

HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to Tablets: 5 mg and 10 mg (3)

use MEMANTINE HYDROCHLORIDE Tablets USP safely and effectively. See full prescribing information for MEMANTINE HYDROCHLORIDE Tablets USP.

MEMANTINE hydrochloride tablets USP for oral use Initial U.S. Approval: 2003

----INDICATIONS AND USAGE-----Memantine Hydrochloride Tablet, USP is an N-methyl-D-aspartate elimination of memantine, resulting in increased plasma levels of (NMDA) receptor antagonist indicated for the treatment of memantine. (5.1, 7.1) moderate to severe dementia of the Alzheimer's type. (1) ----DOSAGE AND ADMINISTRATION---

· May be taken with or without food. (2) to a maintenance dose of 10 mg twice daily. A minimum of 1 week

Pharma Inc 1-877-244-9825 or go to www.stridesshasun.com of treatment with the previous dose should be observed before or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. increasing the dose. (2)

----CONTRAINDICATIONS---Memantine hydrochloride tablets are contraindicated in patients

-- DOSAGE FORMS AND STRENGTHS-

with known hypersensitivity to memantine hydrochloride or to any excipients used in the formulation. (4) ----WARNINGS AND PRECAUTIONS-- \cdot Conditions that raise urine pH may decrease the urinary

-----ADVERSE REACTIONS-Most common adverse reactions (≥ 5 % and greater than placebo) are dizziness, headache, confusion and constipation. (6.1) Initial dose is 5 mg once daily. Increase dose in 5 mg increments

To report SUSPECTED ADVERSE REACTIONS, contact Strides

Severe renal impairment: recommended dose is 5 mg twice daily.

See 17 for Patient Counseling Information and FDA-approved patient labeling. Revised: 05/2017

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Information are not listed.

FULL PRESCRIBING INFORMATION 1 INDICATIONS AND USAGE

8.4 Pediatric Use

Memantine Hydrochloride Tablets USP are indicated for the treatment of moderate to severe dementia of the Alzheimer's type.

2 DOSAGE AND ADMINISTRATION he recommended starting dose of memantine hydrochloride is 5 mg once daily. The dose should be increased in 5 mg increments to 10 mg/day (5 mg twice daily), 15 mg/day (5 mg and 10 mg as separate doses), and 20 mg/day (10 mg twice daily). The minimum recommended interval between dose increases is one week. The dosage shown to be effective in controlled clinical trials is 20 mg/day. $Memantine \ \ hydrochloride \ \ can \ \ be \ \ taken \ \ with \ \ or \ \ without \ food. \ \ If \ \ a \ \ patient \ \ misses \ \ a \ \ single \ \ dose \ \ of \ \ memantine \ \ \ hydrochloride, \ \ that$ patient should not double up on the next dose. The next dose should be taken as scheduled. If a patient fails to take memantine

hydrochloride tablets for several days, dosing may need to be resumed at lower doses and retitrated as described above Special Populations A target dose of 5 mg twice daily is recommended in patients with severe renal impairment (creatinine clearance of 5 to 29 mL/min

based on the Cockroft-Gault equation) Memantine hydrochloride should be administered with caution to patients with severe hepatic impairment [see Clinical Pharmacology

3 DOSAGE FORMS AND STRENGTHS Memantine Hydrochloride Tablets, USP 5 mg: Tan colored, capsule-shaped, film-coated tablets debossed with "M5" on one side and plain

on the other side. Memantine Hydrochloride Tablets, USP 10 mg: Gray, capsule-shaped, film-coated tablets debossed with "M10" on one side and plain on the other side. 4 CONTRAINDICATIONS

Memantine hydrochloride tablets are contraindicated in patients with known hypersensitivity to memantine hydrochloride or to any excipients used in the formulation

Conditions that raise urine pH may decrease the urinary elimination of memantine resulting in increased plasma levels of memantine [see Drug Interactions (7.1)]

ADVERSE REACTIONS 6.1 Clinical Trials Experience

Memantine hydrochloride was evaluated in eight double-blind placebo-controlled trials involving a total of 1862 dementia (Alzheimer's disease, vascular dementia) patients (940 patients treated with memantine hydrochloride and 922 patients treated with placebo) for Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug

cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. Adverse Events Leading to Discontinuation In placebo-controlled trials in which dementia patients received doses of memantine hydrochloride up to 20 mg/day, the likelihood

of discontinuation because of an adverse reaction was the same in the memantine hydrochloride group (10.1%) as in the placebo group (11.5%). No individual adverse reaction was associated with the discontinuation of treatment in 1% or more of memantine hydrochloride-treated patients and at a rate greater than placebo. Most Common Adverse Reactions

than placebo) in patients treated with memantine hydrochloride were dizziness, headache, confusion and constipation. Table 1 lists all adverse reactions that occurred in at least 2% of patients treated with memantine hydrochloride and at an incidence greater than placebo.

