ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg film-coated tablets
Nemdatine 10 mg film-coated tablets
Nemdatine 15 mg film-coated tablets
Nemdatine 20 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Nemdatine 5 mg

Each film-coated tablet contains 5 mg of memantine hydrochloride equivalent to 4.15 mg memantine.

Nemdatine 10 mg

Each film-coated tablet contains 10 mg of memantine hydrochloride equivalent to 8.31 mg memantine.

Nemdatine 15 mg

Each film-coated tablet contains 15 mg of memantine hydrochloride equivalent to 12.46 mg memantine.

Nemdatine 20 mg

Each film-coated tablet contains 20 mg of memantine hydrochloride equivalent to 16.62 mg memantine.

Excipient(s) with known effect:

Nemdatine 5 mg film-coated tablets

Each film-coated tablet contains 0.47 mg lactose monohydrate.

Nemdatine 10 mg film-coated tablets

Each film-coated tablet contains 0.95 mg lactose monohydrate.

Nemdatine 15 mg film-coated tablets

Each film-coated tablet contains 1.42 mg lactose monohydrate.

Nemdatine 20 mg film-coated tablets

Each film-coated tablet contains 1.89 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet).

Nemdatine 5 mg film-coated tablets

White, oval shaped, biconvex film-coated tablet, 8 mm x 4.5 mm in size, with the marking “M5”

engraved on one side.

Nemdatine 10 mg film-coated tablets

White, capsule-shaped, biconvex film-coated tablet, 9.8 mm x 4.9 mm in size, with score line and the marking “M 10” engraved on the scored side.

The tablet can be divided into equal doses.

Nemdatine 15 mg film-coated tablets

Orange, oval shaped, biconvex film-coated tablet, 11.4 mm x 6.4 mm in size, with the marking “M15” engraved on one side.

Nemdatine 20 mg film-coated tablets

Dark pink, oval shaped, biconvex film-coated tablet, 12.6 mm x 7 mm in size, with the marking “M20” engraved on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of adult patients with moderate to severe Alzheimer’s disease.

4.2 Posology and method of administration

Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer’s dementia.

Posology

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.

Adults

Dose titration

The maximum daily dose is 20 mg per day. 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 one 5 mg film-coated tablet (5 mg) or half a 10 mg film-coated tablet (5 mg) per day for 7 days.

Week 2 (day 8-14):
The patient should take two 5 mg film-coated tablets (10 mg) or one 10 mg film-coated tablet (10 mg) per day for 7 days.

Week 3 (day 15-21):
The patient should take three 5 mg film-coated tablets (15 mg) or one 15 mg film-coated tablet (15 mg) per day for 7 days.

From Week 4 on:
The patient should take four 5 mg film-coated tablets (20 mg), two 10 mg film-coated tablets (20 mg) or one 20 mg film-coated tablet (20 mg) per day.

Maintenance dose

The recommended maintenance dose is 20 mg per day.

Elderly
On the basis of the clinical studies, the recommended dose for patients over the age of 65 years is 20 mg per day (four 5 mg film-coated tablets (20 mg), two 10 mg film-coated tablets (20 mg) or one 20 mg film-coated tablet (20 mg) once a day) as described above.

Renal impairment
In patients with mildly impaired renal function (creatinine clearance 50 − 80 ml/min) no dose adjustment is required. In patients with moderate renal impairment (creatinine clearance 30 – 49 ml/min) daily dose should be 10 mg per day. If tolerated well after at least 7 days of treatment, the dose could be increased up to 20 mg/day according to standard titration scheme. In patients with severe renal impairment (creatinine clearance 5 – 29 ml/min) daily dose should be 10 mg per day.

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 Nemdatine is not recommended in patients with severe hepatic impairment.

Paediatric population
No data are available.

Method of administration

Nemdatine should be administered orally once a day and should be taken at the same time every day. The film-coated tablets can be taken with or without food.

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 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.

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption 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

There are no or limited amount of data from the use of memantine in pregnant women. 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.

Breast-feeding

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, Nemdatine 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

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 %).

Tabulated list of adverse reactions

The following Adverse Reactions listed in the table below have been accumulated in clinical studies with memantine and since its introduction in the market.

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). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE REACTION
Infections and infestations	Uncommon	Fungal infections
Immune system disorders	Common	Drug hypersensitivity
Psychiatric disorders	Common	Somnolence
	Uncommon	Confusion
	Uncommon	Hallucinations[1]
	Not known	Psychotic reactions[2]
Nervous system disorders	Common	Dizziness
	Common	Balance disorders
	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
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
	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 reactions 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 listed in Appendix V.

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 of gastrointestinal origin (vomiting and diarrhoea).

In the most extreme case of overdose, the patient survived the oral intake of a total of 2,000 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: Psychoanaleptics, other Anti-dementia drugs, ATC code: N06DX01.

Mechanism of action

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 efficacy and safety

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

Tablet cores for 5, 10, 15 and 20 mg film-coated tablets

Microcrystalline cellulose
Crospovidone Type A
Talc
Magnesium stearate

Tablet coat for 5, 10, 15 and 20 mg film-coated tablets

Hypromellose 6cP
Titanium dioxide (E171)
Lactose monohydrate
Macrogol 3350
Triacetin

Additional for 15 mg film-coated tablets

Iron oxide yellow, red and black (E172)

Additional for 20 mg film-coated tablets

Iron oxide red and yellow (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Blisters: 2 years.

HDPE bottles: use within 100 days after opening.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PVC/PVDC-Aluminium blisters.

Nemdatine 10 mg and 20 mg film-coated tablets:
HDPE bottle.

Pack sizes
Nemdatine 5 mg film-coated tablets:
Blister packs: 42 and 98 film-coated tablets.

Nemdatine 10 mg film-coated tablets:
Blister packs: 28, 30, 42, 50, 56, 60, 98 and 112 film-coated tablets.
HDPE bottle: 100 film-coated tablets.

Nemdatine 15 mg film-coated tablets:
Blister packs: 7, 42 and 98 film-coated tablets.

