*
- Inability to perform actions or formulate certain words *(less frequent)*
- Increased libido *(less frequent)*
- Ringing in the ears *(less frequent)*

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF REMCEPT XL:

Store at or below 25 °C.

Do not remove capsule from blister until required for use.

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

Keep the HDPE container tightly closed.

Keep the HDPE bottle in the carton container.

Do not take this medicine after the expiry date which is clearly marked on the blister and outside of the box.

Return any expired or unused medicine to your pharmacist for safe disposal. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

KEEP OUT OF REACH OF CHILDREN.

7. PRESENTATION OF REMCEPT XL:

Packs of 28's or 30's prolonged release hard capsules packed in glossy, transparent, PVC/PE/PVDC film and aluminium foil, shiny on the inside and dull (matte) on the outside blisters in a cardboard carton.

White opaque, round HDPE bottles with a white plastic child-resistant tamper-evident screw cap and an aperture for desiccant in packs of 100's prolonged release hard capsules in a cardboard carton.

8. IDENTIFICATION OF REMCEPT XL:

REMCEPT XL 8 mg: Opaque white-white size 2 hard gelatine capsules containing one round biconvex tablet of 8 mg

REMCEPT XL 16 mg: Opaque, flesh-flesh size 2 hard gelatine capsules containing two round biconvex tablets of 8 mg

REMCEPT XL 24 mg: Opaque orange-orange size 2 hard gelatine capsules containing three round biconvex tablets of 8 mg

9. REGISTRATION NUMBERS:

REMCEPT XL 8 mg: 46/5.3/0998

REMCEPT Xl. 16 mg: 46/5.3/0999

REMCEPT XL 24 mg: 46/5.3/1000

10. NAME AND ADDRESS OF REGISTRATION HOLDER

Actavis Pharma (Pty) Ltd
Maxwell Office Park
Magwa Crescent West
Waterfall City
Midrand
2090
Tel No.: 011 055 0200

11. DATE OF PUBLICATION:

Date of Registration: 29 September 2017

VOUBILJET

SKEDULERINGSTATUS:

S4

EIENDOMSNAAM, STERKTE EN FARMASEUTIESE VORM:

REMCEPT XL 8 mg (Verlengde-vrystelling harde kapsules)

REMCEPT XL 16 mg (Verlengde-vrystelling harde kapsules)

REMCEPT XL 24 mg (Verlengde-vrystelling harde kapsules)

Lees hierdie hele brosjure versigtig voordat jy begin om REMCEPT XL te neem.

- Hou hierdie brosjure. Jy mag dit weer moet lees.
- Indien jy verdere vrae het, vra asseblief jou dokter of jou apteker daaroor.
- **REMCEPT XL** is vir jou persoonlik voorgeskryf en jy behoort nie jou medisyne met ander persone te deel nie. Dit kan hulle skade aandoen, al is hulle simptome dieselfde as joune.

1. WAT REMCEPT XL BEVAT:

Die aktiewe bestanddeel is:

REMCEPT XL verlengde-vrystellingkapsules bevat galantamienhidrobromied, onderskeidelik ekwivalent aan 8 mg, 16 mg en 24 mg galantamienbasis.

Die ander bestanddele is:

Etielsellulose, eritrosien FD&C Rooi 3, gelatien, hipromellose, Indigo-karmosyn FD&C Blou 2, magnesiumstearaat, mikrokristallyne sellulose, rooi ysteroksied (E172), titaandioksied (E172), geel ysteroksied (E172).

Suikervry.

2. WAARVOOR REMCEPT XL GEBRUIK WORD:

REMCEPT XL word gebruik vir:

- die behandeling van simptome van demensie wat aan Alzheimer se siekte verwant is.

3. VOORDAT JY REMCEPT XL NEEM:

Moenie REMCEPT XL neem: indien jy hipersensitief (allergies) is vir galantamien of enige van die ander bestanddele van **REMCEPT XL** (sien **WAT REMCEPT XL BEVAT**).

