SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

<Product name> 10 mg/ml oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution contains 10 mg of memantine hydrochloride equivalent to 8.31 mg memantine.

Excipient with known effect: Each one millilitre of solution contains 100.25 mg sorbitol (E420).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.
The solution is clear, colourless to light yellowish and odourless.

Kommentiert [OM1]: V_IB_B.II.d.1.z. (PL/H/0405/001/IB/006) Change of the specification of Appearance of the finished product submitted parallel

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of patients with moderate to severe Alzheimer's disease.

4.2 Posology and method of administration

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Posology

Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. Therapy should only be started if a caregiver is available who will regularly monitor the intake of the medicinal product by the patient. Diagnosis should be made according to current guidelines. The tolerance and dosing of memantine should be reassessed on a regular basis, preferably within three months after start of treatment. Thereafter, the clinical benefit of memantine and the patient's tolerance of treatment should be reassessed on a regular basis according to current clinical guidelines. Maintenance treatment can be continued for as long as a therapeutic benefit is favourable and the patient tolerates treatment with memantine. Discontinuation of memantine should be considered when evidence of a therapeutic effect is no longer present or if the patient does not tolerate treatment.

~~Posology~~

Adults:
Dose titration
The maximum daily dose is 20 mg once daily. In order to reduce the risk of undesirable effects the maintenance dose is achieved by upward titration of 5 mg per week over the first 3 weeks as follows:

Week 1 (day 1-7):
The patient should take 0.5 ml solution (5 mg) per day for 7 days.

Week 2 (day 8-14):

The patient should take 1 ml solution (10 mg) per day for 7 days.

Week 3 (day 15-21):
The patient should take 1.5 ml solution (15 mg) per day for 7 days.

From Week 4 on:
The patient should take 2 ml solution (20 mg) once a day.

Maintenance dose
The recommended maintenance dose is 20 mg (2 ml solution) per day.

Older people~~: Elderly~~: On the basis of the clinical studies, the recommended dose for patients over the age of 65 years is 20 mg per day (2 ml solution) as described above.

~~*Paediatric population:* <Product name> is not recommended for use in children below 18 years due to a lack of data on safety and efficacy.~~

Hepatic impairment: In patients with mild or moderate hepatic impaired function (Child-Pugh A and Child-Pugh B) no dose adjustment is needed. No data on the use of memantine in patients with severe hepatic impairment are available. Administration of <Product name> in patients with severe hepatic impairment is not recommended.

Children and adolescents: <Product name>~~ Axura~~ is not recommended for use in children below 18 years due to a lack of data on safety and efficacy.~~—~~
~~to a lack of data on safety and efficacy.~~

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Method of administration
<Product name> should be taken once daily at the same time each day. The solution can be taken with or without food. The solution must not be poured into the mouth directly from the bottle or the syringe, but should be dosed onto a spoon or into a glass of water using the syringe. For detailed instructions on the preparation and handling of the product see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Caution is recommended in patients with epilepsy, former history of convulsions or patients with predisposing factors for epilepsy.

Concomitant use of other N-methyl-D-aspartate (NMDA)-antagonists such as amantadine, ketamine or dextromethorphan should be avoided. These compounds act at the same receptor system as memantine, and therefore adverse reactions (mainly central nervous system (CNS)-related may be more frequent or more pronounced (see also section 4.5).

Some factors that may raise urine pH (see section 5.2 “Elimination”) may necessitate careful monitoring of the patient. These factors include drastic changes in diet, e.g. from a carnivore to a vegetarian diet, or a massive ingestion of alkalising gastric buffers. Also, urine pH may be elevated by states of renal tubulary acidosis (RTA) or severe infections of the urinary tract with *Proteus bacteria*.

In most clinical trials, patients with recent myocardial infarction, uncompensated congestive heart failure (NYHA III-IV), or uncontrolled hypertension were excluded. As a consequence,

only limited data are available and patients with these conditions should be closely supervised.