Nemdatine 20 mg film-coated tablets:
Blister packs: 28, 42, 56 and 98 film-coated tablets.
HDPE bottle: 100 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Actavis Group PTC ehf.
Dalshraun 1
220 Hafnarfjörður
Iceland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/001
EU/1/13/824/002
EU/1/13/824/003
EU/1/13/824/004
EU/1/13/824/005
EU/1/13/824/006
EU/1/13/824/007
EU/1/13/824/008
EU/1/13/824/009
EU/1/13/824/010
EU/1/13/824/019
EU/1/13/824/011
EU/1/13/824/012
EU/1/13/824/013
EU/1/13/824/014
EU/1/13/824/015
EU/1/13/824/016
EU/1/13/824/017
EU/1/13/824/020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 April 2013
Date of latest renewal: 8 January 2018

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg film-coated tablets
Nemdatine 10 mg film-coated tablets
Nemdatine 15 mg film-coated tablets
Nemdatine 20 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Nemdatine 5 mg

Each film-coated tablet contains 5 mg of memantine hydrochloride equivalent to 4.15 mg memantine.

Nemdatine 10 mg

Each film-coated tablet contains 10 mg of memantine hydrochloride equivalent to 8.31 mg memantine.

Nemdatine 15 mg

Each film-coated tablet contains 15 mg of memantine hydrochloride equivalent to 12.46 mg memantine.

Nemdatine 20 mg

Each film-coated tablet contains 20 mg of memantine hydrochloride equivalent to 16.62 mg memantine.

Excipient(s) with known effect:

Nemdatine 5 mg film-coated tablets

Each film-coated tablet contains 0.47 mg lactose monohydrate.

Nemdatine 10 mg film-coated tablets

Each film-coated tablet contains 0.95 mg lactose monohydrate.

Nemdatine 15 mg film-coated tablets

Each film-coated tablet contains 1.42 mg lactose monohydrate.

Nemdatine 20 mg film-coated tablets

Each film-coated tablet contains 1.89 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet).

Nemdatine 5 mg film-coated tablets

White, oval shaped, biconvex film-coated tablets, 8 mm x 4.5 mm in size, with the marking “M5”

engraved on one side.

Nemdatine 10 mg film-coated tablets

White, capsule-shaped, biconvex film-coated tablets, 9.8 mm x 4.9 mm in size, with score line and the marking “M 10” engraved on the scored side. The tablet can be divided into equal doses.

Nemdatine 15 mg film-coated tablets

Orange, oval shaped, biconvex film-coated tablets, 11.4 mm x 6.4 mm in size, with the marking “M15” engraved on one side.

Nemdatine 20 mg film-coated tablets

Dark pink, oval shaped, biconvex film-coated tablets, 12.6 mm x 7 mm in size, with the marking “M20” engraved on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of adult patients with moderate to severe Alzheimer’s disease.

4.2 Posology and method of administration

Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer’s dementia.

Posology

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.

Adults

Dose titration

The recommended starting dose is 5 mg per day which is stepwise increased over the first 4 weeks of treatment reaching the recommended maintenance dose as follows:

Week 1 (day 1-7):
The patient should take one 5 mg film-coated tablet per day (white, oval-shaped) for 7 days.

Week 2 (day 8-14):
The patient should take one 10 mg film-coated tablet per day (white, capsule shaped) for 7 days.

Week 3 (day 15-21):
The patient should take one 15 mg film-coated tablet per day (orange, oval shaped) for 7 days.

Week 4 (day 22-28):
The patient should take one 20 mg film-coated tablet per day (dark pink, oval shaped) for 7 days.

The maximum daily dose is 20 mg per day.

Maintenance dose

The recommended maintenance dose is 20 mg per day.

Elderly
On the basis of the clinical studies, the recommended dose for patients over the age of 65 years is 20 mg per day (20 mg once a day) as described above.

Renal impairment
In patients with mildly impaired renal function (creatinine clearance 50 − 80 ml/min) no dose adjustment is required. In patients with moderate renal impairment (creatinine clearance 30 – 49 ml/min) daily dose should be 10 mg per day. If tolerated well after at least 7 days of treatment, the dose could be increased up to 20 mg/day according to standard titration scheme. In patients with severe renal impairment (creatinine clearance 5 – 29 ml/min) daily dose should be 10 mg per day.

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 Nemdatine is not recommended in patients with severe hepatic impairment.

Paediatric population
No data are available.

Method of administration

Nemdatine should be administered orally once a day and should be taken at the same time every day. The film-coated tablets can be taken with or without food.

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 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.

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption 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

There are no or limited amount of data from the use of memantine in pregnant women. 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.

Breast-feeding

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, Nemdatine 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

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 %).

Tabulated list of adverse reactions

The following Adverse Reactions listed in the table below have been accumulated in clinical studies with memantine and since its introduction in the market.

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). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE REACTION
Infections and infestations	Uncommon	Fungal infections
Immune system disorders	Common	Drug hypersensitivity
Psychiatric disorders	Common	Somnolence
	Uncommon	Confusion
	Uncommon	Hallucinations[1]
	Not known	Psychotic reactions[2]
Nervous system disorders	Common	Dizziness
	Common	Balance disorders
	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
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
	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 reactions 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 listed in Appendix V.

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 of gastrointestinal origin (vomiting and diarrhoea).

In the most extreme case of overdose, the patient survived the oral intake of a total of 2,000 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: Psychoanaleptics, other Anti-dementia drugs, ATC code: N06DX01.

Mechanism of action

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 efficacy and safety

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

Tablet cores for 5, 10, 15 and 20 mg film-coated tablets

Microcrystalline cellulose
Crospovidone Type A
Talc
Magnesium stearate

Tablet coat for 5 mg and 10 mg film-coated tablets

Hypromellose 6cP
Titanium dioxide (E171)
Lactose monohydrate
Macrogol 3350
Triacetin

Tablet coat for 15 mg film-coated tablets

Hypromellose 6cP
Lactose monohydrate
Titanium dioxide (E171)
Macrogol 3350
Triacetin
Iron oxide yellow, red and black (E172)

Tablet coat for 20 mg film-coated tablets

Hypromellose 6cP
Titanium dioxide (E171)
Lactose monohydrate
Macrogol 3350
Triacetin
Iron oxide red and yellow (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PVC/PVDC-Aluminium blisters.

