PACKAGE INSERT FOR MEMINIST 10

SCHEDULING STATUS
S4

PROPRIETARY NAME AND DOSAGE FORM
MEMINIST 10 film-coated tablets

COMPOSITION
Active ingredient:
Each film-coated tablet contains 10 mg memantine hydrochloride
Inactive ingredients:
Colloidal anhydrous silica, crospovidone, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, purified talc and titanium dioxide.
Sugar-free.

PHARMACOLOGICAL CLASSIFICATION
A 5.11 Medicines affecting autonomic function. Others.

PHARMACOLOGICAL ACTION
Pharmacodynamic properties
Memantine is a voltage dependant, moderate-affinity non-competitive antagonist of the NMDA-type glutamate receptor. It blocks the effects of pathologically elevated tonic levels of glutamate that may lead to neuronal dysfunction. Memantine interacts with the Mg^{2+} binding site of the channel to prevent excessive activation, while sparing normal function. Increasing evidence suggests that malfunctioning of glutamatergic neurotransmission, in particular at *N*-methyl-D-aspartate (NMDA)-receptors, contributes to both expression of symptoms and disease progression in neurodegenerative dementia.

Pharmacokinetic properties
Absorption:
Memantine has an absolute bioavailability of approximately 100 %. Peak plasma concentrations are achieved between 3 - 8 hours. There is no indication that food influences the absorption of memantine.

Linearity:
The pharmacokinetics of memantine are linear in the dose range between 10 - 40 mg.

Distribution:
The volume of distribution is approximately 10 l/kg. About 45 % of memantine is bound to plasma protein.

Biotransformation:
Approximately 80 % of the circulating memantine-related material is present as the parent compound. The main metabolites are *N*-3,5-dimethyl-gludantan, the isomeric mixture of 4- and 6-hydroxy-memantine, and 1-nitroso-3,4-dimethyl-adamantane. None of these metabolites exhibits NMDA-antagonistic activity, and *in vitro* no P450 catalysed metabolism has been detected.

Elimination:
Memantine is eliminated in a monoexponential manner, with a terminal half-life of 60 - 100 hours. The total clearance of memantine amounts to 170 ml/min/1,73 m^2, and part of total renal clearance is achieved by tubular secretion. Renal handling involves tubular reabsorption and is probably mediated by cation transport proteins. Alkaline urine conditions may reduce renal elimination of memantine (see **WARNINGS AND SPECIAL PRECAUTIONS**).

Special populations:
Renal impairment:
A significant correlation between creatinine clearance and total renal clearance of memantine has been observed in elderly patients with normal and reduced renal function (creatine clearance of 50 - 100 ml/min/1,73 m^2) (see **DOSAGE AND DIRECTIONS FOR USE**).
Hepatic impairment:
The effects of liver impairment on the pharmacokinetics of memantine have not been evaluated. As memantine is metabolised only to a minor extent, and into metabolites with no NMDA-antagonistic activity, the pharmacokinetics of memantine are not expected to produce clinically significant changes in patients with mild to moderate hepatic impairment.

INDICATIONS
MEMINIST 10 is indicated for the treatment of patients with moderately severe to severe Alzheimer's disease. Efficacy has not been established beyond 6 months.

CONTRAINDICATIONS
- Hypersensitivity to memantine or to any of the excipients in **MEMINIST 10** (see **COMPOSITION**).
- Children and adolescents under the age of 18 years, as safety and efficacy have not been established.

WARNINGS AND SPECIAL PRECAUTIONS
MEMINIST 10 therapy is not recommended for patients with severe renal impairment (creatinine clearance less than 9 ml/min/1,73 m^2) as no data are available (see **DOSAGE AND DIRECTIONS FOR USE**).

Under alkaline conditions the rate of elimination of **MEMINIST 10** is reduced (see **Pharmacokinetic properties**). Factors that may raise urine pH therefore may necessitate careful monitoring of the patient. These factors include drastic changes in diet, e.g. from a diet rich in meat products to a vegetarian diet, or a massive ingestion of alkalising gastric buffers. Urine pH may also be elevated by states of renal tubular acidosis (RTA) or severe infections of the urinary tract with *Proteus* bacteria.
Caution is recommended in patients at risk of convulsions.

Concomitant use of *N*-methyl-D-aspartate (NMDA)-antagonists, such as amantadine, ketamine or dextromethorphan, with **MEMINIST 10** should be avoided. These compounds act at the same receptor system as **MEMINIST 10**, and therefore side effects (mainly central nervous system (CNS)-related) may be more frequent or more pronounced (see **INTERACTIONS**). Limited data are available on patients with recent myocardial infarction, congestive heart failure (NYHA III-IV) and uncontrolled hypertension. These patients should be closely supervised.

Effects on ability to drive and use machines
MEMINIST 10 may change reactivity and outpatients should be warned to take special care when driving a vehicle or operating machinery. Moderately severe to severe Alzheimer's disease also usually causes impairment of driving performance and compromises the ability to use machinery.

INTERACTIONS
- The effects of L-dopa, dopaminergic agonists and anticholinergics may be enhanced by concomitant treatment with **MEMINIST 10**.
- The effects of barbiturates and neuroleptics may be reduced during concomitant treatment with **MEMINIST 10**.
- **MEMINIST 10** may alter the effects of the antispasmodic medicines dantrolene and baclofen, and a dosage adjustment may be necessary.
- Use of other NMDA antagonists such as amantadine, ketamine or dextromethorphan with **MEMINIST 10** should be avoided, as it may increase the incidence and severity of pharmatoxic psychosis.
- Medicines such as cimetidine, ranitidine, procainamide, quinidine, quinine and nicotine, that use the same renal cationic transport system as amantadine, may interact with **MEMINIST 10** leading to a potential risk of increased plasma levels.
- **MEMINIST 10** decreases the area under the curve (AUC) and peak plasma concentration (C_{max}) of hydrochlorothiazide by 20 %.