Excipients: The oral solution contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Due to the pharmacological effects and the mechanism of action of memantine the following interactions may occur:

- The mode of action suggests that the effects of L-dopa, dopaminergic agonists, and anticholinergics may be enhanced by concomitant treatment with NMDA-antagonists such as memantine. The effects of barbiturates and neuroleptics may be reduced. Concomitant administration of memantine with the antispasmodic agents, dantrolene or baclofen, can modify their effects and a dose adjustment may be necessary.
- Concomitant use of memantine and amantadine should be avoided, owing to the risk of pharmacotoxic psychosis. Both compounds are chemically related NMDA-antagonists. The same may be true for ketamine and dextromethorphan (see also section 4.4). There is one published case report on a possible risk also for the combination of memantine and phenytoin.
- Other active substances such as cimetidine, ranitidine, procainamide, quinidine, quinine and nicotine that use the same renal cationic transport system as amantadine may also possibly interact with memantine leading to a potential risk of increased plasma levels.
- There may be a possibility of reduced serum level of hydrochlorothiazide (HCT) when memantine is co-administered with HCT or any combination with HCT.
- In post-marketing experience isolated cases with international normalized ratio (INR) increases have been reported in patients concomitantly treated with warfarin. Although no causal relationship has been established, close monitoring of prothrombin time or INR is advisable for patients concomitantly treated with oral anticoagulants.

In single-dose pharmacokinetic (PK) studies in young healthy subjects no relevant active substance-active substance interaction of memantine with glyburide/metformin or donepezil was observed.

In a clinical study in young healthy subjects no relevant effect of memantine on the pharmacokinetics of galantamine was observed.

Memantine did not inhibit CYP 1A2, 2A6, 2C9, 2D6, 2E1, 3A, flavin containing monooxygenase, epoxide hydrolase or sulphation *in vitro*.

4.6 Fertility, pregnancy and lactation

Pregnancy
For memantine, no clinical data on exposed pregnancies are available. Animal studies indicate a potential for reducing intrauterine growth at exposure levels, which are identical or slightly higher than at human exposure (see section 5.3). The potential risk for humans is unknown. Memantine should not be used during pregnancy unless clearly necessary.

Breastfeeding
It is not known whether memantine is excreted in human breast milk but, taking into consideration the lipophilicity of the substance, this probably occurs. Women taking memantine should not breast-feed.

Fertility
No adverse effects of memantine were noted on non-clinical male and female fertility studies.

4.7 Effects on ability to drive and use machines

Moderate to severe Alzheimer's disease usually causes impairment of driving performance and compromises the ability to use machinery. Furthermore, memantine has minor or moderate influence on the ability to drive and use machines such that outpatients should be warned to take special care.

4.8 Undesirable effects

Summary of the safety profile

Formatiert: Englisch (USA)

In clinical trials in mild to severe dementia, involving 1,784 patients treated with memantine and 1,595 patients treated with placebo, the overall incidence rate of adverse reactions with memantine did not differ from those with placebo; the adverse reactions were usually mild to moderate in severity. The most frequently occurring adverse reactions with a higher incidence in the memantine group than in the placebo group were dizziness (6.3% vs 5.6%, respectively), headache (5.2% vs 3.9%), constipation (4.6% vs 2.6%), somnolence (3.4% vs 2.2%) and hypertension (4.1% vs 2.8%).
The following Adverse Reactions listed in the Table below have been accumulated in clinical studies with memantine and since its introduction in the market. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Tabulated list of adverse reactions

Formatiert: Englisch (USA)

Adverse reactions are ranked according to system organ class, using the following convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to < 1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Infections and infestations	
Uncommon	Fungal infections
Immune system disorders	
Common	Drug hypersensitivity
Psychiatric disorders	
Common	Somnolence
Uncommon	Confusion Hallucinations[1]
Not known	Psychotic reactions[2]
Nervous system disorders	
Common	Dizziness Balance disorder
Uncommon	Gait abnormal
Very rare	Seizures
Cardiac disorders	
Uncommon	Cardiac failure