Each pack contains 28 film-coated tablets (7 film-coated tablets of 5 mg, 7 film-coated tablets of 10 mg, 7 film-coated tablets of 15 mg and 7 film-coated tablets of 20 mg) in a wallet pack or as a pack of 4 blisters in 4 separate immediate cartons and one outer carton.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Actavis Group PTC ehf.
Dalshraun 1
220 Hafnarfjörður
Iceland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/018
EU/1/13/824/021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 April 2013
Date of latest renewal: 8 January 2018

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Actavis Ltd.
BLB 015-016 Bulebel Industrial Estate
Zejtun ZTN 3000
Malta

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR BLISTER PACK

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 5 mg of memantine hydrochloride equivalent to 4.15 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

42 film-coated tablets
98 film-coated tablets

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/001 42 film-coated tablets
EU/1/13/824/002 98 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR BLISTER PACK

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 10 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 10 mg of memantine hydrochloride equivalent to 8.31 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets
30 film-coated tablets
42 film-coated tablets
50 film-coated tablets
56 film-coated tablets
60 film-coated tablets
98 film-coated tablets
112 film-coated tablets

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/003 28 film-coated tablets
EU/1/13/824/004 30 film-coated tablets
EU/1/13/824/005 42 film-coated tablets
EU/1/13/824/006 50 film-coated tablets
EU/1/13/824/007 56 film-coated tablets
EU/1/13/824/008 60 film-coated tablets
EU/1/13/824/009 98 film-coated tablets
EU/1/13/824/010 112 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 10 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 10 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 10 mg of memantine hydrochloride equivalent to 8.31 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

100 film-coated tablets

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

Do not store above 25°C.

Use within 100 days after opening.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/019

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

LABEL FOR BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 10 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 10 mg of memantine hydrochloride equivalent to 8.31 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose.

4. PHARMACEUTICAL FORM AND CONTENTS

100 tablets

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

Do not store above 25°C.

Use within 100 days after opening.

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

[Actavis Group PTC ehf. Logo]

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/019

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR BLISTER PACK

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 15 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 15 mg of memantine hydrochloride equivalent to 12.46 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 film-coated tablets
42 film-coated tablets
98 film-coated tablets

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/011 7 film-coated tablets
EU/1/13/824/012 42 film-coated tablets
EU/1/13/824/013 98 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 15 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON AND WALLET FOR 28 TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE – Frontside

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg
Nemdatine 10 mg
Nemdatine 15 mg
Nemdatine 20 mg
film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 5, 10, 15 or 20 mg of memantine hydrochloride equivalent to 4.15, 8.31, 12.46 or 16.62 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets

Treatment initiation pack.
Each pack of 28 film-coated tablets for a 4 week treatment schedule contains:
7 film-coated tablets of Nemdatine 5 mg
7 film-coated tablets of Nemdatine 10 mg
7 film-coated tablets of Nemdatine 15 mg
7 film-coated tablets of Nemdatine 20 mg

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/018

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 5 mg, 10 mg, 15 mg, 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON AND WALLET FOR 28 TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE – Inside

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg
Nemdatine 10 mg
Nemdatine 15 mg
Nemdatine 20 mg
film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

memantine hydrochloride

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Each pack with 28 film-coated tablets for a 4 week treatment schedule contains:
Week 1: 7 film-coated tablets of Nemdatine 5 mg
Week 2: 7 film-coated tablets of Nemdatine 10 mg
Week 3: 7 film-coated tablets of Nemdatine 15 mg
Week 4: 7 film-coated tablets of Nemdatine 20 mg

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.

Read the package leaflet before use.

One tablet daily.

For continuation of your treatment please consult your doctor.

Nemdatine 5 mg
Week 1
Day 1, 2, 3, 4, 5, 6, 7

Nemdatine 10 mg
Week 2
Day 8, 9, 10, 11, 12, 13, 14

Nemdatine 15 mg
Week 3
Day 15, 16, 17, 18, 19, 20, 21

Nemdatine 20 mg
Week 4
Day 22, 23, 24, 25, 26, 27, 28

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

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

9. SPECIAL STORAGE CONDITIONS

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

[Actavis Group PTC ehf. Logo]

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/018

13. BATCH NUMBER

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 10 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 15 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 20 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING.

CARTON FOR BLISTER PACK

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 20 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 20 mg of memantine hydrochloride equivalent to 16.62 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets
42 film-coated tablets
56 film-coated tablets
98 film-coated tablets

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/014 28 film-coated tablets
EU/1/13/824/015 42 film-coated tablets
EU/1/13/824/016 56 film-coated tablets
EU/1/13/824/017 98 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 20 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Mon.
Tue.
Wed.
Thu.
Fri.
Sat.
Sun.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING.

CARTON FOR BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 20 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 20 mg of memantine hydrochloride equivalent to 16.62 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

100 film-coated tablets

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

Do not store above 25°C.

Use within 100 days after opening.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/020

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING.

LABEL FOR BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 20 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 20 mg of memantine hydrochloride equivalent to 16.62 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose.

4. PHARMACEUTICAL FORM AND CONTENTS

100 tablets

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

Do not store above 25°C.

Use within 100 days after opening.

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

[Actavis Group PTC ehf. Logo]

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/020

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR 28 TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE – OUTER CARTON (WITH BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg
Nemdatine 10 mg
Nemdatine 15 mg
Nemdatine 20 mg
film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 5, 10, 15 or 20 mg of memantine hydrochloride equivalent to 4.15, 8.31, 12.46 or 16.62 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Treatment initiation pack.

Treatment initiation pack with 28 (4x7) film-coated tablets for a 4 week treatment schedule:
7 film-coated tablets of Nemdatine 5 mg
7 film-coated tablets of Nemdatine 10 mg
7 film-coated tablets of Nemdatine 15 mg
7 film-coated tablets of Nemdatine 20 mg

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.

Read the package leaflet before use.

For continuation of your treatment please consult your doctor.

Week 1: Take one tablet daily of Nemdatine 5 mg.

Week 2: Take one tablet daily of Nemdatine 10 mg.

Week 3: Take one tablet daily of Nemdatine 15 mg.

Week 4: Take one tablet daily of Nemdatine 20 mg.

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/021

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 5 mg, 10 mg, 15 mg, 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR 7 TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE –IMMEDIATE CARTON (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 5 mg of memantine hydrochloride equivalent to 4.15 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.

Read the package leaflet before use.

One tablet daily.

For continuation of your treatment please consult your doctor.

Week 1

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/021

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS FOR TREATMENT INITIATION PACK

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 5 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Week 1

Mon.
Tue.
Wed.
Thu.
Fri.
Sat.
Sun.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR 7 TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE –IMMEDIATE CARTON (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 10 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 10 mg of memantine hydrochloride equivalent to 8.31 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.

Read the package leaflet before use.

One tablet daily.

For continuation of your treatment please consult your doctor.

Week 2

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/021

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS FORTREATMENT INITIATION PACK

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 10 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Week 2

Mon.
Tue.
Wed.
Thu.
Fri.
Sat.
Sun.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR 7 TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE –IMMEDIATE CARTON (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 15 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 15 mg of memantine hydrochloride equivalent to 12.46 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.