Table 1: Adverse Reactions Reported in Controlled Clinical Trials in at Least 2% of Patients Receiving Memantine Hydrochloride and at a Higher Frequency than Placebo-treated Patients

Adverse Reaction	(N = 922) %	(N = 940) %
Body as a Whole		
Fatigue	1	2
Pain	1	3
Cardiovascular System		
Hypertension	2	4
Central and Peripheral Nervous System		
Dizziness	5	7
Headache	3	6
Gastrointestinal System		
Constipation	3	5
Vomiting	2	3
Musculoskeletal System		
Back pain	2	3
Psychiatric Disorders		
Confusion	5	6
Somnolence	2	3
Hallucination	2	3
Respiratory System	_	
Coughing	3	4
Dyspnea	1	2

The overall profile of adverse reactions and the incidence rates for individual adverse reactions in the subpopulation of patients with moderate to severe Alzheimer's disease were not different from the profile and incidence rates described above for the overall dementia population.

Memantine hydrochloride has not been systematically evaluated in patients with a seizure disorder. In clinical trials of memantine hydrochloride, seizures occurred in 0.2% of patients treated with memantine hydrochloride and 0.5% of patients treated with placebo.

6.2 Postmarketing Experience The following adverse reactions have been identified during post-approval use of memantine. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal

relationship to drug exposure. These reactions include: $Blood\ and\ Lymphatic\ System\ Disorders-a granulocytosis,\ leukopenia\ (including\ neutropenia),\ pancytopenia,\ thrombocytopenia,\ thrombotic$ thrombocytopenic purpura.

Cadriac Disorders – cardiac failure congestive Gastrointestinal Disorders – pancreatitis. Hepatobiliary Disorders – hepatitis.

Psychiatric Disorders - suicidal ideation

Renal and Urinary Disorders – acute renal failure (including increased creatinine and renal insufficiency). Skin Disorders - Stevens Johnson syndrome.

DRUG INTERACTIONS 7.1 Drugs that Make the Urine Alkaline

The clearance of memantine was reduced by about 80% under alkaline urine conditions at pH 8. Therefore, alterations of urine pH towards the alkaline condition may lead to an accumulation of the drug with a possible increase in adverse effects. Urine pH is altered by diet, drugs (e.g. carbonic anhydrase inhibitors, sodium bicarbonate) and clinical state of the patient (e.g. renal tubular acidosis or severe infections of the urinary tract). Hence, memantine should be used with caution under these conditions

7.2 Use with Other N-methyl-D-aspartate (NMDA) Antagonists
The combined use of memantine hydrochloride with other NMDA antagonists (amantadine, ketamine, and dextromethorphan) has not been systematically evaluated and such use should be approached with caution.

8 USE IN SPECIFIC POPULATIONS

Teratogenic Effect:

There are no adequate and well-controlled studies of memantine in pregnant women. Memantine hydrochloride should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

emantine given orally to pregnant rats and pregnant rabbits during the period of organogenesis was not teratogenic up to the highest doses tested (18 mg/kg/day in rats and 30 mg/kg/day in rabbits, which are 9 and 30 times, respectively, the maximum recommended human dose [MRHD] on a mg/m² basis).

Slight maternal toxicity, decreased pup weights and an increased incidence of non-ossified cervical vertebrae were seen at an oral dose of 18 mg/kg/day in a study in which rats were given oral memantine beginning pre-mating and continuing through the postpartum period. Slight maternal toxicity and decreased pup weights were also seen at this dose in a study in which rats were treated from day 15 of gestation through the postpartum period. The no-effect dose for these effects was 6 mg/kg, which is 3 times the MRHD on a mg/m² basis. 8.3 Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when memantine hydrochloride is administered to a nursing mother.