Vascular disorders	
Common	Hypertension
Uncommon	Venous thrombosis/thromboembolism
Respiratory, thoracic and mediastinal disorders	
Common	Dyspnoea ~~disorders~~
Gastrointestinal disorders	
Common	Constipation
Uncommon	Vomiting
Not known	Pancreatitis[2]
Hepatobiliary disorders	
Common	Elevated liver function test
Not known	Hepatitis
General disorders and administration site conditions	
Common	Headache ~~site conditions~~
Uncommon	Fatigue

[1] Hallucinations have mainly been observed in patients with severe Alzheimer´s disease.

[2] Isolated cases reported in post-marketing experience

Alzheimer's disease has been associated with depression, suicidal ideation and suicide. In post- marketing experience these events have been reported in patients treated with memantine.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system <to be completed nationally>.

4.9 Overdose

Only limited experience with overdose is available from clinical studies and post-marketing experience.

Symptoms: Relative large overdoses (200 mg and 105 mg/day for 3 days, respectively) have been associated with either only symptoms of tiredness, weakness and/or diarrhoea or no symptoms. In the overdose cases below 140 mg or unknown dose the patients revealed symptoms from central nervous system (confusion, drowsiness, somnolence, vertigo, agitation, aggression, hallucination and gait disturbance) and/or gastrointestinal origin (vomiting and diarrhoea).

In the most extreme case of overdose, the patient survived the oral intake of a total of 2000 mg memantine with effects on the central nervous system (coma for 10 days, and later diplopia and agitation). The patient received symptomatic treatment and plasmapheresis. The patient recovered without permanent sequelae.

In another case of a large overdose, the patient also survived and recovered. The patient had received 400 mg memantine orally. The patient experienced central nervous system symptoms such as restlessness, psychosis, visual hallucinations, proconvulsiveness, somnolence, stupor, and unconsciousness.

Treatment: In the event of overdose, treatment should be symptomatic. No specific antidote for intoxication or overdose is available. Standard clinical procedures to remove active substance material, e.g. gastric lavage, carbo medicinalis (interruption of potential entero-hepatic recirculation), acidification of urine, forced diuresis should be used as appropriate.

In case of signs and symptoms of general central nervous system (CNS) overstimulation, careful symptomatic clinical treatment should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Anti-dementia drugs, ATC code: N06DX01.

There is increasing evidence that malfunctioning of glutamatergic neurotransmission, in particular at NMDA-receptors, contributes to both expression of symptoms and disease progression in neurodegenerative dementia.

Memantine is a voltage-dependent, moderate-affinity uncompetitive NMDA-receptor antagonist. It modulates the effects of pathologically elevated tonic levels of glutamate that may lead to neuronal dysfunction.

Clinical studies:
A pivotal monotherapy study in a population of patients suffering from moderate to severe Alzheimer's disease (mini mental state examination (MMSE) total scores at baseline of 3 - 14) included a total of 252 outpatients. The study showed beneficial effects of memantine treatment in comparison to placebo at 6 months (observed cases analysis for the clinician´s interview based impression of change (CIBIC-plus): p=0.025; Alzheimer´s disease cooperative study – activities of daily living (ADCS-ADLsev): p=0.003; severe impairment battery (SIB): p=0.002).

A pivotal monotherapy study of memantine in the treatment of mild to moderate Alzheimer's disease (MMSE total scores at baseline of 10 to 22) included 403 patients. Memantine-treated patients showed a statistically significantly better effect than placebo-treated patients on the primary endpoints: Alzheimer´s disease assessment scale (ADAS-cog) (p=0.003) and CIBIC-plus (p=0.004) at week 24 last observation carried forward (LOCF). In another monotherapy study in mild to moderate Alzheimer's disease a total of 470 patients (MMSE total scores at baseline of 11-23) were randomised. In the prospectively defined primary analysis statistical significance was not reached at the primary efficacy endpoint at week 24.