- Indien jy ernstige lewer- of niersiekte het
- Indien jy probleme met urinêre uitvloei het of besig is om van ‘n blaasoperasie te herstel.

Neem spesiale sorg met REMCEPT XL:

- **REMCEPT XL** moet slegs onder die toesig van jou dokter geneem word, hy/sy sal jou gereeld moniteer nadat jou toestand gediagnoseer is.

- Vertel jou dokter dadelik as jy van ‘n veluitslag bewus word, omdat **REMCEPT XL** ernstige velreaksies kan veroorsaak, insluitend ‘n potensieel lewensbedreigende reaksie wat Stevens-Johnson-sindroom genoem word (‘n perskleurige veluitslag) of blase wat etter bevat (sien **MOONTLIKE NEWE-EFFEKTE**).
- jy mag gewigsverlies ondervind, wat deur jou dokter tydens jou behandeling gemoniteer sal word
- Indien jy enige hartkondisie het, of enige medikasie soos digoksien of beta-blokkeerders neem, moet jy jou dokter daarvan vertel voordat jy **REMCEPT XL** neem, omdat dit nodig sal wees om jou harttempo te moniteer
- Indien jy ‘n ulkus of ‘n geskiedenis van ulkusse het, of as jy anti-inflammatories medisyne neem
- Indien enige obstruksie in jou maag het of tans van chirurgie herstel
- Indien jy aan aanvalle of Parkinson se siekte ly
- Indien jy ‘n geskiedenis van ernstige asma of longinfeksie het
- Indien jy ly aan probleme met urinêre uitvloei of besig is om te herstel van ‘n blaasoperasie.

Inname van REMCEPT XL saam met voedsel en drank:
Dit word aanbeveel dat **REMCEPT XL** saam met voedsel geneem word om enige newe-effekte wat sonder voedsel mag voorkom, te verminder.

Swangerskap en borsvoeding:
Indien jy swanger is of jou baba borsvoed, moet jy asseblief jou dokter, apteker of ander gesondheidsorgdeskundige raadpleeg vir advies voordat jy **REMCEPT XL** neem.

Jy behoort REMCEPT XL nie te neem:

- indien jy swanger is, swangerskap oorweeg of as jy vermoed dat jy swanger is;
- as jy jou baba borsvoed

Indien jy swanger word terwyl jy **REMCEPT XL** neem, moet jy asseblief jou dokter dadelik raadpleeg .

Bestuur en gebruik van masjiene:
Jy mag duiseligheid en belemmerde visie ondervind terwyl jy **REMCEPT XL** neem. Moenie bestuur, masjiene gebruik, of enigiets anders doen wat gevaarlik kan wees totdat jy weet hoe jy op **REMCEPT XL** reageer, veral tydens die eerste weke van jou behandeling.

Neem van ander medisyne saam met REMCEPT XL:
Jy moet altyd jou gesondheidsorgdeskundige daarvan vertel indien jy enige ander medisyne neem. (Dit sluit komplementêre of tradisionele medisyne in.)

Vertel asseblief jou dokter indien jy enige van die volgende medisyne neem: Ambenonium, donepesiel, neostigmien, piridostigmien, rivastigmien (om spierswakheid te behandel), pilokarpien

(om gloukoom te behandel)

- Hartmedikasie soos digoksien, betablokkeerders en amiodaroon (sien **Neem spesiale sorg met REMCEPT XL**)
- Voedsel vertraag die absorpsie van **REMCEPT XL**, maar dit behoort saam met voedsel geneem te word om die newe-effekte te verminder
- Paroksetien of fluoksetien (om depressie te behandel), ketokonasool (om swaminfeksies te behandel), eritromisien (antibiotikum) omdat dit die vlakke van **REMCEPT XL** in jou bloed mag verhoog en newe-effekte soos naarheid en braking mag verhoog

Vertel jou dokter voor chirurgie indien jy **REMCEPT XL** neem.

4. HOE OM REMCEPT XL TE NEEM:

Moenie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie.
Neem **REMCEPT XL** altyd presies volgens jou dokter se instruksies. Jy behoort met jou dokter of apteker te gesels indien jy onseker is.