PREGNANCY AND LACTATION
The safety and efficacy of **MEMINIST 10** have not been established in pregnant and lactating women.

DOSAGE AND DIRECTIONS FOR USE
Treatment should be initiated and supervised by a medical practitioner experienced in the diagnosis and treatment of Alzheimer's dementia. Therapy should only be started if a caregiver is available who will regularly monitor medicine intake by the patient. Diagnosis should be made according to current guidelines.

Adults:
The maximum daily dose is 20 mg per day.

In order to reduce the risk of side effects, the maintenance dose is achieved by upward titration of 5 mg per week over the first 3 weeks as follows:
Treatment should be started with 5 mg per day (half a tablet in the morning) during the 1st week. In the 2nd week 10 mg per day (half a tablet twice a day), and in the 3rd week 15 mg per day is recommended (one tablet in the morning and half a tablet in the afternoon). From the 4th week on, treatment can be continued with the recommended maintenance dose of 20 mg per day (one tablet twice a day).

The tablets can be taken with or without food.

Elderly:
The recommended dose for patients > 65 years of age is 20 mg per day (10 mg twice a day) as described above.

Renal impairment:
In patients with normal to mildly impaired renal function (serum creatinine levels of up to 130 µmol/l) no dose reduction is needed.
In patients with moderate renal impairment (creatinine clearance 40 - 60 ml/min/1,73 m^2) the dose should be reduced to 10 mg per day.
No data are available for patients with severely reduced kidney function (see **WARNINGS AND SPECIAL PRECAUTIONS**).

Hepatic impairment:
There are no data on the use of **MEMINIST 10** in patients with hepatic impairment.

SIDE EFFECTS
Blood and the lymphatic system disorders
Frequency unknown: Thrombocytopenia

Endocrine disorders
Frequency unknown: Acute pancreatitis, hypoglycaemia

Metabolism and nutrition disorders
Less frequent: Anorexia
Frequency unknown: Hyperlipidaemia

Psychiatric disorders
Frequent: Agitation, hallucinations, insomnia
Less frequent: Depression, somnolence

Nervous system disorders
Frequent: Confusion, dizziness, headache
Less frequent: Anxiety, abnormal gait
Frequency unknown: Dyskinesia, grand mal convulsions, neuroleptic malignant syndrome, tardive dyskinesia, carpal tunnel syndrome, restlessness

Cardiac disorders
Frequency unknown: Atrioventricular block, prolonged QT interval, supraventricular tachycardia, tachycardia

Vascular disorders
Less frequent: Hypertension
Frequency unknown: Cerebral infarction, intracranial haemorrhage, claudication

Respiratory, thoracic and mediastinal disorders
Frequent: Coughing
Less frequent: Bronchitis, dyspnoea, upper respiratory tract infection
Frequency unknown: Aspiration pneumonia

Gastrointestinal disorders
Less frequent: Vomiting, constipation, diarrhoea, nausea
Frequency unknown: Ileus, colitis, dysphagia, gastritis, gastro-oesophageal reflux

Hepatobiliary disorders
Frequency unknown: Hepatic failure

Skin and subcutaneous tissue disorders
Frequency unknown: Stevens-Johnson syndrome

Musculoskeletal, connective tissue and bone disorders
Less frequent: Hypertonia (increased muscle tone), arthralgia, back pain
Frequency unknown: Bone fracture

Renal and urinary disorders
Frequent: Urinary incontinence
Less frequent: Cystitis, urinary tract infection
Frequency unknown: Acute renal failure

Reproductive system and breast disorders
Less frequent: Increased libido
Frequency unknown: Impotence

General disorders and administrative site conditions
Frequent: Inflicted injury
Less frequent: Peripheral oedema, tiredness, fatigue, influenza-like syndrome, pain
Frequency unknown: Chest pain, malaise

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
See **SIDE EFFECTS**.
Treatment of overdosage should be symptomatic and supportive.

IDENTIFICATION
Off-white, capsule shaped, biconvex, film-coated tablets, debossed with "M" and 10 on either side of the break line on one side and break line on other side.

PRESENTATION
Clear transparent triplex (PVC/PE/PVDC) film blister strips with aluminium foil containing 10 tablets. Six blister strips are packed in an outer carton.

STORAGE INSTRUCTIONS
Store at or below 25 °C.
Keep blister strips in outer carton until required for use.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER
46/5.11/0427

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
Unichem S.A. (Pty) Ltd.
1st Floor, Pinewood Park, Lonsdale Road, Pinelands, Cape Town 7405

MARKETED BY
Forrester Pharma (Pty) Ltd.
13 Pasita Street, Rosen Heights, Rosen Park, Bellville, 7530

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LI0052/15A

PATIENT INFORMATION LEAFLET FOR MEMINIST 10

SCHEDULING STATUS
Schedule 4

PROPRIETARY NAME AND DOSAGE FORM
MEMINIST 10 film-coated tablets

Please read all of this leaflet carefully before taking MEMINIST 10
- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or your pharmacist.
- **MEMINIST 10** 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 MEMINIST 10 CONTAINS
Active ingredient:
Each film-coated tablet contains 10 mg memantine hydrochloride.

Inactive ingredients:
Colloidal anhydrous silica, crospovidone, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, purified talc and titanium dioxide.
Sugar-free.

2. WHAT MEMINIST 10 IS USED FOR
Alzheimer's disease is a form of dementia which is a brain disorder that negatively affects a person's ability to carry out daily activities.
MEMINIST 10 is used to treat the symptoms of Alzheimer's disease such as memory loss.

3. BEFORE YOU TAKE MEMINIST 10
Do not take MEMINIST 10:
- If you are allergic (hypersensitive) to memantine or to any of the ingredients of **MEMINIST 10** (see **WHAT MEMINIST 10 CONTAINS**).
  MEMINIST 10 should not be used in children and adolescents under the age of 18 years.