A meta-analysis of patients with moderate to severe Alzheimer's disease (MMSE total scores <–20) from the six phase III, placebo-controlled, 6-month studies (including monotherapy studies and studies with patients on a stable dose of acetylcholinesterase inhibitors) showed that there was a statistically significant effect in favour of memantine treatment for the cognitive, global, and functional domains. When patients were identified with concurrent worsening in all three domains, results showed a statistically significant effect of memantine in preventing worsening, as twice as many placebo-treated patients as memantine-treated patients showed worsening in all three domains (21% vs. 11%, p<0.0001).

5.2 Pharmacokinetic properties

Absorption: Memantine has an absolute bioavailability of approximately 100%. t_{max} is between 3 and 8 hours. There is no indication that food influences the absorption of memantine.

Distribution: Daily doses of 20 mg lead to steady-state plasma concentrations of memantine ranging from 70 to 150 ng/ml (0.5 - 1 µmol) with large interindividual variations. When daily doses of 5 to 30 mg were administered, a mean cerebrospinal fluid (CSF)/serum ratio of 0.52 was calculated. The volume of distribution is around 10 l/kg. About 45% of memantine is bound to plasma-proteins.

Biotransformation: In man, about 80% of the circulating memantine-related material is present as the parent compound. Main human metabolites are N-3,5-dimethyl-gludantan, the isomeric mixture of 4- and 6-hydroxy-memantine, and 1-nitroso-3,5-dimethyl-adamantane. None of these metabolites exhibit NMDA-antagonistic activity. No cytochrome P 450 catalysed metabolism has been detected *in vitro.*

In a study using orally administered ^{14}C-memantine, a mean of 84% of the dose was recovered within 20 days, more than 99% being excreted renally.

Elimination: Memantine is eliminated in a monoexponential manner with a terminal $t_{½}$ of 60 to 100 hours. In volunteers with normal kidney function, total clearance (Cl_{tot}) amounts to 170 ml/min/1.73 m² and part of total renal clearance is achieved by tubular secretion.

Renal handling also involves tubular reabsorption, probably mediated by cation transport proteins. The renal elimination rate of memantine under alkaline urine conditions may be reduced by a factor of 7 to 9 (see section 4.4). Alkalisation of urine may result from drastic changes in diet, e.g. from a carnivore to a vegetarian diet, or from the massive ingestion of alkalising gastric buffers.

Linearity: Studies in volunteers have demonstrated linear pharmacokinetics in the dose range of 10 to 40 mg.

Pharmacokinetic/pharmacodynamic relationship: At a dose of memantine of 20 mg per day the CSF levels match the k_i-value (k_i = inhibition constant) of memantine, which is 0.5 µmol in human frontal cortex.

5.3 Preclinical safety data

In short term studies in rats memantine like other NMDA-antagonists have induced neuronal vacuolisation and necrosis (Olney lesions) only after doses leading to very high peak serum concentrations. Ataxia and other preclinical signs have preceded the vacuolisation and necrosis. As the effects have neither been observed in long term studies in rodents nor in non-rodents, the clinical relevance of these findings is unknown.

Ocular changes were inconsistently observed in repeat dose toxicity studies in rodents and dogs, but not in monkeys. Specific ophthalmoscopic examinations in clinical studies with memantine did not disclose any ocular changes.

Phospholipidosis in pulmonary macrophages due to accumulation of memantine in lysosomes was observed in rodents. This effect is known from other active substances with cationic amphiphilic properties. There is a possible relationship between this accumulation and the

vacuolisation observed in lungs. This effect was only observed at high doses in rodents. The clinical relevance of these findings is unknown.