8.4 Pediatric Use

The majority of people with Alzheimer's disease are 65 years and older. In the clinical studies of memantine hydrochloride the mean age of patients was approximately 76; over 90% of patients were 65 years and older, 60% were 75 years and older, and 12% were at or above 85 years of age. The efficacy and safety data presented in the clinical trial sections were obtained from these patients. There were no clinically meaningful differences in most adverse events reported by patient groups ≥65 years old and <65 year old 8.6 Renal Impairment

No dosage adjustment is needed in patients with mild or moderate renal impairment. A dosage reduction is recommended in patients with severe renal impairment [see Dosage and Administration (2) and Clinical Pharmacology (12.3)] 8.7 Hepatic Impairment

No dosage adjustment is needed in patients with mild or moderate hepatic impairment. Memantine hydrochloride should be administered with caution to patients with severe hepatic impairment [see Dosage and Administration (2) and Clinical Pharmacology (12.3)]. 10 OVERDOSAGE

Signs and symptoms most often accompanying memantine overdosage in clinical trials and from worldwide marketing experience, alone or in combination with other drugs and/or alcohol, include agitation, asthenia, bradycardia, confusion, coma, dizziness, ECG changes, increased blood pressure, lethargy, loss of consciousness, psychosis, restlessness, slowed movement, sommolence, stupor, unsteady gait, visual hallucinations, vertigo, vomiting, and weakness. The largest known ingestion of memantine worldwide was 2.0 grams in a patient who took memantine in conjunction with unspecified antidiabetic medications. The patient experienced coma, diplopia, and agitation, but subsequently recovered. Fatal outcome has been very rarely reported with memantine, and the relationship to memantine was unclear.

Because strategies for the management of overdose are continually evolving, it is advisable to contact a poison control center to determine the latest recommendations for the management of an overdose of any drug. As in any cases of overdose, general supportive measures should be utilized, and treatment should be symptomatic. Elimination of memantine can be enhanced by acidification of urine 11 DESCRIPTION

Memantine hydrochloride USP is an orally active NMDA receptor antagonist. The chemical name for memantine hydrochloride is 1-amino-3,5-dimethyladamantane hydrochloride with the following structural formula:

The molecular formula is $C_{12}H_{21}N \bullet HCl$ and the molecular weight is 215.77. Memantine HCl, USP occurs as a fine white to off-white powder,

Memantine Hydrochloride Tablets USP are available for oral administration as capsule-shaped, film-coated tablets containing 5 mg and 10 mg of memantine hydrochloride. The tablets also contain the following inactive ingredients: microcrystalline cellulose, colloidal silicon dioxide, talc, croscarmellose sodium, and magnesium stearate. In addition the following inactive ingredients are also present as components of the film coat: hypromellose, titanium dioxide, polyethylene glycol, FD&C yellow #6 and FD&C blue #2 (5 mg tablets), and hypromellose, titanium dioxide, polyethylene glycol and black iron oxide (10 mg tablets)

12 CLINICAL PHARMACOLOGY 12.1 Mechanism of Action

Persistent activation of central nervous system N-methyl-D-aspartate (NMDA) receptors by the excitatory amino acid glutamate has been hypothesized to contribute to the symptomatology of Alzheimer's disease. Memantine is postulated to exert its therapeutic effect through its action as a low to moderate affinity uncompetitive (open-channel) NMDA receptor antagonist which binds preferentially to the NMDA receptor-operated cation channels. There is no evidence that memantine prevents or slows neurodegeneration in patients with

Alzheimer's disease.

12.2 Pharmacodynamics

Memantine showed low to negligible affinity for GABA, benzodiazepine, dopamine, adrenergic, histamine and glycine receptors and for voltage-dependent Ca²⁺, Na⁺ or K⁺ channels. Memantine also showed antagonistic effects at the 5HT₃ receptor with a potency similar to that for the NMDA receptor and blocked nicotinic acetylcholine receptors with one-sixth to one-tenth the potency. In vitro studies have shown that memantine does not affect the reversible inhibition of acetylcholinesterase by donepezil, galantamine

ring oral administration memantine is highly absorbed with peak concentrations reached in about 3 to 7 hours. Memantine has linear pharmacokinetics over the therapeutic dose range. Food has no effect on the absorption of memantine

The mean volume of distribution of memantine is 9 to 11 L/kg and the plasma protein binding is low (45%)

Memantine undergoes partial hepatic metabolism. The hepatic microsomal CYP450 enzyme system does not play a significant role in the

Elimination Memantine is excreted predominantly (about 48%) unchanged in urine and has a terminal elimination half-life of about 60 to 80 hours. The remainder is converted primarily to three polar metabolites which possess minimal NMDA receptor antagonistic activity: the N-glucuronide conjugate, 6-hydroxy memantine, and 1-nitroso deaminated memantine. A total of 74% of the administered dose is excreted as the sum of the parent drug and the N-glucuronide conjugate. Renal clearance involves active tubular secretion moderated by

Pharmacokinetics in Specific Populations Following multiple dose administration of memantine hydrochloride 20 mg daily, females had about 45% higher exposure than males, but there was no difference in exposure when body weight was taken into account.