Take special care with MEMINIST 10:
Before you take **MEMINIST 10** tell your doctor:
- If you have a severe kidney disorder.
- If you have recently changed or intend to change your diet significantly (such as from normal diet to vegetarian diet), if you suffer from a condition called renal tubular acidosis or RTA (an excess of acid-forming substances in the blood due to a kidney disorder) or if you suffer from severe infections of the urinary tract, as your doctor may need to adjust the dose of **MEMINIST 10**.
- If you suffer from epilepsy or have a history of seizures or fits.
- If you recently had a heart attack or have a heart disorder.
- If you have a history of high and uncontrolled blood pressure.

Taking MEMINIST 10 with food or drink:
MEMINIST 10 may be taken with or without food.

Pregnancy and breastfeeding:
If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional before taking **MEMINIST 10**.
Do not take **MEMINIST 10** if you are pregnant, suspect you are pregnant or planning to become pregnant. Contact you doctor immediately.
Do not take **MEMINIST 10** if you are breastfeeding your baby.

Driving and using machinery:
MEMINIST 10 may impair your ability to drive a vehicle and use machinery.
Do not drive a vehicle, operate machinery or perform any activities that require concentration until you know how **MEMINIST 10** affects you.

Taking other medicines with MEMINIST 10:
Always tell your healthcare professional if you are taking any other medicine (this includes complementary or traditional medicines).
In particular, tell your doctor if you are taking any of the following medicines:
- Dextromethorphan (a type of cough medicine).
- Dantrolene, baclofen (used as muscle relaxants).
- Cimetidine, ranitidine (used to treat stomach ulcers or heartburn).
- Hydrochlorothiazide (water pill or any medicine used to manage high blood pressure that is in combination with hydrochlorothiazide).
- Anticholinergics (used to treat movement disorders or intestinal cramps).
- Anticonvulsants (used to prevent and relieve seizures or fits).
- Barbiturates (used to induce sleep).
- Dopaminergic agonists, such as L-dopa (used to treat Parkinson's disease) or bromocriptine (used to treat high levels of the hormone prolactin in your body).
- Neuroleptics (used in the treatment of mental disorders).
- Amantadine (used to treat Parkinson's disease).
- Ketamine (used as anaesthetic during surgery).
- Procainamide or quinidine (used to treat an abnormal heartbeat).
- Quinine (used to reduce fever and treat malaria).
- Nicotine (used as an aid to stop smoking and prevent withdrawal symptoms).

Not all medicines that may interact with MEMINIST 10 are included in this leaflet.

4. HOW TO TAKE MEMINIST 10
- Do not share medicines prescribed for you with any other person.
- Your caregiver will help you take your medication exactly as directed by your doctor. You should check with your doctor or pharmacist if you are unsure.
- When starting your treatment your doctor will start off with a small dose and gradually increase the dose. This allows your doctor to make sure that you have the right dose that helps your condition and avoids any unwanted symptoms.
- The usual dose is:
- Week 1: 5 mg per day (half a tablet in the morning).
- Week 2: 10 mg per day (half a tablet twice a day).
- Week 3: 15 mg per day (one tablet in the morning and half a tablet in the afternoon).
- Week 4: 20 mg per day (one tablet twice a day).
- The maximum dose is 20 mg per day.
- Your doctor will adjust your dose accordingly if you are elderly or suffer from moderate kidney problems.
- Make sure to take **MEMINIST 10** at the same time each day and try to avoid missing any doses.
- Your doctor will tell you how long your treatment with **MEMINIST 10** will last. If you have the impression that the effects of **MEMINIST 10** is too strong or too weak, tell your doctor or pharmacist.

If you take more MEMINIST 10 than you should:
In the event of overdosage, consult your doctor or pharmacist as soon as possible. If neither is available, contact the nearest hospital or poison centre. Take this leaflet and any remaining tablets with you, so that the doctor knows what you have taken.

If you forget to take MEMINIST 10:
If you have missed your dose by only a few hours, take the missed dose as soon as you remember and then continue with your normal schedule. However, if it is almost time for your next dose, skip the missed dose and take your next dose at the usual time. Do not take a double dose to make up for a missed dose.

5. POSSIBLE SIDE EFFECTS
MEMINIST 10 can have side effects.
Not all side effects reported for MEMINIST 10 are included in this leaflet. Should your general health worsen or you experience any untoward effects while taking MEMINIST 10, please consult your doctor, pharmacist or other healthcare professional for advice.
If any of the following happens, stop taking **MEMINIST 10** and tell your doctor immediately or go to the casualty department at your nearest hospital:
- Swelling of your hands, feet, ankles, face, mouth or throat, which may cause difficulty in swallowing or breathing.
- Rash or itching.
- Fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to **MEMINIST 10.** You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
The following side effects occur frequently:
- Shortness of breath.
- Loss of bladder control.

The following side effect occurs less frequently:
- Bladder infection (painful or burning urination, frequent urge to urinate).

The following side effects can occur but the frequencies are not known:
- Yellowing of your skin and eyes, also called jaundice or liver failure.
- Chest pain.
- Changes in the way your heart beats (beating faster than normal).
- Stroke (weakness, loss of sensation, slurred speech, difficult movement, loss of sight).
- Unexplained bruising, pin point bleeds on your skin, nosebleeds or bleeding gums.
- Inhalation of foreign material (such as food, mucus or saliva) causing infection of your lungs (chest pain, shortness of breath, wheezing, cough with sputum, blood or odour).
- Seizures.
- Neuroleptic malignant syndrome (NMS) (fever, tight/stiff muscles, altered mental status (feeling confused, agitated or disoriented), changes in the way your heart beats, changes in your pulse rate or blood pressure and increased sweating).
- Tardive dyskinesia (uncontrolled and repetitive movements of your lips, tongue, face, arms or legs, or excessive blinking of your eyes).
- Severe, painful, blistering skin rash known as Stevens-Johnson syndrome.
- Kidney failure (weakness, tiredness, nausea, vomiting or changes in the amount of urine).