No genotoxicity has been observed following testing of memantine in standard assays. There was no evidence of any carcinogenicity in life long studies in mice and rats. Memantine was not teratogenic in rats and rabbits, even at maternally toxic doses, and no adverse effects of memantine were noted on fertility. In rats, foetal growth reduction was noted at exposure levels, which are identical or slightly higher than at human exposure.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potassium sorbate (E202)
Sorbitol, liquid 70 % (non crystallising) (E420)
Water, purified

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.
Once opened, the contents of the bottle should be used within 6 months.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Amber glass bottles (Type III) with a screw cap (Polyethylene) and graduated oral syringe (Polypropylene) and oral syringes adaptor (Polyethylene). The glass bottles of <Product name> containing 50 ml or 100 ml solution, are packed in cardboard boxes containing a 2 ml oral syringe graduated from 0.5 ml to 2.0 ml in increments of 0.5 ml and an adaptor for the syringe.

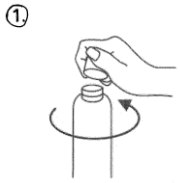
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

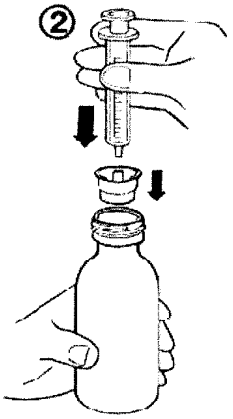
Any unused product or waste material should be disposed of in accordance with local requirements.

The solution must not be poured directly into the mouth from the bottle or syringe. Transfer the dose onto a spoon or into a glass of water.

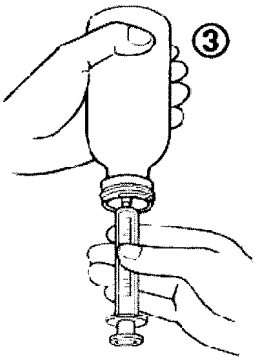
- Opening the bottle: Twist the cap anticlockwise to open (Fig. 1).



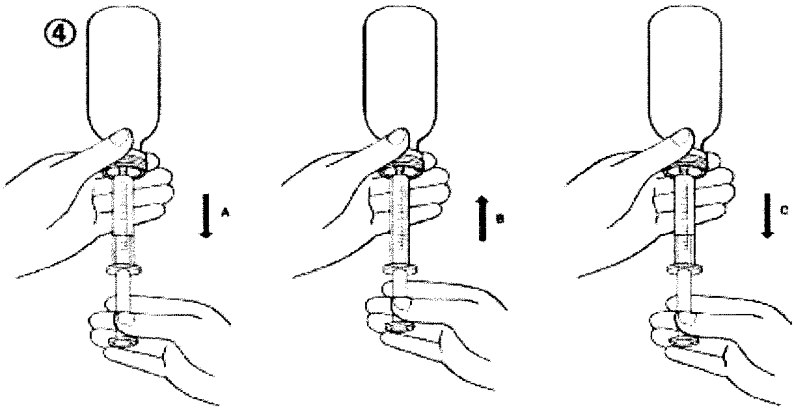
- Insert the oral syringe adaptor into the bottle neck (Fig. 2). Make sure that the adaptor is tightly fitted.
- Take the oral syringe and insert it into the adaptor opening (Fig. 2).



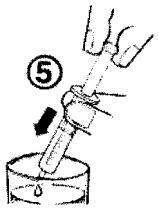
- Turn the bottle upside down (Fig. 3).



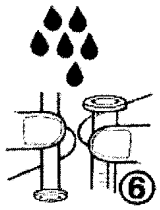
- Fill the oral syringe with a small amount of solution, by slightly pulling out the plunger (Fig. 4A). Then, press the plunger back in to remove any air bubbles (Fig. 4B). Next, pull the plunger up to the mark in millilitres (ml) corresponding to the dose prescribed by the doctor (Fig. 4C).



- Turn the bottle the right way up. Remove the oral syringe from the adaptor.
- Empty the contents of the oral syringe onto a spoon or into a glass of water, by pushing the plunger as far as it will go into the oral syringe (Fig. 5).



- Drink the entire contents of the glass or spoon.
- Rinse out the oral syringe with water only (Fig. 6).



- Close the bottle with the screw closure.

The solution must not be poured directly into the mouth from the bottle or syringe. Transfer the dose onto a spoon or into a glass of water.