The pharmacokinetics of memantine hydrochloride in young and elderly subjects are similar. Renal Impairment

Memantine pharmacokinetics were evaluated following single oral administration of 20 mg memantine HCl in 8 subjects with mild renal impairment (creatinine clearance, CLcr, >50 to 80 mL/min), 8 subjects with moderate renal impairment (CLcr 30 to 49 mL/min), 7 subjects with severe renal impairment (CLcr 5 to 29 mL/min) and 8 healthy subjects (CLcr > 80 mL/min) matched as closely as possible by age, weight and gender to the subjects with renal impairment. Mean AUC $_{0...}$ increased by 4%, 60%, and 115% in subjects with mild, moderate, and severe renal impairment, respectively, compared to healthy subjects. The terminal elimination half-life increased by 18%, 41%, and 95% in subjects with mild, moderate, and severe renal impairment, respectively, compared to healthy subjects. No dosage adjustment is recommended for patients with mild and moderate renal impairment. Dosage should be reduced in patients with severe renal impairment [see Dosage and Administration (2)].

Hepatic Impairment Memantine pharmacokinetics were evaluated following the administration of single oral doses of 20 mg in 8 subjects with moderate hepatic impairment (Child-Pugh Class B, score 7 to 9) and 8 subjects who were age-, gender-, and weight-matched to the hepatically-impaired subjects. There was no change in memantine exposure (based on C_{max} and AUC) in subjects with moderate hepatic impairment as compared with healthy subjects. However, terminal elimination half-life increased by about 16% in subjects with moderate hepatic impairment as compared with healthy subjects. No dose adjustment is recommended for patients with mild and moderate hepatic impairment. Memantine should be administered with caution to patients with severe hepatic impairment as the pharmacokinetics of memantine have not been evaluated in that population.

Drug-Drug Interactions

Use with Cholinesterase Inhibitors Coadministration of memantine with the AChE inhibitor donepezil HCl did not affect the pharmacokinetics of either compound. Furthermore, memantine did not affect AChE inhibition by donepezil. In a 24-week controlled clinical study in patients with moderate to severe Alzheimer's disease, the adverse event profile observed with a combination of memantine hydrochloride and donepezil was similar to that of donepezil alone.

Effect of Memantine Hydrochloride on the Metabolism of Other Drugs In vitro studies conducted with marker substrates of CYP450 enzymes (CYP1A2, -2A6, -2C9, 2D6, -2E1, -3A4) showed minimal inhibition of these enzymes by memantine. In addition, in vitro studies indicate that at concentrations exceeding those associated with efficacy. memantine does not induce the cytochrome P450 isozymes CYP1A2, -2C9, -2E1 and -3A4/5. No pharmacokinetic interactions wi drugs metabolized by these enzymes are expected.

Pharmacokinetic studies evaluated the potential of memantine for interaction with warfarin, and buproprion. Memantine did not affect the pharmacokinetics of the CYP2B6 substrate buproprion or its metabolite hydroxybuproprion. Furthermore, memanting did not affect the pharmacokinetics or pharmacodynamics of warfarin as assessed by the prothrombin INR. Effect of Other Drugs on Memantine Hydrochloride

Memantine is predominantly renally eliminated, and drugs that are substrates and/or inhibitors of the CYP450 system are not expected to alter the metabolism of memantine. Drugs Eliminated via Renal Mechanisms

Because memantine is eliminated in part by tubular secretion, coadministration of drugs that use the same renal cationic system, including plasma levels of both agents. However, coadministration of memantine hydrochloride and HCTZ/TA did not affect the bioavailability of either memantine or TA, and the bioavailability of HCTZ decreased by 20%. In addition, coadministration of memantine with the

hydrochloride tablets before you start taking it and each t get a refill. There may be new information. This information take the place of talking to your doctor about your condition or your treatment.

What are memantine hydrochloride tablets?

Memantine hydrochloride tablets are a prescription medicine used for the treatment of moderate to severe dementia in people with Alzheimer's disease. Memantine hydrochloride tablets belongs to a class of medicines called NMDA (N-methyl-D

belongs to a class aspartate) inhibitors.

It is not known if memantine hydrochloride tablets are safe and effective in children.