Read the package leaflet before use.

One tablet daily.

For continuation of your treatment please consult your doctor.

Week 3

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/021

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS FOR TREATMENT INITIATION PACK

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 15 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Week 3

Mon.
Tue.
Wed.
Thu.
Fri.
Sat.
Sun.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING.

CARTON FOR 7 TABLETS – TREATMENT INITIATION PACK – 4 WEEK TREATMENT SCHEDULE –IMMEDIATE CARTON (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 20 mg film-coated tablets

memantine hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 20 mg of memantine hydrochloride equivalent to 16.62 mg memantine.

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

7 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.

Read the package leaflet before use.

One tablet daily.

For continuation of your treatment please consult your doctor.

Week 4

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

Do not store above 25°C.

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

Actavis Group PTC ehf.
220 Hafnarfjörður
Iceland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/824/021

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nemdatine 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR TABLETS FOR TREATMENT INITIATION PACK

1. NAME OF THE MEDICINAL PRODUCT

Nemdatine 20 mg tablets

memantine hydrochloride

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[Actavis Group PTC ehf. Logo]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Week 4

Mon.
Tue.
Wed.
Thu.
Fri.
Sat.
Sun.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Nemdatine 5 mg film-coated tablets
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 Nemdatine is and what it is used for

How does Nemdatine work
Nemdatine contains the active substance memantine hydrochloride. Nemdatine 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. Nemdatine belongs to a group of medicines called NMDA-receptor antagonists. Nemdatine acts on these NMDA-receptors improving the transmission of nerve signals and the memory.

What is Nemdatine used for
Nemdatine is used for the treatment of adult patients with moderate to severe Alzheimer's disease.

2. What you need to know before you take Nemdatine

Do not take Nemdatine
- if you are allergic to memantine hydrochloride or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Nemdatine
- 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 Nemdatine 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
Nemdatine is not recommended for children and adolescents under the age of 18 years.

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

In particular, Nemdatine 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 Nemdatine.

Nemdatine 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 and breast-feeding
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.

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

Breast-feeding
Women taking Nemdatine 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, Nemdatine may change your reactivity, making driving or operating machinery inappropriate.

Nemdatine contains lactose monohydrate
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Nemdatine

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

Dosage
The recommended dose of Nemdatine for adults and older people is 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	One 5 mg tablet
Week 2	Two 5 mg tablets
Week 3	Three 5 mg tablets
Week 4 and beyond	Four 5 mg tablets once a day

The usual starting dose is one tablet once a day (1x 5 mg) for the first week. This is increased to two tablets once a day (1x 10 mg) in the second week and to three tablets once a day (1x 15 mg) in the third week. From the fourth week on, the usual dose is 4 tablets once a day (1x 20 mg).

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
Nemdatine 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 tablets should be swallowed with some water. The tablets can be taken with or without food.

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

If you take more Nemdatine than you should
- In general, taking too much Nemdatine 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 Nemdatine, contact your doctor or get medical advice, as you may need medical attention.

If you forget to take Nemdatine
- If you find you have forgotten to take your dose of Nemdatine, 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)
- Headache, sleepiness, constipation, elevated liver function test, dizziness, balance disorders, shortness of breath, high blood pressure and drug hypersensitivity

Uncommon (affects 1 to 10 users in 1,000)
- 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)
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nemdatine

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 blister after 'EXP'. The expiry date refers to the last day of that month.

Do not store above 25°C.

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 Nemdatine contains
- The active substance is memantine hydrochloride. Each film-coated tablet contains 5 mg memantine hydrochloride equivalent to 4.15 mg memantine.

- The other ingredients are: *Tablet core:* Microcrystalline cellulose, crospovidone Type A, talc and magnesium stearate. *Tablet coat (Opadry II White 33G28435):* Hypromellose 6cP, titanium dioxide (E171), lactose monohydrate, macrogol 3350 and triacetin.

What Nemdatine looks like and contents of the pack
Nemdatine 5 mg film-coated tablets (tablets) are white, oval shaped, biconvex, 8 mm x 4.5 mm in size, with the marking "M5" engraved on one side.

Pack sizes
Blister packs: 42 and 98 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Actavis Group PTC ehf.
Dalshraun 1
220 Hafnarfjörður
Iceland

Manufacturer
Actavis Ltd.
BLB 015-016 Bulebel Industrial Estate
Zejtun ZTN 3000
Malta

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Teva Pharma Belgium N.V./S.A./AG
Tél/Tel: +32 38207373

България
Тева Фарма ЕАД
Тел: +359 24899585

Česká republika
Teva Pharmaceuticals CR, s.r.o.
Tel: +420 251007111

Danmark
Teva Denmark A/S
Tlf: +45 44985511

Deutschland
ratiopharm GmbH
Tel: +49 73140202

Eesti
UAB Teva Baltics Eesti filiaal
Tel: +372 6610801

Ελλάδα
TEVA HELLAS A.E.
Τηλ: +30 2118805000

España
Teva Pharma, S.L.U.
Tel: +34 913873280

France
Teva Santé
Tél: +33 155917800

Hrvatska
Pliva Hrvatska d.o.o.
Tel: +385 13720000

Ireland
Teva Pharmaceuticals Ireland
Tel: +44 2075407117

Ísland
Teva Pharma Iceland ehf.
Sími: +354 5503300

Lietuva
UAB Teva Baltics
Tel: +370 52660203

Luxembourg/Luxemburg
ratiopharm GmbH
Allemagne/Deutschland
Tél/Tel: +49 73140202

Magyarország
Teva Gyógyszergyár Zrt.
Tel: +36 12886400

Malta
Teva Pharmaceuticals Ireland
L-Irlanda
Tel: +44 2075407117

Nederland
Teva Nederland B.V.
Tel: +31 8000228400

Norge
Teva Norway AS
Tlf: +47 66775590

Österreich
ratiopharm Arzneimittel Vertriebs-GmbH
Tel: +43 1970070

Polska
Teva Pharmaceuticals Polska Sp. z o.o.
Tel: +48 223459300

Portugal
Teva Pharma - Produtos Farmacêuticos, Lda.
Tel: +351 214767550

România
Teva Pharmaceuticals S.R.L.
Tel: +40 212306524

Slovenija
Pliva Ljubljana d.o.o.
Tel: +386 15890390

Slovenská republika
TEVA Pharmaceuticals Slovakia s.r.o.
Tel: +421 257267911

Italia
Teva Italia S.r.l.
Tel: +39 028917981

Κύπρος
TEVA HELLAS A.E.
Ελλάδα
Τηλ: +30 2118805000

Latvija
UAB Teva Baltics filiāle Latvijā
Tel: +371 67323666

Suomi/Finland
Teva Finland Oy
Puh/Tel: +358 201805900

Sverige
Teva Sweden AB
Tel: +46 42121100

United Kingdom (Northern Ireland)
Accord Healthcare Ireland Ltd.
Ireland
Tel: +353 214619040

This leaflet was last revised in {MM/YYYY}

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Package leaflet: Information for the patient

Nemdatine 10 mg film-coated tablets
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 Nemdatine is and what it is used for

How does Nemdatine work
Nemdatine contains the active substance memantine hydrochloride. Nemdatine 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. Nemdatine belongs to a group of medicines called NMDA-receptor antagonists. Nemdatine acts on these NMDA-receptors improving the transmission of nerve signals and the memory.