REMCEPT XL kapsules behoort een keer daagliks in die oggend, verkieslik saam met voedsel, geneem te word.
Die aanbevole aanvangsdosis is 8 mg/dag.
Jou dokter mag jou dosis aanpas afhangende van jou toestand en jou reaksie op die medisyne.

Kinders:

Die gebruik van **REMCEPT XL** by kinders word nie aanbeveel nie.

Indien jy meer REMCEPT XL neem as wat jy behoort te neem:

In ’n geval van oordosering, raadpleeg jou dokter of apteker. Indien beide onbeskikbaar is, moet jy die naaste hospitaal of gifbeheersentrum kontak.
In ‘n geval van oordosis, mag jy naarheid, braking, maagkrampe, spierswakheid of duiseligheid ondervind.

Indien jy vergeet om REMCEPT XL te neem:

Dit is belangrik dat jy jou medisyne elke dag neem. As jy egter vergeet om een of meer dosisse te neem, moet jy ‘n dosis neem sodra jy dit onthou en dan voortgaan soos voorgeskryf op ‘n normale daaglikse dosis.
Moenie ‘n dubbele dosis neem om op te maak vir vergete individuele dosisse nie.

Effekte wanneer behandeling met REMCEPT XL gestaak word:

Dit is belangrik dat jy met die behandelingskursus aanhou. Moenie die inname van **REMCEPT XL** staak nie, tensy jou dokter vir jou instruksies gee om dit te doen.

5. MOONTLIK NEWE-EFFEKTE:

REMCEPT XL kan newe-effekte veroorsaak. Nie alle newe-effekte wat vir **REMCEPT XL** aangemeld is, word in hierdie brosjure ingesluit nie.

Indien jou algemene gesondheid sou vererger terwyl jy **REMCEPT XL** neem, moet jy asseblief jou dokter, apteker of ander gesondheidsorgdeskundige vir advies raadpleeg.

Indien enige van die volgende plaasvind, moet jy die inname van **REMCEPT XL** staak en dadelik vir jou dokter daarvan vertel of na die noodafdeling by jou naaste hospitaal gaan:

- Swelling van die hande, voete, enkels, lippe, mond of keel wat probleme met asemhaling mag veroorsaak.
- veluitslag of jeuk.

Dit is almal baie ernstige newe-effekte. Indien jy dit het, het jy moontlik ’n ernstige allergiese reaksie teen **REMCEPT XL** gehad. Jy mag dringende mediese aandag of hospitalisering nodig hê.

Vertel vir jou dokter dadelik daarvan of gaan na die noodafdeling by jou naaste hospitaal indien jy van enige van die volgende bewus word:

- Baie stadige hartklop wat jou duiselig laat voel, ‘n vinnige hartklop, ‘n onreëlmatige hartklop, ‘n hartaanval (met simptome soos borspyn, sweet en kortasem).
- Hoë of lae bloeddruk, gevoel van duiseligheid wanneer jy opstaan, swelling van die hande en voete, blosing, neusbloeding.
- Stevens-Johnson-sindroom (‘n ernstige velversteuring, met ‘n perskleurige veluitslag) of blase op die vel wat etter bevat.
- Selfmoordgedagtes en -neigings, depressie, sien of hoor dinge wat nie bestaan nie, verwarring en angs.
- Aanvalle (stuipe), belemmerde visie.
- Mond- of keelinfeksie.
- Lewerprobleme.
- Urienweginfeksie, probleme met urinering, bloed in die urine, urineer meer dikwels as gewoonlik, onvermoë om te urineer of gevoel om snags te urineer.

Dit is almal ernstige newe-effekte. Jy mag dringende mediese aandag nodig hê.