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

Tell your doctor as soon as possible if you notice any of the following:
The following side effects occur more frequently:
- Feeling confused or agitated.
- Hallucinations (seeing, hearing or sensing things that are not real).
- Difficulty sleeping (insomnia).
- Headache or dizziness.
- Coughing.
- Inflicted injury.

The following side effects occur less frequently:
- Anorexia (severe weight loss).
- Feeling depressed or anxious.
- Drowsiness.
- Changes in the way you walk.
- Involuntary muscle movements.
- Carpal tunnel syndrome (numbness, pain or tingling in your hand or arm).
- Restlessness.
- High blood pressure.
- Claudication (pain or cramping in your lower legs while walking or exercising).
- Nausea (feeling sick) or vomiting (being sick).
- Constipation or diarrhoea.
- Increased muscle tone or spams.
- Joint or back pain.
- Increased sex drive.
- Swelling of your hands, feet, arms or legs due to water retention.
- Tiredness.
- Flu-like symptoms (headache, aching muscles, tiredness).
- Generalised pain.

The following side effects can occur but the frequencies are not known:
- High fat levels in your blood when tests are done.
- Pancreatitis (pain of your stomach are radiating to your back).
- Low blood sugar levels (confusion, dizziness, headaches, pale skin and increased heartrate).
- Intestinal obstruction caused by slow bowel movements (cramping, bloating, inability to go to the bathroom, nausea or vomiting).
- Stomach upset.
- Difficulty swallowing.
- Heartburn.
- Bone fracture.
- Inability to develop or maintain an erection.
- General discomfort.

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

6. STORING AND DISPOSING OF MEMINIST 10
- Store at or below 25 °C.
- Keep blister strips in outer carton until required for use.
- **STORE ALL MEDICINES OUT OF REACH OF CHILDREN.**
- Do not use after the expiry date printed on the label or carton.
- Return all unused medicine to your pharmacist.
- Do not dispose unused medicine in drains and sewerage systems (e.g. toilets).

7. PRESENTATION OF MEMINIST 10
Clear transparent triplex (PVC/PE/PVDC) film blister strips with aluminium foil containing 10 tablets. Six blister strips are packed in an outer carton.

8. IDENTIFICATION OF MEMINIST 10
Off white, capsule shaped, biconvex, film-coated tablets, debossed with "M" and 10 on either side of the break line on one side and break line on other side.

9. REGISTRATION NUMBER
46/5.11/0427

10. NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
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11. MARKETED BY
Forrester Pharma (Pty) Ltd.
13 Pasita Street, Rosen Heights, Rosen Park, Bellville, 7530

12. DATE OF PUBLICATION

FORRESTER PHARMA

LI0051/15A

VOUBILJET VIR MEMINIST 10

SKEDULERINGSTATUS
S4

EIENDOMSNAAM EN DOSEERVORM
MEMINIST 10 filmbedekte tablette

SAMESTELLING
Aktiewe bestanddeel:
Elke filmbedekte tablet bevat 10 mg memantienhidrochloried.
Onaktiewe bestanddele:
Kolloïdale anhidriese silika, krospovidoon, hipromellose, magnesiumstearaat, mikrokristallyne sellulose, poliëtileenglikol, povidoon, gesuiwerde talk en titaandioksied.
Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE
A 5.11 Medisynes wat outonomiese funksie beïnvloed. Ander.

FARMAKOLOGIESE WERKING
Farmakodinamiese eienskappe
Memantien is 'n volt-afhanklike, nie-kompeterende antagonis van die NMDA-tipe glutamaatreseptor met matige affiniteit. Dit blokkeer die effekte van patologies verhoogde toniese vlakke van glutamaat wat mag lei tot neuronale disfunksie. Memantien het wisselwerking met die Mg^{2+}-bindingsetel van die kanaal om sodoende oormatige aktivering te voorkom, terwyl dit normale funksie behou. Toenemende bewyse dui daarop dat wanfunksionering van glutamatergiese neuro-oordrag, in besonder by *N*-metiel-D-aspartaat (NMDA)-reseptore, bydra tot sowel uitdrukking van simptome en siekteprogressie in neurodegeneratiewe demensie.

Farmakokinetiese eienskappe
Absorpsie:
Die absolute biobeskikbaarheid van memantien is ongeveer 100 %. Piek plasmakonsentrasies word tussen 3 – 8 uur bereik. Daar is geen aanduiding dat voedsel die absorpsie van memantien beïnvloed nie.

Lineariteit:
Die farmakokinetika van memantien is lineêr in die dosisreikwydte van 10 – 40 mg.

Verspreiding:
Die volume van verspreiding is ongeveer 10 l/kg. Sowat 45 % van die memantien is gebind aan plasmaproteïen.

Biotransformasie:
Ongeveer 80 % van die sirkulerende memantien-verwante materiaal is teenwoordig as die moederverbinding. Die belangrikste metaboliete is *N*-3,5-dimetiel-gludantaan, die isomeriese mengsel van 4- en 6-hidroksimemantien, en 1-nitroso-3,5-dimetiel-adamantaan. Geen van hierdie metaboliete vertoon NMDA-antagonistiese werking nie, en *in vitro* is geen metabolisme gekataliseer deur P450 waargeneem nie.

Eliminasie:
Memantien word op 'n mono-eksponensiële wyse geëlimineer, met 'n terminale halfleeftyd van 60 – 100 uur. Die totale opruiming van memantien beloop 170 ml/min/1,73 m^2 en totale renale opruiming word gedeeltelik deur tubulêre sekresie bereik. Hantering deur die niere behels tubulêre herabsorpsie en word waarskynlik deur katioontransportproteïene bemiddel. Renale eliminasie van memantien mag onder alkaliese toestande verminder word (kyk **WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS**).

Spesiale bevolkingsgroepe:
Renale belemmering:
'n Beduidende korrelasie tussen kreatinienopruiming en totale renale opruiming van memantien is waargeneem in bejaarde pasiënte met normale en verminderde nierfunksie (kreatinienopruiming van 50 – 100 ml/min/1,73 m^2) (kyk **DOSIS EN GEBRUIKSAANWYSINGS**).