Who should not take memantine hydrochloride tablets?

Do not take memantine hydrochloride tablets if you a allergic to memantine or any of the ingredients in memantin hydrochloride tablets. See the end of this leaflet for a comple list of ingredients in memantine hydrochloride tablets.

What should I tell my doctor before taking memantine hydrochloride tablets?

Before you take memantine hydrochloride tablets, tell your doctor if you: have or have had bladder or kidney problems have or have had problems passing urine have or have had seizures

MAKE ANY CHANGE TO THE ARTWORK WITHOUT WRITTEN INSTRUCTIONS FROM PDC.

are pregnant or plan to become pregnant. memantine hydrochloride will harm your unk have any other medical conditions

are breastfeeding or plan to breastfeed. memantine hydrochloride passes into You and your doctor should decide if you whydrochloride tablets or breastfeed.

if you will take memantine

Tell your doctor about all the medicines you take, including orescription and non-prescription medicines, vitamins, and herbal medicines may affect each other. Taking memantine hydrochloride tablets with other medicines can cause serious side effects.

Especially tell your doctor if you take:

other NMDA antagonists such as amantadine, ketamine and dextromethorphan

Ask your doctor or pharmacist for a list of these are not sure. medicines that make your urine anhydrase inhibitors and sodium b

alkaline such as carbonic

Know the medicines you take. Keep a list of them to show you doctor and pharmacist when you get a new medicine. How should I take memantine hydrochloride tablets?

Your doctor will tell you how many mablets to take and when to take them

Do not use any tablets of memantine hydrochloride that are damaged or show signs of tampering. you forget to take one dose of none one of none of not double up on the next dose. If you take too many memantine hydrochloride tablets, call your doctor or poison control center at 1-800-222-1222 right away, or go to the nearest hospital emergency room.

Perporation required.

Front side 360 x 420mm



MEMANTINE HYDROCHLORIDE

Patient Information

ARTWORK DETAIL LABEL

Product	Memantine HCI Tablets				
Buyer/Country	STRIDES PHARMA INC.	Component	Out sert with medication Guide		
Dimension	360 X 420 mm with Perforation as indicated.			Pack	NA
New Item Code	1034766	Old Item Code	NA		
Colour Shades	BLACK	1		No. of Colours	1
Change Control No.	NA			Artwork Version	1.0
Design/Style	Front & Back Printing. To be suppiled in folde	d size of 33 mm	x 33mm		
Substrate	40 / 45 GSM Paper.				
Special Instructions	PRINTING CLARITY TO BE CLEAR AND SHA	RP.			
Autocartonator Requirements	NA				
Caution to the printe	r: Before processing, please ensure that the ARTWC	PRK received for pr	inting is exactly in line	with APPROVED A	ARTW

provided to you. In case of any FONTS/DESIGN are Mis-matching with the APPROVED ARTWORK, please inform PDC for further action. DO NOT

antihyperglycemic drug Glucovance* (glyburide and metformin HCl) did not affect the pharmacokinetics of memantine, metformin and glyburide. Furthermore, memantine did not modify the serum glucose lowering effect of Glucovance*, indicating the absence of a pharmacodynamic interaction. Drugs Highly Bound to Plasma Proteins Because the plasma protein binding of memantine is low (45%), an interaction with drugs that are highly bound to plasma proteins, such as warfarin and digoxin, is unlikely 13 NONCLINICAL TOXICOLOGY 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility There was no evidence of carcinogenicity in a 113-week oral study in mice at doses up to 40 mg/kg/day (10 times the maximum recommended human dose [MRHD] on a mg/m² basis). There was also no evidence of carcinogenicity in rats orally dosed at up to 40 mg/kg/day for 71 weeks followed by 20 mg/kg/day (20 and 10 times the MRHD on a mg/m² basis, respectively) through 128 weeks. Memantine produced no evidence of genotoxic potential when evaluated in the in vitro S. typhimurium or E. coli reverse mutation assay an *in vitro* chromosomal aberration test in human lymphocytes, an *in vitro* cytogenetics assay for chromosome damage in rats, and the *in vivo* mouse micronucleus assay. The results were equivocal in an *in vitro* gene mutation assay using Chinese hamster V79 cells. No impairment of fertility or reproductive performance was seen in rats administered up to 18 mg/kg/day (9 times the MRHD on a mg/m² basis) orally from 14 days prior to mating through gestation and lactation in females, or for 60 days prior to mating in male: 13.2 Animal Toxicology and/or Pharmacology
Memantine induced neuronal lesions (vacuolation and necrosis) in the multipolar and pyramidal cells in cortical layers III and IV of the