What is Nemdatine used for
Nemdatine is used for the treatment of adult patients with moderate to severe Alzheimer's disease.

2. What you need to know before you take Nemdatine

Do not take Nemdatine
- if you are allergic to memantine hydrochloride or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Nemdatine
- 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 Nemdatine 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
Nemdatine is not recommended for children and adolescents under the age of 18 years.

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

In particular, Nemdatine 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 Nemdatine.

Nemdatine 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 and breast-feeding
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.

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

Breast-feeding
Women taking Nemdatine 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, Nemdatine may change your reactivity, making driving or operating machinery inappropriate.

Nemdatine contains lactose monohydrate
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Nemdatine

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

Dosage
The recommended dose of Nemdatine for adults and older people is 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	Half a 10 mg tablet
Week 2	One 10 mg tablet
Week 3	One and a half 10 mg tablets
Week 4 and beyond	Two 10 mg tablets once a day

The usual starting dose is half a tablet once a day (1x 5 mg) for the first week. This is increased to one tablet once a day (1x 10 mg) in the second week and to 1 and a half tablets once a day (1x 15 mg) in the third week. From the fourth week on, the usual dose is 2 tablets once a day (1x 20 mg).

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
Nemdatine 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 tablets should be swallowed with some water. The tablets can be taken with or without food.

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

If you take more Nemdatine than you should
- In general, taking too much Nemdatine 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 Nemdatine, contact your doctor or get medical advice, as you may need medical attention.

If you forget to take Nemdatine
- If you find you have forgotten to take your dose of Nemdatine, 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)
- Headache, sleepiness, constipation, elevated liver function test, dizziness, balance disorders, shortness of breath, high blood pressure and drug hypersensitivity

Uncommon (affects 1 to 10 users in 1,000)
- 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)
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nemdatine

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, blister and bottle label after 'EXP'. The expiry date refers to the last day of that month.

Do not store above 25°C.

<[For HDPE bottle only:]>
Use within 100 days after opening.

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 Nemdatine contains
- The active substance is memantine hydrochloride. Each film-coated tablet contains 10 mg memantine hydrochloride equivalent to 8.31 mg memantine.

- The other ingredients are: *Tablet core:* Microcrystalline cellulose, crospovidone Type A, talc and magnesium stearate. *Tablet coat (Opadry II White 33G28435):* Hypromellose 6cP, titanium dioxide (E171), lactose monohydrate, macrogol 3350 and triacetin.

What Nemdatine looks like and contents of the pack
Nemdatine 10 mg film-coated tablets (tablets) are white, capsule-shaped, biconvex, 9.8 mm x 4.9 mm in size, with score line and the marking "M 10" engraved on the scored side

Pack sizes
Blister packs: 28, 30, 42, 50, 56, 60, 98 and 112 film-coated tablets.
Bottle: 100 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Actavis Group PTC ehf.
Dalshraun 1
220 Hafnarfjörður
Iceland

Manufacturer
Actavis Ltd.
BLB 015-016 Bulebel Industrial Estate
Zejtun ZTN 3000
Malta

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Teva Pharma Belgium N.V./S.A./AG
Tél/Tel: +32 38207373

България
Тева Фарма ЕАД
Тел: +359 24899585

Česká republika
Teva Pharmaceuticals CR, s.r.o.
Tel: +420 251007111

Danmark
Teva Denmark A/S
Tlf: +45 44985511

Deutschland
ratiopharm GmbH
Tel: +49 73140202

Eesti
UAB Teva Baltics Eesti filiaal
Tel: +372 6610801

Ελλάδα
TEVA HELLAS A.E.
Τηλ: +30 2118805000

España
Teva Pharma, S.L.U.
Tel: +34 913873280

France
Teva Santé
Tél: +33 155917800

Hrvatska
Pliva Hrvatska d.o.o.
Tel: +385 13720000

Ireland
Teva Pharmaceuticals Ireland
Tel: +44 2075407117

Lietuva
UAB Teva Baltics
Tel: +370 52660203

Luxembourg/Luxemburg
ratiopharm GmbH
Allemagne/Deutschland
Tél/Tel: +49 73140202

Magyarország
Teva Gyógyszergyár Zrt.
Tel: +36 12886400

Malta
Teva Pharmaceuticals Ireland
L-Irlanda
Tel: +44 2075407117

Nederland
Teva Nederland B.V.
Tel: +31 8000228400

Norge
Teva Norway AS
Tlf: +47 66775590

Österreich
ratiopharm Arzneimittel Vertriebs-GmbH
Tel: +43 1970070

Polska
Teva Pharmaceuticals Polska Sp. z o.o.
Tel: +48 223459300

Portugal
Teva Pharma - Produtos Farmacêuticos, Lda.
Tel: +351 214767550

România
Teva Pharmaceuticals S.R.L.
Tel: +40 212306524

Slovenija
Pliva Ljubljana d.o.o.
Tel: +386 15890390

Ísland
Teva Pharma Iceland ehf.
Sími: +354 5503300

Italia
Teva Italia S.r.l.
Tel: +39 028917981

Κύπρος
TEVA HELLAS A.E.
Ελλάδα
Τηλ: +30 2118805000

Latvija
UAB Teva Baltics filiāle Latvijā
Tel: +371 67323666

Slovenská republika
TEVA Pharmaceuticals Slovakia s.r.o.
Tel: +421 257267911

Suomi/Finland
Teva Finland Oy
Puh/Tel: +358 201805900

Sverige
Teva Sweden AB
Tel: +46 42121100

United Kingdom (Northern Ireland)
Accord Healthcare Ireland Ltd.
Ireland
Tel: +353 214619040

This leaflet was last revised in {MM/YYYY}

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Package leaflet: Information for the patient

Nemdatine 15 mg film-coated tablets
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 Nemdatine is and what it is used for

How does Nemdatine work
Nemdatine contains the active substance memantine hydrochloride. Nemdatine 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. Nemdatine belongs to a group of medicines called NMDA-receptor antagonists. Nemdatine acts on these NMDA-receptors improving the transmission of nerve signals and the memory.