- Opening the bottle: Press down on the screw closure and twist it anticlockwise (Fig. 1).

7. MARKETING AUTHORISATION HOLDER

<To be completed nationally>

8. MARKETING AUTHORISATION NUMBER(S)

<To be completed nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<To be completed nationally>

10. DATE OF REVISION OF THE TEXT

<To be completed nationally>

Package leaflet: Information for the user

<Product name> 10 mg/ml oral solution
Memantine hydrochloride

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What <Product name> is and what it is used for

How does <Product name> work
<Product name>~~Axura~~ contains the active substance memantine -hydrochloride.
<Product name> belongs to a group of medicines known as anti-dementia medicines.

Memory loss in Alzheimer's disease is due to a disturbance of message signals in the brain. The brain contains so-called N-methyl-D-aspartate (NMDA)-receptors that are involved in transmitting nerve signals important in learning and memory. <Product name> belongs to a group of medicines called NMDA- receptor antagonists. <Product name> acts on these NMDA-receptors improving the transmission of nerve signals and the memory.

What is <Product name> used for
<Product name> is used for the treatment of patients with moderate to severe Alzheimer's disease.

2. What you need to know before you take <Product name>

Do not take <Product name>:
- if you are allergic (hypersensitive) to memantine hydrochloride or any of the other ingredients of this medicine (listed in section 6).

Formatiert: Englisch (USA)

Warnings and precautions
Talk to your doctor or pharmacist before taking <Product name>
- if you have a history of epileptic seizures
- if you have recently experienced a myocardial infarction (heart attack), or if you are suffering from congestive heart failure or from an uncontrolled hypertension (high blood pressure).

In these situations the treatment should be carefully supervised, and the clinical benefit of <Product name> reassessed by your doctor on a regular basis.

- If you suffer from renal impairment (kidney problems), your doctor should closely monitor your kidney function and if necessary adapt the memantine doses accordingly.

- The use of medicinal products called amantadine (for the treatment of Parkinson´s disease), ketamine (a substance generally used as an anaesthetic), dextromethorphan (generally used to treat cough) and other NMDA-antagonists at the same time should be avoided.

Children and adolescents
<Product name> is not recommended for children and adolescents under the age of 18 years.

Other medicines and <Product name>
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular, <Product name> may change the effects of the following medicines and their dose may need to be adjusted by your doctor:

amantadine, ketamine, dextromethorphan
dantrolene, baclofen
cimetidine, ranitidine, procainamide, quinidine, quinine, nicotine
hydrochlorothiazide (or any combination with hydrochlorothiazide)
anticholinergics (substances generally used to treat movement disorders or intestinal cramps)
anticonvulsants (substances used to prevent and relieve seizures)
barbiturates (substances generally used to induce sleep)
dopaminergic agonists (substances such as L-dopa, bromocriptine)
neuroleptics (substances used in the treatment of mental disorders)
oral anticoagulants

If you go into hospital, let your doctor know that you are taking <Product name>.

<Product name> with food and drink
You should inform your doctor if you have recently changed or intend to change your diet substantially (e.g. from normal diet to strict vegetarian diet) or if you are suffering from states of renal tubulary acidosis (RTA, an excess of acid-forming substances in the blood due to renal dysfunction (poor kidney function)) or severe infections of the urinary tract (structure that carries urine), as your doctor may need to adjust the dose of your medicine.

Pregnancy, breast-feeding ~~and fertility~~
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. ~~The use of memantine in pregnant women is not recommended.~~

Pregnancy: The use of memantine in pregnant women is not recommended.

Breast-Feeding: Women taking <Product name> should not breast-feed.

Driving and using machines
Your doctor will tell you whether your illness allows you to drive and to use machines safely. Also, <Product name> may change your reactivity, making driving or operating machinery inappropriate.

<Product name> contains sorbitol
This medicinal product contains sorbitol. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product. Your doctor will advise you.