Vertel jou dokter indien jy van enige van die volgende bewus word:

- Verminderde aptyt (*dikwels*), verminderde gewig (*dikwels*), dehidrasie (*minder dikwels*), hoë bloedsuiker (*minder dikwels*), voel slaperig (*dikwels*).
- Naarheid (*dikwels*), braking (*dikwels*), hardlywigheid (*dikwels)*, voel opgeblaas (*dikwels*), maagpyn en -ongemak (*dikwels*), diarree (*dikwels*), slegte spysvertering (*dikwels*).
- Droë mond (*minder dikwels*), hik (*minder dikwels*), verhoogde speekselproduksie (*minder dikwels*), rektale bloeding (*minder dikwels*), donker stoelgang (*minder dikwels*), braakbewegings (*minder dikwels*), probleme met sluk (*minder dikwels*)
- Toename in sweet (*minder dikwels*).

- Hoofpyn (*dikwels*), tremor (*dikwels*), duiseligheid (*frekwent*), “naalde en spelde” (*minder dikwels*), onwillekeurige spiersametrekkings (*minder dikwels*), verlies aan beweging (*minder dikwels*), beenkrampe (*minder dikwels*).
- Metaalagtige smaak in die mond (*minder dikwels*).
- Onvermoë om aksies uit te voer of om sekere woorde te formuleer (*minder dikwels*).
- Verhoogde libido (*minder dikwels*).
- Gesuis in die ore (*minder dikwels*).

Indien jy bewus word van enige newe-effekte wat nie in hierdie brosjure genoem word nie, moet jy asseblief jou dokter of apteker daarvan vertel.

6. BERGING EN WEGDOENING VAN REMCEPT XL:

Bewaar by benede 25 ^{o}C.
Moenie ‘n kapsule uit die stulpverpakking verwyder, totdat dit vir gebruik benodig word nie.
Hou die stulpverpakking in die oorspronklike buitenste houer totdat dit benodig word vir gebruik.
Hou die HDPE-houer dig toe.
Hou die HDPE-houer in die kartondoos.
Moenie hierdie medisyne na die vervaldatum wat duidelik op die stulpverpakking en die buitekant van die kartondoos gemerk is, gebruik nie.
Gee enige vervalle of ongebruikte medisyne terug aan jou apteker vir veilige wegdoening. Moenie ongebruikte medisyne in dreine of rioolsisteme (bv. toilette) weggooi nie.
HOU BUITE BEREIK VAN KINDERS.

7. AANBIEDING VAN REMCEPT XL:

Verpakkings van 28 of 30 verlengde-vrystelling, harde kapsules verpak in glansende, deurskynende PVC/PE/PVDC-film en aluminiumfoelie, glansend aan die binnekant en dof (mat) aan die buitekant, stulpverpakkings in ‘n kartondoos.

Wit ondeurskynende, ronde HDPE-bottels met ‘n wit plastiek kinderbestande, peuterbestande skroefdop en ‘n opening vir ‘n droogmiddel in verpakkings van 100 verlengde-vrystelling harde kapsules in ‘n kartondoos.

8. IDENTIFIKASIE VAN REMCEPT XL:

REMCEPT XL 8 mg: Ondeurskynende wit-wit, grootte 2, harde gelatienkapsules wat een ronde bikonvekse tablet van 8 mg bevat.
REMCEPT XL 16 mg: Ondeurskynende vleeskleurige-vleeskleurige, grootte 2, harde gelatienkapsules wat twee ronde bikonvekse tablette van 8 mg bevat.
REMCEPT XL 24 mg: Ondeurskynende oranje-oranje, grootte 2, harde gelatienkapsules wat drie ronde bikonvekse tablette van 8 mg bevat.

9. REGISTRASIENOMMERS:

REMCEPT XL 8 mg: 46/5.3/0998

REMCEPT Xl. 16 mg: 46/5.3/0999

REMCEPT XL 24 mg: 46/5.3/1000

10. NAAM EN ADRES VAN DIE REGISTRASIEHOUER:

Actavis Pharma (Edms) Bpk.
Maxwell Kantoorpark
Magwa singel Wes
Waterfall City
Midrand
2090
Tel Nr.: 011 055 0200

11. DATUM VAN PUBLIKASIE:

Datum van registrasie: 29 September 2017