posterior clingulate and retrosplenial neocortices in rats, similar to those which are known to occur in rodents administered other NMDA receptor antagonists. Lesions were seen after a single dose of memantine. In a study in which rats were given daily oral doses of memantine for 14 days, the no-effect dose for neuronal necrosis was 6 times the maximum recommended human dose of 20 mg/day on a mg/m² basis In acute and repeat-dose neurotoxicity studies in female rats, oral administration of memantine and donepezil in combination resulted in actue and repeat-dose neurooxicity studies in ternale rats, or a administration or inernatione and donepezh in combination resulted in increased incidence, severity, and distribution of neurodegeneration compared with memantine alone. The no-effect levels of the combination were associated with clinically relevant plasma memantine and donepezil exposures. The relevance of these findings to humans is unknown.

14 CLINICAL STUDIES

The effectiveness of memantine hydrochloride as a treatment for patients with moderate to severe Alzheimer's disease was demonstrated in 2 randomized, double-blind, placebo-controlled clinical studies (Studies 1 and 2) conducted in the United States that assessed both cognitive function and day to day function. The mean age of patients participating in these two trials was 76 with a range of 50 to 93 years. Approximately 66% of patients were female and 91% of patients were Caucasian. A third study (Study 3), carried out in Latvia, enrolled patients with severe dementia, but did not assess cognitive function as a planned endpoint. Study Outcome Measures: In each U.S. study, the effectiveness of memantine hydrochloride was determined using both an instrument designed to evaluate overall function through caregiver-related assessment, and an instrument that measures cognition. Both studies showed that patients on memantine hydrochloride experienced significant improvement on both measures compared to placebo.

Day-to-day function was assessed in both studies using the modified Alzheimer's disease Cooperative Study - Activities of Daily Living inventory (ADCS-ADL). The ADCS-ADL consists of a comprehensive battery of ADL questions used to measure the functional capabilities of patients. Each ADL term is rated from the highest level of independent performance to complete loss. The investigator performs the inventory by interviewing a caregiver familiar with the behavior of the patient. A subset of 19 items, including ratings of the patient's ability to eat, dress, bathe, telephone, travel, shop, and perform other household chores has been validated for the assessment of patients with moderate to severe dementia. This is the modified ADCS-ADL, which has a scoring range of 0 to 54, with the lower scores indicating

The ability of memantine hydrochloride to improve cognitive performance was assessed in both studies with the Severe Impairment Battery (SIB), a multi-item instrument that has been validated for the evaluation of cognitive function in patients with moderate to severe dementia. The SIB examines selected aspects of cognitive performance, including elements of attention, orientation, language, memory, visuospatial ability, construction, praxis, and social interaction. The SIB scoring range is from 0 to 100, with lower scores indicating greater cognitive impairment.

Study 1 (Twenty-Eight-Week Study)
In a study of 28 weeks duration, 252 patients with moderate to severe probable Alzheimer's disease (diagnosed by DSM-IV and NINCDS-ADRDA criteria, with Mini-Mental State Examination scores ≥ 3 and ≤ 14 and Global Deterioration Scale Stages 5 to 6) were randomized to memantine hydrochloride or placebo. For patients randomized to memantine hydrochloride, treatment was initiated at 5 mg once daily and increased weekly by 5 mg/day in divided doses to a dose of 20 mg/day (10 mg twice a day).

Effects on the ADCS-ADL Figure 1 shows the time course for the change from baseline in the ADCS-ADL score for patients in the two treatment groups completing the 28 weeks of the study. At 28 weeks of treatment, the mean difference in the ADCS-ADL change scores for the memantine hydrochloride-treated patients compared to the patients on placebo was 3.4 units. Using an analysis based on all patients and carrying their last study ntine hydrochloride treatment was statistically significantly superior to placeb

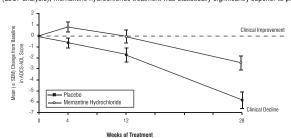


Figure 1: Time course of the change from baseline in ADCS-ADL score for patients completing 28 weeks of treatment. Figure 2 shows the cumulative percentages of patients from each of the treatment groups who had attained at least the change in the ADCS-ADL shown on the X axis. The curves show that both patients assigned to memantine hydrochloride and placebo have a wide range of responses and generally show deterioration (a negative change in ADCS-ADL compared to baseline), but that the memantine hydrochloride group is more likely to show a smaller decline or an improvement. (In a cumulative distribution display, a curve for

an effective treatment would be shifted to the left of the curve for placebo, while an ineffective or deleterious treatment would be superimposed upon or shifted to the right of the curve for placebo).