What is Nemdatine used for
Nemdatine is used for the treatment of adult patients with moderate to severe Alzheimer's disease.

2. What you need to know before you take Nemdatine

Do not take Nemdatine
- if you are allergic to memantine hydrochloride or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Nemdatine
- 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 Nemdatine 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
Nemdatine is not recommended for children and adolescents under the age of 18 years.

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

In particular, Nemdatine 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 Nemdatine.

Nemdatine 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 and breast-feeding
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.

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

Breast-feeding
Women taking Nemdatine 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, Nemdatine may change your reactivity, making driving or operating machinery inappropriate.

Nemdatine contains lactose monohydrate
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Nemdatine

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

Dosage
The recommended dose of Nemdatine for adults and older people is 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	One 5 mg tablet
Week 2	One 10 mg tablet
Week 3	One 15 mg tablet
Week 4 and beyond	One 20 mg tablet once a day

The usual starting dose is 5 mg memantine once a day for the first week. This is increased to 10 mg memantine in the second week and to 15 mg memantine once a day in the third week. From the fourth week on, the usual dose is 20 mg memantine once a day.

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
Nemdatine 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 tablets should be swallowed with some water. The tablets can be taken with or without food.

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

If you take more Nemdatine than you should
- In general, taking too much Nemdatine 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 Nemdatine, contact your doctor or get medical advice, as you may need medical attention.

If you forget to take Nemdatine
- If you find you have forgotten to take your dose of Nemdatine, 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)
- Headache, sleepiness, constipation, elevated liver function test, dizziness, balance disorders, shortness of breath, high blood pressure and drug hypersensitivity

Uncommon (affects 1 to 10 users in 1,000)
- 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)
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nemdatine

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 blister after 'EXP'. The expiry date refers to the last day of that month.

Do not store above 25°C.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Nemdatine contains
- The active substance is memantine hydrochloride. Each film-coated tablet contains 15 mg memantine hydrochloride equivalent to 12.46 mg memantine.

- The other ingredients are: *Tablet core:* Microcrystalline cellulose, crospovidone Type A, talc and magnesium stearate. *Tablet coat (Opadry II Orange 33G230001):* Hypromellose 6cP, titanium dioxide (E171), lactose monohydrate, macrogol 3350, triacetin and iron oxide yellow, red and black (E172).

What Nemdatine looks like and contents of the pack
Nemdatine 15 mg film-coated tablets (tablets) are orange, oval shaped, biconvex, 11.4 mm x 6.4 mm in size, with the marking "M15" engraved on one side.

Pack sizes
Blister packs: 7, 42 and 98 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Actavis Group PTC ehf.
Dalshraun 1
220 Hafnarfjörður
Iceland

Manufacturer
Actavis Ltd.
BLB 015-016 Bulebel Industrial Estate
Zejtun ZTN 3000
Malta

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Teva Pharma Belgium N.V./S.A./AG
Tél/Tel: +32 38207373

България
Тева Фарма ЕАД
Тел: +359 24899585

Česká republika
Teva Pharmaceuticals CR, s.r.o.
Tel: +420 251007111

Danmark
Teva Denmark A/S
Tlf: +45 44985511

Deutschland
ratiopharm GmbH
Tel: +49 73140202

Eesti
UAB Teva Baltics Eesti filiaal
Tel: +372 6610801

Ελλάδα
TEVA HELLAS A.E.
Τηλ: +30 2118805000

España
Teva Pharma, S.L.U.
Tel: +34 913873280

France
Teva Santé
Tél: +33 155917800

Hrvatska
Pliva Hrvatska d.o.o.
Tel: +385 13720000

Ireland
Teva Pharmaceuticals Ireland
Tel: +44 2075407117

Lietuva
UAB Teva Baltics
Tel: +370 52660203

Luxembourg/Luxemburg
ratiopharm GmbH
Allemagne/Deutschland
Tél/Tel: +49 73140202

Magyarország
Teva Gyógyszergyár Zrt.
Tel: +36 12886400

Malta
Teva Pharmaceuticals Ireland
L-Irlanda
Tel: +44 2075407117

Nederland
Teva Nederland B.V.
Tel: +31 8000228400

Norge
Teva Norway AS
Tlf: +47 66775590

Österreich
ratiopharm Arzneimittel Vertriebs-GmbH
Tel: +43 1970070

Polska
Teva Pharmaceuticals Polska Sp. z o.o.
Tel: +48 223459300

Portugal
Teva Pharma - Produtos Farmacêuticos, Lda.
Tel: +351 214767550

România
Teva Pharmaceuticals S.R.L.
Tel: +40 212306524

Slovenija
Pliva Ljubljana d.o.o.
Tel: +386 15890390

Ísland
Teva Pharma Iceland ehf.
Sími: +354 5503300

Italia
Teva Italia S.r.l.
Tel: +39 028917981

Κύπρος
TEVA HELLAS A.E.
Ελλάδα
Τηλ: +30 2118805000

Latvija
UAB Teva Baltics filiāle Latvijā
Tel: +371 67323666

Slovenská republika
TEVA Pharmaceuticals Slovakia s.r.o.
Tel: +421 257267911

Suomi/Finland
Teva Finland Oy
Puh/Tel: +358 201805900

Sverige
Teva Sweden AB
Tel: +46 42121100

United Kingdom (Northern Ireland)
Accord Healthcare Ireland Ltd.
Ireland
Tel: +353 214619040

This leaflet was last revised in {MM/YYYY}

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Package leaflet: Information for the patient

Nemdatine 5 mg film-coated tablets
Nemdatine 10 mg film-coated tablets
Nemdatine 15 mg film-coated tablets
Nemdatine 20 mg film-coated tablets
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 Nemdatine is and what it is used for

How does Nemdatine work
Nemdatine contains the active substance memantine hydrochloride. Nemdatine 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. Nemdatine belongs to a group of medicines called NMDA-receptor antagonists. Nemdatine acts on these NMDA-receptors improving the transmission of nerve signals and the memory.