Hepatiese belemmering:
Die uitwerking van lewerbelemmering op die farmakokinetika van memantien is nie geëvalueer nie. Aangesien memantien slegs in 'n klein mate gemetaboliseer word, en na metaboliete met geen NMDA-antagonistiese werking nie, word nie verwag dat die farmakokinetika van memantien klinies betekenisvolle veranderings in pasiënte met ligte tot matige lewerbelemmering sal veroorsaak nie.

INDIKASIES
MEMINIST 10 word aangedui vir die behandeling van pasiënte met matige tot ernstige Alzheimer se siekte. Effektiwiteit vir 'n tydperk langer as 6 maande, is nie bepaal nie.

KONTRA-INDIKASIES
- Hipersensitiwiteit vir memantien of enige van die onaktiewe bestanddele in **MEMINIST 10** (kyk **SAMESTELLING**).
- Kinders en adolessente jonger as 18 jaar, aangesien veiligheid en doeltreffendheid nie bepaal is nie.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS
MEMINIST 10 terapie word nie aanbeveel vir pasiënte met ernstige renale belemmering nie (kreatinienopruiming minder as 9 ml/min/1,73 m^2), aangesien daar geen data beskikbaar is nie (kyk **DOSIS EN GEBRUIKSAANWYSINGS**).

Onder alkaliese toestande is die tempo van eliminasie van **MEMINIST 10** verlaag (kyk **Farmakokinetiese eienskappe**). Faktore wat die pH van die urine kan verhoog mag dit dus nodig maak om die pasiënt noukeurig te moniteer. Hierdie faktore sluit in drastiese veranderings in die dieet, bv. van 'n dieet ryk aan vleisprodukte na 'n vegetariese dieet, of 'n baie groot inname van alkaliserende gastriese buffers. Urinêre pH kan ook styg weens toestande van renale tubulêre asidose (RTA) of erge infeksies van die urienweg met *Proteus* bakterieë.

Versigtigheid word aanbeveel in pasiënte met 'n risiko vir konvulsies.

Gelyktydige gebruik van *N*-metiel-D-aspartaat (NMDA)-antagoniste, soos amantadien, ketamien of dekstrometorfaan, saam met **MEMINIST 10** moet vermy word. Hierdie verbindings werk by dieselfde reseptorsisteem as **MEMINIST 10**, en gevolglik mag newe-effekte (hoofsaaklik verwant aan die sentrale senuweesisteem (SSS)) meer dikwels en meer uitgesproke wees (kyk **INTERAKSIES**).
Beperkte data is beskikbaar vir pasiënte met onlangse miokardiale infarksie, kongestiewe hartversaking (NYHA III-IV) en ongekontroleerde hipertensie. Hierdie pasiënte moet noukeurig gemoniteer word.

Effekte op die vermoë om te bestuur en masjiene te gebruik
MEMINIST 10 mag reaksievermoë verander en buitepasiënte moet gewaarsku word om spesiale sorg te neem wanneer 'n voertuig bestuur of masjinerie hanteer word. Matige tot erge Alzheimer se siekte veroorsaak ook belemmering van bestuursvermoë en die vermoë om masjinerie te gebruik.

INTERAKSIES
- Die effekte van L-dopa, dopaminergiese agoniste en anticholinergiese middels mag versterk word deur gelyktydige behandeling met **MEMINIST 10**.
- Die uitwerking van barbiturate en neuroleptiese middels mag verminder word gedurende gelyktydige behandeling met **MEMINIST 10**.
- **MEMINIST 10** mag die effekte van die antispasmodiese middels dantroleen en baklofeen wysig, en 'n aanpassing van die dosis mag nodig wees.
- Die gebruik van ander NMDA-antagoniste, soos amantadien, ketamien of dekstrometorfaan saam met **MEMINIST 10** moet vermy word, aangesien dit die insidensie en ernstigheidsgraad van farmatoksiese psigose kan verhoog.
- Medisynes soos simetidien, ranitidien, prokaïenamied, kinidien, kinien en nikotien, wat dieselfde renale katioontransportsisteem as amantadien gebruik, mag ook wisselwerking met **MEMINIST 10** toon, met 'n potensiële risiko van verhoogde plasmavlakke.
- **MEMINIST 10** verminder die area onder die kurwe (AOK) en piek plasmakonsentrasie (C_{maks}) van hidrochloortiasied met 20 %.

SWANGERSKAP EN BORSVOEDING
Die veiligheid en doeltreffendheid van **MEMINIST 10** is nie by swanger en borsvoedende vrouens bepaal nie.

DOSIS EN GEBRUIKSAANWYSINGS
'n Mediese praktisyn ervare in die diagnose en behandeling van Alzheimer se demensie, moet die behandeling begin en toesig hou daaroor. Terapie moet slegs begin word indien 'n versorger beskikbaar is wat die pasiënt se medisyne-inname gereeld sal moniteer. Diagnose moet volgens huidige riglyne gemaak word.

Volwassenes:
Die maksimum daaglikse dosis is 20 mg per dag.
Ten einde die risiko van newe-effekte te verminder, word die instandhoudingsdosis deur opwaartse titrasie van 5 mg per week oor die eerste 3 weke soos volg bereik:
Behandeling moet met 5 mg daagliks ('n halwe tablet soggens) gedurende die 1ste week begin word. In die 2de week word 10 mg per dag ('n halwe tablet twee keer per dag) en in die 3de week 15 mg per dag (een tablet in die oggend en 'n halwe tablet in die middag) aanbeveel. Van die 4de week verderaan, kan behandeling voortgesit word met die aanbevole instandhoudingsdosis van 20 mg per dag (een tablet twee keer per dag).

Die tablette kan met of sonder kos geneem word.

Bejaardes:
Die aanbevole dosis vir pasiënte > 65 jaar is 20 mg per dag (10 mg twee keer per dag) soos hierbo beskryf.