ADCS-ADL Change from Basel

Figure 3 shows the time course for the change from baseline in SIB score for the two treatment groups over the 28 weeks of the study. At 28 weeks of treatment, the mean difference in the SIB change scores for the memantine hydrochloride-treated patients compared to the patients on placebo was 5.7 units. Using an LOCF analysis, memantine hydrochloride treatment was statistically significantly

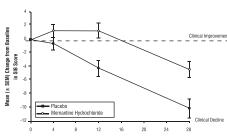


Figure 3: Time course of the change from baseline in SIB score for patients completing 28 weeks of treatment. Figure 4 shows the cumulative percentages of patients from each treatment group who had attained at least the measure of change in SIB score shown on the X axis. The curves show that both patients assigned to memantine hydrochloride and placebo have a wide range of responses and generally show deterioration, but that the memantine hydrochloride group is more likely to show a smaller decline or

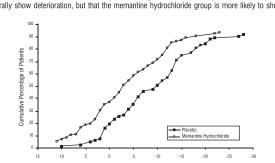


Figure 4: Cumulative percentage of patients completing 28 weeks of double-blind treatment with specified changes from baseline

In a study of 24 weeks duration, 404 patients with moderate to severe probable Alzheimer's disease (diagnosed by NINCDS-ADRDA criteria. with Mini-Mental State Examination scores ≥ 5 and ≤ 14) who had been treated with donepezil for at least 6 months and who had been on a stable dose of donepezil for the last 3 months were randomized to memantine hydrochloride or placebo while still receiving donepezil. For patients randomized to memantine hydrochloride, treatment was initiated at 5 mg once daily and increased weekly by 5 mg/day in divided

Figure 5 shows the time course for the change from baseline in the ADCS-ADL score for the two treatment groups over the 24 weeks of the study. At 24 weeks of treatment, the mean difference in the ADCS-ADL change scores for the memantine hydrochloride/donepezil treated patients (combination therapy) compared to the patients on placebo/donepezil (monotherapy) was 1.6 units. Using an LOCF analysis, memantine hydrochloride/donepezil treatment was statistically significantly superior to placebo/done

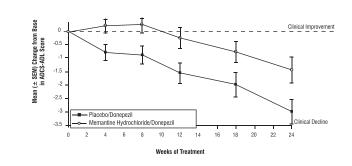
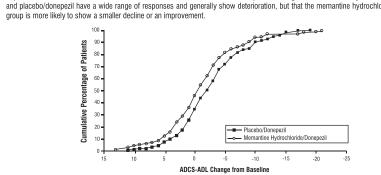


Figure 5: Time course of the change from baseline in ADCS-ADL score for patients completing 24 weeks of treatment. Figure 6 shows the cumulative percentages of patients from each of the treatment groups who had attained at least the measure of improvement in the ADCS-ADL shown on the X axis. The curves show that both patients assigned to memantine hydrochloride/donepezil and placebo/donepezil have a wide range of responses and generally show deterioration, but that the memantine hydrochloride/donepezil



Effects on the SIB

Figure 7 shows the time course for the change from baseline in SIB score for the two treatment groups over the 24 weeks of the study. At 24 weeks of treatment, the mean difference in the SIB change scores for the memantine hydrochloride/donepezil-treated patients compared to the patients on placebo/donepezil was 3.3 units. Using an LOCF analysis, memantine hydrochloride/donepezil treatment was statistically significantly superior to placebo/donepezil.

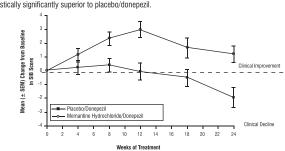


Figure 7: Time course of the change from baseline in SIB score for patients completing 24 weeks of treatment. Figure 8 shows the cumulative percentages of patients from each treatment group who had attained at least the measure of improvement in SIB score shown on the X axis. The curves show that both patients assigned to memantine hydrochloride/donepezil and placebo/donepezil have a wide range of responses, but that the memantine hydrochloride/donepezil group is more likely to show an improvement or a smaller

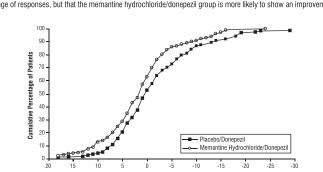


Figure 8: Cumulative percentage of patients completing 24 weeks of double-blind treatment with specified changes from baseline in SIB scores.