What is Nemdatine used for
Nemdatine is used for the treatment of adult patients with moderate to severe Alzheimer's disease.

2. What you need to know before you take Nemdatine

Do not take Nemdatine
- if you are allergic to memantine hydrochloride or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Nemdatine
- 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 Nemdatine 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
Nemdatine is not recommended for children and adolescents under the age of 18 years.

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

In particular, Nemdatine 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 Nemdatine.

Nemdatine 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 and breast-feeding
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.

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

Breast-feeding
Women taking Nemdatine 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, Nemdatine may change your reactivity, making driving or operating machinery inappropriate.

Nemdatine contains lactose monohydrate
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Nemdatine

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

The Nemdatine treatment initiation pack is only to be used for the beginning of the treatment with Nemdatine.

Dosage
The recommended treatment dose of 20 mg per day is achieved by a gradual increase of the Nemdatine dose during the first 3 weeks of treatment. The treatment scheme is also indicated on the treatment initiation pack. Take one tablet once a day.

Week 1 (day 1-7):
Take one 5 mg tablet once a day (white, oval-shaped) for 7 days.

Week 2 (day 8-14):
Take one 10 mg tablet once a day (white, capsule shaped) for 7 days.

Week 3 (day 15-21):
Take one 15 mg tablet once a day (orange, oval shaped) for 7 days.

Week 4 (day 22-28):
Take one 20 mg tablet per day (dark pink, oval shaped) for 7 days.

Week 1	5 mg tablet
Week 2	10 mg tablet
Week 3	15 mg tablet
Week 4 and beyond	20 mg tablets once a day

Maintenance dose
The recommended daily dose is 20 mg once a day.
For continuation of the treatment please consult your doctor.

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
Nemdatine 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 tablets should be swallowed with some water. The tablets can be taken with or without food.

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

If you take more Nemdatine than you should
- In general, taking too much Nemdatine 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 Nemdatine, contact your doctor or get medical advice, as you may need medical attention.

If you forget to take Nemdatine
- If you find you have forgotten to take your dose of Nemdatine, 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)
- Headache, sleepiness, constipation, elevated liver function test, dizziness, balance disorders, shortness of breath, high blood pressure and drug hypersensitivity

Uncommon (affects 1 to 10 users in 1,000)
- 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)
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nemdatine

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 blister after 'EXP'. The expiry date refers to the last day of that month.

Do not store above 25°C.

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 Nemdatine contains
- The active substance is memantine hydrochloride. Each film-coated tablet contains 5, 10, 15, or 20 mg memantine hydrochloride equivalent to 4.15, 8.31, 12.46 or 16.62 mg memantine.

- The other ingredients for Nemdatine 5, 10, 15 and 20 mg film-coated tablets are: *Tablet core:* Microcrystalline cellulose, crospovidone Type A, talc and magnesium stearate. *Tablet coat:* Hypromellose 6cP, titanium dioxide (E171), lactose monohydrate, macrogol 3350 and triacetin. The 15 mg tablets furthermore contain iron oxide yellow, red and black (E172). The 20 mg tablets furthermore contain iron oxide red and yellow (E172).

What Nemdatine looks like and contents of the pack
Nemdatine 5 mg film-coated tablets (tablets) are white, oval shaped, biconvex, 8 mm x 4.5 mm in size, with the marking “M5” engraved on one side.
Nemdatine 10 mg film-coated tablets (tablets) are white, capsule-shaped, biconvex, 9.8 mm x 4.9 mm in size, with score line and the marking “M 10” engraved on the scored side.
Nemdatine 15 mg film-coated tablets (tablets) are orange, oval shaped, biconvex, 11.4 mm x 6.4 mm in size, with the marking “M15” engraved on one side.
Nemdatine 20 mg film-coated tablets (tablets) are dark pink, oval shaped, biconvex, 12.6 mm x 7 mm in size, with the marking “M20” engraved on one side.

One treatment initiation pack contains 28 tablets in 4 blisters in a wallet pack or a multipack of 4 blisters in 4 separate immediate cartons and one outer carton with 7 tablets of Nemdatine 5 mg, 7 tablets of Nemdatine 10 mg, 7 tablets of Nemdatine 15 mg and 7 tablets of Nemdatine 20 mg.

Marketing Authorisation Holder
Actavis Group PTC ehf.
Dalshraun 1
220 Hafnarfjörður
Iceland

Manufacturer
Actavis Ltd.
BLB 015-016 Bulebel Industrial Estate
Zejtun ZTN 3000
Malta

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Teva Pharma Belgium N.V./S.A./AG
Tél/Tel: +32 38207373

България
Тева Фарма ЕАД
Тел: +359 24899585

Česká republika
Teva Pharmaceuticals CR, s.r.o.
Tel: +420 251007111

Danmark
Teva Denmark A/S
Tlf: +45 44985511

Deutschland
ratiopharm GmbH
Tel: +49 73140202

Eesti
UAB Teva Baltics Eesti filiaal
Tel: +372 6610801

Lietuva
UAB Teva Baltics
Tel: +370 52660203

Luxembourg/Luxemburg
ratiopharm GmbH
Allemagne/Deutschland
Tél/Tel: +49 73140202

Magyarország
Teva Gyógyszergyár Zrt.
Tel: +36 12886400

Malta
Teva Pharmaceuticals Ireland
L-Irlanda
Tel: +44 2075407117

Nederland
Teva Nederland B.V.
Tel: +31 8000228400

Norge
Teva Norway AS
Tlf: +47 66775590

Ελλάδα
TEVA HELLAS A.E.
Τηλ: +30 2118805000

España
Teva Pharma, S.L.U.
Tel: +34 913873280

France
Teva Santé
Tél: +33 155917800

Hrvatska
Pliva Hrvatska d.o.o.
Tel: +385 13720000

Ireland
Teva Pharmaceuticals Ireland
Tel: +44 2075407117

Ísland
Teva Pharma Iceland ehf.
Sími: +354 5503300

Italia
Teva Italia S.r.l.
Tel: +39 028917981

Κύπρος
TEVA HELLAS A.E.
Ελλάδα
Τηλ: +30 2118805000

Latvija
UAB Teva Baltics filiāle Latvijā
Tel: +371 67323666

Österreich
ratiopharm Arzneimittel Vertriebs-GmbH
Tel: +43 1970070

Polska
Teva Pharmaceuticals Polska Sp. z o.o.
Tel: +48 223459300

Portugal
Teva Pharma - Produtos Farmacêuticos, Lda.
Tel: +351 214767550

România
Teva Pharmaceuticals S.R.L.
Tel: +40 212306524

Slovenija
Pliva Ljubljana d.o.o.
Tel: +386 15890390

Slovenská republika
TEVA Pharmaceuticals Slovakia s.r.o.
Tel: +421 257267911

Suomi/Finland
Teva Finland Oy
Puh/Tel: +358 201805900

Sverige
Teva Sweden AB
Tel: +46 42121100

United Kingdom (Northern Ireland)
Accord Healthcare Ireland Ltd.
Ireland
Tel: +353 214619040

This leaflet was last revised in {MM/YYYY}

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.