Renale belemmering:
In pasiënte met normale tot ligte belemmering van nierfunksie (serumkreatinienvlakke van tot 130 μmol/l) is geen dosisaanpassing nodig nie.
In pasiënte met matige nierfunksiebelemmering (kreatinienopruiming 40 – 60 ml/min/1,73 m^2) moet die dosis verminder word na 10 mg per dag.
Geen data is beskikbaar vir pasiënte met ernstig verminderde nierfunksie nie (kyk **WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS**).

Hepatiese belemmering:
Daar is geen data beskikbaar vir die gebruik van **MEMINIST 10** by pasiënte met hepatiese belemmering nie.

NEWE-EFFEKTE
Bloed- en limfsisteemversteurings
Frekwensie onbekend: Trombositopenie

Endokriene versteurings
Frekwensie onbekend: *Akute pankreatitis, hipoglisemie*

Metabolisme en voedingsversteurings
Minder dikwels: Anoreksie
Frekwensie onbekend: Hiperlipidemie

Psigiatriese versteurings
Dikwels: Prikkelbaarheid, hallusinasies, slaaploosheid
Minder dikwels: Depressie, slaperigheid

Senuweesisteemversteurings
Dikwels: Verwarring, duiseligheid, hoofpyn
Minder dikwels: Angstigheid, abnormale loopgang
Frekwensie onbekend: Diskinesie, grand mal konvulsies, neuroleptiese kwaadaardige sindroom, tardiewe diskinesie, karpaletonnelsindroom, rusteloosheid

Kardiale versteurings
Frekwensie onbekend: Atrioventrikulêre blok, verlengde QT-interval, supraventrikulêre tagikardie, tagikardie

Vaskulêre versteurings
Minder dikwels: Hipertensie
Frekwensie onbekend: Serebrale infarksie, intrakraniale bloeding, kloudikasie

Respiratoriese, torakale en mediastinale versteurings
Dikwels: Hoes
Minder dikwels: Brongitis, dispnee, boonste lugweginfeksie
Frekwensie onbekend: Aspirasie-pneumonie

Gastro-intestinale versteurings
Minder dikwels: Braking, hardlywigheid, diarree, naarheid
Frekwensie onbekend: Ileus, kolitis, disfagie, gastritis, gastro-esofageale refluks

Hepatobiliêre versteurings
Frekwensie onbekend: Lewerversaking

Vel- en subkutane weefselversteurings
Frekwensie onbekend: Stevens-Johnsonsindroom

Muskuloskeletale, bindweefsel- en skeletbeenversteurings
Minder dikwels: Hipertonie (verhoogde spiertonus), artralgie, rugpyn
Frekwensie onbekend: Skeletbeenfraktuur

Nier- en urienwegversteurings
Dikwels: Urinêre inkontinensie
Minder dikwels: Sistitis, urienweginfeksie
Frekwensie onbekend: Akute nierversaking

Voortplantingstelsel- en borsversteurings
Minder dikwels: Verhoogde libido
Frekwensie onbekend: Impotensie

Algemene versteurings en toestande by die plek van toediening
Dikwels: Toegediende besering
Minder dikwels: Perifere edeem, moegheid, uitputting, griepagtige sindroom, pyn
Frekwensie onbekend: Borskaspyn, algemene gevoel van ongesteldheid

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN
Kyk **NEWE-EFFEKTE.**
Behandeling van oordosering moet simptomaties en ondersteunend wees.

IDENTIFIKASIE
Naaswit, kapsulevormige, bikonvekse, filmbedekte tablette, met "M" en 10 aan weerskante van die breeklyn aan die een kant ingepers en met 'n breeklyn aan die ander kant.

AANBIEDING
Helder, deursigtige tripleks (PVC/PE/PVDC) film stulpstroke met aluminiumfoelie wat 10 tablette bevat. Ses stulpstroke word in 'n buitenste karton verpak.

BEWARINGINSTRUKSIES
Bêre by of onder 25 °C.
Hou die stulpstroke in die buitenste karton tot nodig vir gebruik.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER
46/5.11/0427

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PASIËNTINLIGTINGSBLAD VIR MEMINIST 10

SKEDULERINGSTATUS
Skedule 4

EIENDOMSNAAM EN DOSEERVORM
MEMINIST 10 filmbedekte tablette

Lees asseblief hierdie hele inligtingsblad noukeurig voordat u begin om MEMINIST 10 te gebruik.
- Hou hierdie inligtingsblad. Dit mag nodig wees dat u dit later weer lees.
- Indien u verdere vrae het, vra asseblief u dokter of apteker.
- **MEMINIST 10** is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit mag skadelik wees vir hulle, selfs al het hulle dieselfde simptome as u.

1. WAT MEMINIST 10 BEVAT
Aktiewe bestanddeel:
Elke filmbedekte tablet bevat 10 mg memantienhidrochloried.

Onaktiewe bestanddele:
Kolloïdale anhidriese silika, krospovidoon, hipromellose, magnesiumstearaat, mikrokristallyne sellulose, poliëtileenglikol, povidoon, gesuiwerde talk en titaandioksied.
Suikervry.

2. WAARVOOR MEMINIST 10 GEBRUIK WORD
Alzheimer se siekte is 'n vorm van demensie wat 'n breinversteuring is wat 'n persoon se vermoë om daaglikse aktiwiteite uit te voer, negatief beïnvloed. **MEMINIST 10** word gebruik om die simptome van Alzheimer se siekte, soos belemmering van geheue, te behandel.

3. VOORDAT U MEMINIST 10 NEEM
Moenie MEMINIST 10 neem nie:
- Indien u allergies (hipersensitief) is vir memantien of vir enige van die bestanddele van **MEMINIST 10** (kyk **WAT MEMINIST 10 BEVAT**).

MEMINIST 10 moet nie in kinders en adolessente jonger as 18 jaar gebruik word nie.