Formatiert: Englisch (USA)

3. How to take <Product name>

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Dosage
0.5 ml contains 5mg memantine hydrochloride.
The recommended dose of <Product name> for adults and elderly patients is 2 ml, equivalent to 20 mg once a day.
In order to reduce the risk of side effects this dose is achieved gradually by the following daily treatment scheme:

week 1	0.5 ml
week 2	1 ml
week 3	1.5 ml
week 4 and beyond	2 ml

The usual starting dose is 0.5 ml (1 x 5 mg) once daily for the first week. This dose is increased in the second week to 1 ml once daily (1 x 10 mg), and in the third week to 1.5 ml (1 x 15 mg) once daily. From the fourth week the recommended dose is 2 ml once daily (1 x 20mg).

Dosage in patients with impaired kidney function
If you have impaired kidney function, your doctor will decide upon a dose that suits your condition. In this case, monitoring of your kidney function should be performed by your doctor at specified intervals.

Administration
<Product name> should be administered orally once a day. To benefit from your medicine you should take it regularly every day at the same time of the day. The solution should be taken with a little water. The solution can be taken with or without food.
For detailed instructions on the preparation and handling of the product see end of this leaflet.

Duration of treatment
Continue to take <Product name> as long as it is of benefit to you. Your doctor should assess your treatment on a regular basis.

If you take more <Product name> than you should
- In general, taking too much <Product name> should not result in any harm to you. You may experience increased symptoms as described in section 4. "Possible side effects".
- If you take a large overdose of <Product name>, contact your doctor or get medical advice, as you may need medical attention.

If you forget to take <Product name>
- If you find you have forgotten to take your dose of <Product name>, wait and take your next dose at the usual time.
- Do not take a double dose to make up for a forgotten dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

In general, the observed side effects are mild to moderate.

Common (affects 1 to 10 users in 100):~~(may affect up to 1 in 10 people):~~
- Headache, sleepiness, constipation, elevated liver function tests, dizziness, balance disorder,

Formatiert: Englisch (USA)

shortness of breath, high blood pressure and drug hypersensitivity

Uncommon (affects 1 to 10 users in 1,000):~~(may affect up to 1 in 100 people):~~

- Tiredness, fungal infections, confusion, hallucinations, vomiting, abnormal gait, heart failure and venous blood clotting (thrombosis/thromboembolism)

Very rare (affects less than 1 user in 10,000):~~(may affect up to 1 in 10,000 people):~~

- Seizures

Not known (frequency cannot be estimated from the available data):

- Inflammation of the pancreas, inflammation of the liver (hepatitis) and psychotic reactions

Alzheimer's disease has been associated with depression, suicidal ideation and suicide. These events have been reported in patients treated with memantine.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system <to be completed nationally>. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store <Product name>

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the bottle label after the EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.
Once opened, the contents of the bottle should be used within 6 months.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What <Product name> contains

- The active substance is memantine hydrochloride. 1 ml solution contains 10 mg memantine hydrochloride which is equivalent to 8.31 mg memantine.
- The other ingredients are: Potassium sorbate (E202), Sorbitol, liquid 70% (non crystallising) (E420) and purified water.

What <Product name> looks like and contents of the pack

<Product name> is presented as a clear, colourless to light yellowish and odourless solution.
Amber glass bottle containing 50 ml or 100 ml solution, packed in cardboard boxes along with a 2ml graduated oral syringe (graduated from 0.5 ml to 2.0 ml in increments of 0.5 ml), an oral syringe adaptor and screw cap

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

<To be completed nationally>

Formatiert: Englisch (USA)

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Kommentiert [OM2]: V_IB_B.II.d.1.z. (PL/H/0405/001/IB/006) Change of the specification of Appearance of the finished product submitted parallel

This medicinal product is authorised in the Member States of the EEA under the following names:

<To be completed nationally>

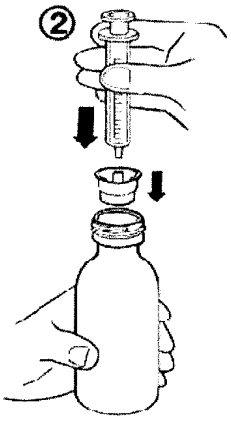
This leaflet was last revised in <MM/YYYY>.
Instruction for proper use

The solution must not be poured directly into the mouth from the bottle or syringe. Transfer the dose onto a spoon or into a glass of water.