Package leaflet: Information for the patient

Nemdatine 20 mg film-coated tablets
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 Nemdatine is and what it is used for

How does Nemdatine work
Nemdatine contains the active substance memantine hydrochloride. Nemdatine 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. Nemdatine belongs to a group of medicines called NMDA-receptor antagonists. Nemdatine acts on these NMDA-receptors improving the transmission of nerve signals and the memory.

What is Nemdatine used for
Nemdatine is used for the treatment of adult patients with moderate to severe Alzheimer's disease.

2. What you need to know before you before you take Nemdatine

Do not take Nemdatine
- if you are allergic to memantine hydrochloride or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Nemdatine
- 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 Nemdatine 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
Nemdatine is not recommended for children and adolescents under the age of 18 years.

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

In particular, Nemdatine 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 Nemdatine.

Nemdatine 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 and breast-feeding
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.

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

Breast-feeding
Women taking Nemdatine 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, Nemdatine may change your reactivity, making driving or operating machinery inappropriate.

Nemdatine contains lactose monohydrate
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Nemdatine

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

Dosage
The recommended dose of Nemdatine for adults and older people is 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. For up-titration other tablet strengths are available.

At the beginning of treatment you will start by using Nemdatine 5 mg film-coated tablets once a day. This dose will be increased weekly by 5 mg until the recommended (maintenance) dose is reached. The recommended maintenance dose is 20 mg once a day, which is reached at the beginning of the 4th week.

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
Nemdatine 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 tablets should be swallowed with some water. The tablets can be taken with or without food.

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

If you take more Nemdatine than you should
- In general, taking too much Nemdatine 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 Nemdatine, contact your doctor or get medical advice, as you may need medical attention.

If you forget to take Nemdatine
- If you find you have forgotten to take your dose of Nemdatine, 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)
- Headache, sleepiness, constipation, elevated liver function test, dizziness, balance disorders, shortness of breath, high blood pressure and drug hypersensitivity

Uncommon (affects 1 to 10 users in 1,000)
- 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)
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nemdatine

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, blister and bottle label after 'EXP'. The expiry date refers to the last day of that month.

Do not store above 25°C.

<[For HDPE bottle only:]>
Use within 100 days after opening.

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 Nemdatine contains
- The active substance is memantine hydrochloride. Each film-coated tablet contains 20 mg memantine hydrochloride equivalent to 16.62 mg memantine.

- The other ingredients are: *Tablet core:* Microcrystalline cellulose, crospovidone Type A, talc and magnesium stearate. *Tablet coat (Opadry II Pink 33G240000):* Hypromellose 6cP, titanium dioxide (E171), lactose monohydrate, macrogol 3350, triacetin and iron oxide red and yellow (E172).

What Nemdatine looks like and contents of the pack
Nemdatine 20 mg film-coated tablets (tablets) are dark pink, oval shaped, biconvex, 12.6 mm x 7 mm in size, with the marking "M20" engraved on one side.

Pack sizes
Blister packs: 28, 42, 56 and 98 film-coated tablets.
Bottle: 100 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Actavis Group PTC ehf.
Dalshraun 1
220 Hafnarfjörður
Iceland

Manufacturer
Actavis Ltd.
BLB 015-016 Bulebel Industrial Estate
Zejtun ZTN 3000
Malta

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Teva Pharma Belgium N.V./S.A./AG
Tél/Tel: +32 38207373

България
Тева Фарма ЕАД
Тел: +359 24899585

Česká republika
Teva Pharmaceuticals CR, s.r.o.
Tel: +420 251007111

Danmark
Teva Denmark A/S
Tlf: +45 44985511

Deutschland
ratiopharm GmbH
Tel: +49 73140202

Eesti
UAB Teva Baltics Eesti filiaal
Tel: +372 6610801

Ελλάδα
TEVA HELLAS A.E.
Τηλ: +30 2118805000

España
Teva Pharma, S.L.U.
Tel: +34 913873280

France
Teva Santé
Tél: +33 155917800

Hrvatska
Pliva Hrvatska d.o.o.
Tel: +385 13720000

Ireland
Teva Pharmaceuticals Ireland
Tel: +44 2075407117

Ísland
Teva Pharma Iceland ehf.
Sími: +354 5503300

Lietuva
UAB Teva Baltics
Tel: +370 52660203

Luxembourg/Luxemburg
ratiopharm GmbH
Allemagne/Deutschland
Tél/Tel: +49 73140202

Magyarország
Teva Gyógyszergyár Zrt.
Tel: +36 12886400

Malta
Teva Pharmaceuticals Ireland
L-Irlanda
Tel: +44 2075407117

Nederland
Teva Nederland B.V.
Tel: +31 8000228400

Norge
Teva Norway AS
Tlf: +47 66775590

Österreich
ratiopharm Arzneimittel Vertriebs-GmbH
Tel: +43 1970070

Polska
Teva Pharmaceuticals Polska Sp. z o.o.
Tel: +48 223459300

Portugal
Teva Pharma - Produtos Farmacêuticos, Lda.
Tel: +351 214767550

România
Teva Pharmaceuticals S.R.L.
Tel: +40 212306524

Slovenija
Pliva Ljubljana d.o.o.
Tel: +386 15890390

Slovenská republika
TEVA Pharmaceuticals Slovakia s.r.o.
Tel: +421 257267911

Italia
Teva Italia S.r.l.
Tel: +39 028917981

Κύπρος
TEVA HELLAS A.E.
Ελλάδα
Τηλ: +30 2118805000

Latvija
UAB Teva Baltics filiāle Latvijā
Tel: +371 67323666

Suomi/Finland
Teva Finland Oy
Puh/Tel: +358 201805900

Sverige
Teva Sweden AB
Tel: +46 42121100

United Kingdom (Northern Ireland)
Accord Healthcare Ireland Ltd.
Ireland
Tel: +353 214619040

This leaflet was last revised in {MM/YYYY}

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.