Neem spesiale sorg met MEMINIST 10:
Voordat u **MEMINIST 10** neem, sê vir u dokter:
- Indien u 'n ernstige niervversteuring het.
- Indien u onlangs u dieet beduidend verander het (soos van 'n normale dieet na 'n vegetariese dieet) of beplan om dit te verander, indien u aan 'n toestand genaamd renale tubulêre asidose of RTA ly ('n oormaat suurvormende middels in die bloed weens 'n niervversteuring) of indien u ly aan ernstige urienweginfeksies, aangesien dit nodig mag wees dat u dokter die dosis van **MEMINIST 10** aanpas.
- Indien u ly aan epilepsie of 'n geskiedenis van stuiptrekkings of toevalle het.
- Indien u onlangs 'n hartaanval gehad het of 'n hartsteuring het.
- Indien u 'n geskiedenis van hoë en ongekontroleerde bloeddruk het.

Die neem van MEMINIST 10 met kos en drinkgoed:
MEMINIST 10 mag met of sonder kos geneem word.

Swangerskap en borsvoeding:
Indien u swanger is of u baba borsvoed, konsulteer asseblief u dokter, apteker of ander gesondheidsorgdeskundige voordat u **MEMINIST 10** neem.
Moenie MEMINIST 10 neem indien u swanger is, vermoed dat u swanger is of beplan om swanger te raak nie. Kontak u dokter onmiddellik.
Moenie MEMINIST 10 neem indien u u baba borsvoed nie.

Bestuur en die gebruik van masjinerie:
MEMINIST 10 mag u vermoë om 'n voertuig te bestuur en masjinerie te hanteer belemmer.
Moenie 'n voertuig bestuur, masjinerie hanteer of enigiets doen wat konsentrasie verg nie, totdat u weet hoe **MEMINIST 10** u beïnvloed.

Die neem van ander medisynes saam met MEMINIST 10:
Sê altyd vir u gesondheidsorgdeskundige indien u enige ander medisyne neem (dit sluit aanvullende of tradisionele medisynes in).
Sê veral vir u dokter indien u enige van die volgende medisynes neem:
- Dekstrometorfaan ('n tipe hoesmedisyne).
- Dantroleen, baklofeen (gebruik as spierverslappers).
- Simetidien, ranitidien (gebruik om maagsere of sooibrand te behandel).
- Hidrochloortiasied (waterpil of enige medisyne wat gebruik word om hoë bloeddruk te beheer in kombinasie met hidrochloortiasied).
- Anticholinergiese middels (gebruik om bewegingstoornisse of buikkrampe te behandel).
- Antikonvulsante (gebruik om stuiptrekkings of toevalle te voorkom en te verlig).
- Barbiturate (gebruik om slaap aan te help).
- Dopaminergiese agoniste, soos L-dopa (gebruik om Parkinson se siekte te behandel) of broomkriptien (gebruik om hoë vlakke van die hormoon prolaktien in u liggaam te behandel).
- Neuroleptika (gebruik in die behandeling van geestesteurings).
- Amantadien (gebruik om Parkinson se siekte te behandel).
- Ketamien (gebruik as anestetikum tydens chirurgie).
- Prokaïenamied of kinidien (gebruik om 'n abnormale hartklop te behandel).
- Kinien (gebruik om koors te verlaag en malaria te behandel).
- Nikotien (gebruik as 'n hulpmiddel om op te hou rook en onttrekkingsimptome te voorkom).

Nie al die medisynes wat wisselwerking met MEMINIST 10 mag hê word in hierdie inligtingsblad ingesluit nie.

4. HOE OM MEMINIST 10 TE NEEM
- Moenie medisyne wat vir u voorgeskryf is, met enigiemand anders deel nie.
- U versorger sal u help om u medikasie te neem presies soos wat u dokter voorgeskryf het. Maak seker by u dokter of apteker indien u twyfel.
- Wanneer die behandeling geïnisieer word, sal u dokter begin met 'n klein dosis en dan die dosis geleidelik verhoog. Dit help u dokter om seker te maak dat u die regte dosis kry om u toestand te help en enige ongewenste simptome te vermy.
- Die gewone dosis is:
- Week 1: 5 mg per dag ('n halwe tablet soggens).
- Week 2: 10 mg per dag ('n halwe tablet twee keer per dag).
- Week 3: 15 mg per dag (een tablet in die oggend en 'n halwe tablet in die middag).
- Week 4: 20 mg per dag (een tablet twee keer per dag).
- Die maksimum dosis is 20 mg per dag.
- U dokter sal u dosis dienooreenkomstig aanpas indien u bejaard is of aan matige nierprobleme ly.
- Verseker dat **MEMINIST 10** op dieselfde tyd elke dag geneem word en probeer om te vermy dat enige dosisse oorgeslaan word.
- U dokter sal vir u sê hoe lank u behandeling met **MEMINIST 10** sal duur. Indien u die indruk kry dat die uitwerking van **MEMINIST 10** te sterk of te swak is, lig u dokter of apteker daaroor in.

Indien u meer MEMINIST 10 neem as wat u moet:
In die geval van oordosering, raadpleeg u dokter of apteker so gou as moontlik. Indien nie een van hulle beskikbaar is nie, kontak die naaste hospitaal of gifsentrum. Neem hierdie inligtingsblad en enige oorblywende tablette saam met u, sodat die dokter kan sien wat u geneem het.

Indien u vergeet om MEMINIST 10 te neem:
Indien u 'n dosis oorgeslaan het en u onthou binne 'n paar uur, neem dit sou gou as moontlik en gaan dan voort met u normale skedule. Indien dit egter amper tyd is vir die volgende dosis, slaan die vergete dosis oor en neem u volgende dosis op die gewone tyd. Moet nie 'n dubbele dosis neem om te vergoed vir die dosis wat oorgeslaan is nie.

5. MOONTLIKE NEWE-EFFEKTE
MEMINIST 10 kan newe-effekte veroorsaak.
Nie alle newe-effekte wat vir MEMINIST 10 aangemeld is, is in hierdie inligtingsblad ingesluit nie. Indien u algemene gesondheid versleg of indien u enige ongunstige effekte ervaar terwyl u MEMINIST 10 neem, konsulteer asseblief u dokter, apteker of ander gesondheidsorgdeskundige.