Study 3 (Twelve-Week Study) In a double-blind study of 12 weeks duration, conducted in nursing homes in Latvia, 166 patients with dementia according to DSM-III-R, a Mini-Mental State Examination score of < 10, and Global Deterioration Scale staging of 5 to 7 were randomized to either memantine hydrochloride or placebo. For patients randomized to memantine hydrochloride, treatment was initiated at 5 mg once daily and increased to 10 mg once daily after 1 week. The primary efficacy measures were the care dependency subscale of the Behavioral Rating Scale for Geriatric Patients (BGP), a measure of day-to-day function, and a Clinical Global Impression of Change (CGI-C), a measure of overall clinical effect. No valid measure of cognitive function was used in this study. A statistically significant treatment difference at 12 weeks that favored memantine hydrochloride over placebo was seen on both primary efficacy measures. Because the patients entered were a mixture of Alzheimer's disease and vascular dementia, an attempt was made to distinguish the two groups and all patients were later designated as having either vascular dementia or Alzheimer's disease, based on their scores on the Hachinski Ischemic Scale at study entry. Only about 50% of the patients had computerized tomography of the brain. For the subset designated as having Alzheimer's disease, a statistically significant treatment effect favoring memantine hydrochloride over placebo at 12 weeks was seen on both the BGP 16 HOW SUPPLIED/STORAGE AND HANDLING

Memantine Hydrochloride Tablets, USP 5 mg: Tan colored, capsule-shaped, film-coated tablets debossed with "M5" on one side and plain

Memantine Hydrochloride Tablets, USP 10 mg: Gray, capsule-shaped, film-coated tablets debossed with "M10" on one side and plain on

tile otilei Side.					
NDC #	Product	Pack Size			
64380-774-01	Memantine Hydrochloride Tablets USP, 5 mg	1 x 10 Unit Dose			
64380-774-30		10 x 10 Unit Dose			
64380-774-03		60's bottle			
64380-745-30	Memantine Hydrochloride Tablets USP, 10 mg	10 x 10 Unit Dose			
64380-745-03		60's bottle			

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature] 17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

To assure safe and effective use of memantine hydrochloride tablets, the following information provided in the patient information section should be discussed with patients and caregivers.

Patients/caregivers should be instructed to follow the dose titration schedule provided by their physician or healthcare professional for memantine hydrochloride. They should be warned not to use any tablets of memantine hydrochloride that are damaged or show signs of tampering.

If a patient misses a single dose of memantine hydrochloride, that patient should not double up on the next dose. The next dose should be taken as scheduled. If a patient fails to take memantine hydrochloride tablets for several days, dosing should not be resumed without consulting that patient's healthcare professional. Manufactured by:

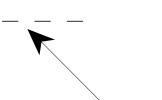
Strides Shasun Limited Bengaluru - 562106, India

Distributed by: Strides Pharma Inc East Brunswick, NJ 08816

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1034766

360 x 420mm



Perporation required.

Memantine hydrochloride tablets may cause side effects What are the possible hydrochloride tablets?

Back side

These are not all the possible side effects of memantine hydrochloride tablets. For more information, ask your doctor or

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. How should I store

ingredients

General information about the amemantine hydrochloride tablets.

Distributed by: Strides Pharma Inc. East Brunswick, NJ 08816 Revised: 05/2017

ARTWORK DETAIL LABEL

Product	Memantine HCI Tablets				
Buyer/Country	STRIDES PHARMA INC.	Component	Out sert with medication Guide		
Dimension	360 X 420 mm with Perforation as indicated.			Pack	NA
New Item Code	1034766	Old Item Code	NA		ı
Colour Shades	BLACK	1		No. of Colours	1
Change Control No.	NA			Artwork Version	1.0
Design/Style	Front & Back Printing. To be suppiled in folder	d size of 33 mm	x 33mm		
Substrate	40 / 45 GSM Paper.				
Special Instructions	PRINTING CLARITY TO BE CLEAR AND SHA	RP.			
Autocartonator Requirements	NA				
Caution to the printe	r: Before processing, please ensure that the ARTWC	RK received for pr	inting is exactly in line	with APPROVED A	ARTW

provided to you. In case of any FONTS/DESIGN are Mis-matching with the APPROVED ARTWORK, please inform PDC for further action. **DO NOT MAKE ANY CHANGE TO THE ARTWORK WITHOUT WRITTEN INSTRUCTIONS FROM PDC.**