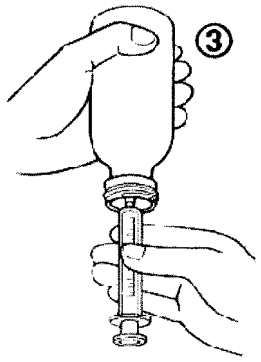
- Opening the bottle: Twist the cap anticlockwise to open (Fig. 1).

①

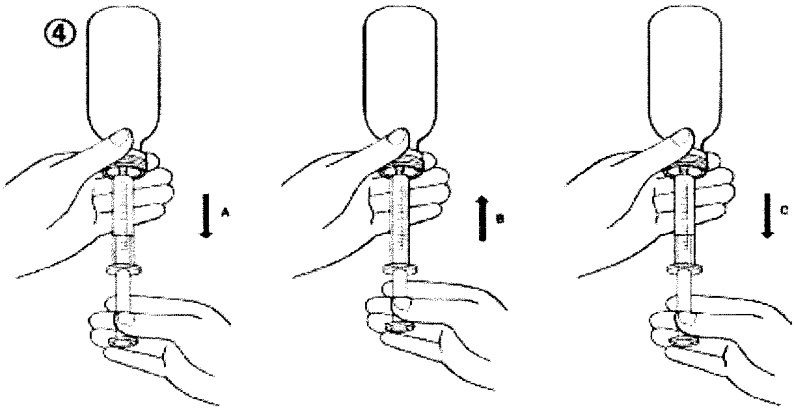
- Insert the oral syringe adaptor into the bottle neck (Fig. 2). Make sure that the adaptor is tightly fitted.
- Take the oral syringe and insert it into the adaptor opening (Fig. 2).



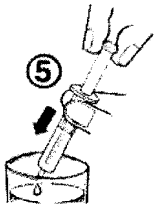
- Turn the bottle upside down (Fig. 3).



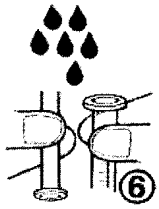
- Fill the oral syringe with a small amount of solution, by slightly pulling out the plunger (Fig. 4A). Then, press the plunger back in to remove any air bubbles (Fig. 4B). Next, pull the plunger up to the mark in millilitres (ml) corresponding to the dose prescribed by the doctor (Fig. 4C).



- Turn the bottle the right way up. Remove the oral syringe from the adaptor.
- Empty the contents of the oral syringe onto a spoon or into a glass of water, by pushing the plunger as far as it will go into the oral syringe (Fig. 5).



- Drink the entire contents of the glass or spoon.
- Rinse out the oral syringe with water only (Fig. 6).



- Close the bottle with the screw closure.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON AND LABEL FOR BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

<Product name> 10 mg/ml oral solution

Memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml of solution contains 10 mg of memantine hydrochloride equivalent to 8.31 mg memantine.

3. LIST OF EXCIPIENTS

Also contains sorbitol (E420) and potassium sorbate (E202) as preservative.
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Oral solution

50 ml
100 ml

Formatiert: Nicht Hervorheben

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Once opened, use within 6 months.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<To be completed nationally>

12. MARKETING AUTHORISATION NUMBER(S)

<To be completed nationally>

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

<Product name> 10 mg/ml oral solution

17. UNIQUE IDENTIFIER – 2D BARCODE

Formatiert: Einzug: Links: 0,21 cm, Rechts: -0,04 cm

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Formatiert: Einzug: Links: 0,21 cm, Rechts: -0,04 cm

PC: {number} [product code]
SN: {number} [serial number]
NN: {number} [national reimbursement number or other national number identifying the medicinal product]