Indien enige van die volgende gebeur, hou op om **MEMINIST 10** te neem en sê onmiddellik vir u dokter of gaan na die ongevalle-afdeling by u naaste hospitaal:
- Swelling van u hande, voete, enkels, gesig, mond of keel, wat probleme mag veroorsaak met sluk of asemhaling.
- Uitslag of gejeuk.
- Floutes.

Hierdie is alles baie ernstige newe-effekte. Indien u dit het, mag u 'n ernstige allergiese reaksie op **MEMINIST 10** gehad het. U mag dringende mediese sorg of hospitalisasie nodig hê.

Sê onmiddellik vir u dokter of gaan na die ongevalle-afdeling by u naaste hospitaal indien u enige van die volgende opmerk:
Die volgende newe-effekte het dikwels voorgekom:
- Kortasemheid.
- Verlies van blaasbeheer.

Die volgende newe-effek kom minder dikwels voor:
- Blaasinfeksie (pyn of brandgevoel met urinering, drang om dikwels te urineer).

Die volgende newe-effekte kan voorkom, maar die frekwensie daarvan is onbekend:
- Vergeling van u vel en oë, ook geelsug of lewerversaking genoem.
- Borskaspyn.
- Veranderings in die manier waarop u hart klop (klop vinniger as gewoonlik).
- Beroerte (swakheid, verlies aan sensasie, sleepspraak, moeilike beweging, sigverlies).
- Onverklaarbare kneusing, speldpuntbloedings op u vel, neusbloedings of bloeiende tandvleise.
- Inaseming van vreemde materiaal (soos voedsel, slym of speeksel) wat longinfeksie (borskaspyn, kortasemheid, gehyg, hoes met sputum, bloed of slegte reuk) veroorsaak.
- Stuiptrekkings/toevalle.
- Neuroleptiese kwaadaardige sindroom (NKS) (koors, stywe spiere, gewysigde geestestoestand (voel verward, prikkelbaar of gedisoriënteer), veranderings in die manier wat u hart klop, veranderings in u polsspoed of bloeddruk en 'n toename in sweetafskeiding).
- Tardiewe diskinesie (ongekontroleerde en herhalende bewegings van u lippe, tong, gesig, arms of bene, of oormatige knip van die oë).
- Erge, pynlike, blaasvormende uitslag van die vel, bekend as Stevens-Johnsonsindroom.
- Niervversaking (swakheid, moegheid, naarheid, braking of veranderings in die hoeveelheid urine).

Hierdie is alles ernstige newe-effekte. U mag dringende mediese aandag nodig hê.

Sê so gou as moontlik vir jou dokter indien jy enige van die volgende opmerk:
Die volgende newe-effekte kom meer dikwels voor:
- Voel verward of rusteloos.
- Hallusinasies (sien, hoor of voel goed wat nie werklik is nie).
- Probleme om te slaap (insomnie/slaaploosheid).
- Hoofpyn of duiseligheid.
- Hoes.
- Toegediende besering.

Die volgende newe-effekte kom minder dikwels voor:
- Anoreksie (erge gewigsverlies).
- Voel depressief of angstig.
- Lomerigheid.
- Veranderings in die manier waarop u loop.
- Onwillekeurige spierbewegings.
- Karpaletonnelsindroom (gevoelloosheid, pyn of tintelende gevoel in u hand of arm).
- Rusteloosheid.
- Hoë bloeddruk.
- Kloudikasie (pyn of krampe in u onderbene terwyl u loop of oefen).
- Naarheid of braking.
- Hardlywigheid of diarree.
- Verhoogde spiertonus of spasmas.
- Gewrig- of rugpyn.
- Verhoogde libido.
- Swelling van u hande, voete, arms of bene weens vogterughouding.
- Moegheid.
- Griepagtige simptome (hoofpyn, seer spiere, moegheid).
- Algemene pyn.

Die volgende newe-effekte kan voorkom maar die frekwensie daarvan is onbekend:
- Hoë vlakke van vette in u bloed wanneer toetse gedoen word.
- Pankreatitis (pyn in die maagarea wat versprei na die rug toe).
- Lae bloedsuikervlakke (verwarring, duiseligheid, hoofpyn, bleek vel en verhoogde hartklop).
- Intestinale obstruksie veroorsaak deur stadige dermbewegings (krampe, opgeblasenheid, maag wil nie werk nie, naarheid of braking).
- Omgekrapte maag.
- Probleme om te sluk.
- Sooibrand.
- Beenfraktuur.
- Onvermoë om 'n ereksie te kry of in stand te hou.
- Algemene gevoel van ongemak.

Indien u enige newe-effekte waarneem wat nie in hierdie inligtingsblad genoem word nie, lig asseblief u dokter of apteker in.

6. BERGING EN WEGDOENING VAN MEMINIST 10
- Bêre by of onder 25 °C.
- Hou die stulpstroke in die buitenste karton tot nodig vir gebruik.
- **STOOR ALLE MEDISYNES BUITE BEREIK VAN KINDERS.**
- Moenie gebruik ná die vervaldatum wat op die etiket of karton gedruk is nie.
- Neem alle ongebruikte medisyne terug na jou apteker.
- Moenie ongebruikte medisyne in dreine en rioolsisteme (bv. toilette) weggooi nie.

7. AANBIEDING VAN MEMINIST 10
Helder, deursigtige tripleks (PVC/PE/PVDC) film stulpstroke met aluminiumfoelie wat 10 tablette bevat. Ses stulpstroke word in 'n buitenste karton verpak.

8. IDENTIFIKASIE VAN MEMINIST 10
Naaswit, kapsulevormige, bikonvekse, filmbedekte tablette, met "M" en 10 aan weerskante van die breeklyn aan die een kant ingepers en met 'n breeklyn aan die ander kant.

9. REGISTRASIENOMMER
46/5.11/0427

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