Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Memantine 10 mg orodispersible tablets
Memantine 20 mg orodispersible tablets

memantine hydrochloride

PL 24837/0198-0199

Consilient Health Limited

LAY SUMMARY

Memantine 10 mg and 20 mg orodispersible tablets
memantine hydrochloride

This is a summary of the Public Assessment Report (PAR) for Memantine 10 mg and 20 mg orodispersible tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Memantine tablets in this lay summary for ease of reading.

For practical information about using Memantine tablets, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What are Memantine tablets and what are they used for?
These products are generic medicines. This means that these medicines are the same as, and considered interchangeable with, reference medicines already authorised, called Ebixa 10 mg and 20 mg film-coated tablets.

Memantine tablets are used for the treatment of patients with moderate to severe Alzheimer's disease.

How do Memantine tablets work?
Memantine tablets contains the active substance memantine hydrochloride. It 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. Memantine belongs to a group of medicines called NMDAreceptor antagonists. Memantine acts on these NMDA receptors improving the transmission of nerve signals and the memory.

How are Memantine tablets used?
The pharmaceutical form of these medicines is orodispersible tablet, and the route of administration is oral (by mouth).

The recommended dose of memantine 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	5 mg once a day
Week 2	10 mg once a day
Week 3	15 mg once a day
Week 4 and beyond	20 mg once a day

Memantine orodispersible tablets cannot be split.

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

Memantine should be administered orally once a day. To benefit from these medicines the patient should take it regularly every day at the same time of the day. The tablet should be placed on the tongue and allowed to dissolve before swallowing with or without water, as the patient prefers. The tablets can be taken with or without food.

For further information on how Memantine tablets are used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Memantine tablets have been shown in studies?
Because Memantine tablets are generic medicines, studies in healthy volunteers have been limited to tests to determine that it is bioequivalent to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the possible side effects of Memantine tablets?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Memantine tablets are generic medicines, its benefits and possible side effects are considered to be the same as for the reference medicines.

Why were Memantine tablets approved?
It was concluded that, Memantine tablets has been shown to be bioequivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

Memantine tablets have been authorised with the condition to perform further studies and/or to provide additional measures to minimise the risk. See section below "What measures are being taken to ensure the safe and effective use of Memantine tablets?"

What measures are being taken to ensure the safe and effective use of Memantine tablets?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Memantine tablets. The RMP details the important risks of Memantine tablets, how these risks can be minimised, any uncertainties about Memantine tablets (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Memantine tablets:

Summary of safety concerns	
Important identified risks	• Hepatic disorders
Important potential risks	• None
Missing information	• None

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Memantine tablets are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Memantine tablets
Marketing authorisations for Memantine tablets were granted in the United Kingdom (UK) on 08 October 2025.

The full PAR for Memantine tablets follows this summary.

This summary was last updated in October 2025.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for **Memantine 10 mg and 20 mg orodispersible tablets** (PL 24837/0198-0199) could be approved.

The products are approved for the following indication(s):
Treatment of adult patients with moderate to severe Alzheimer's disease.

The name of the active substance is memantine hydrochloride which belongs to the pharmacotherapeutic group of psychoanaleptics; other Anti-dementia drugs.
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.

These applications were approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as generic medicines of a suitable originator medicinal products, Ebixa 20 mg film-coated tablets that has been licensed for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the applications are for generic medicinal product of suitable reference products.

With the exception of the bioequivalence study, no new clinical studies were conducted, which is acceptable given that the applications are for generic medicinal products of a suitable reference product(s). The bioequivalence study was conducted in-line with current Good Clinical Practice (GCP).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Marketing authorisations for Memantine tablets were granted in the United Kingdom (UK) on 08 October 2025.

II QUALITY ASPECTS

II.1 Introduction

These products consist of orodispersible tablets; each orodispersible tablet contains 10 mg or 20 mg of memantine hydrochloride, equivalent to 8.31 mg or 16.62 mg of memantine respectively

In addition to memantine hydrochloride, these products also contain the following excipients: microcrystalline cellulose, polacrilin potassium, croscarmellose sodium, peppermint flavouring, aspartame (E-951), mannitol, maize starch, saccharin sodium, silica, colloidal anhydrous and magnesium stearate.

The finished products are packaged in aluminium/Polyamide-Aluminium-PVC blister strips, in a carton in pack sizes of 28 or 112 tablets (10 mg strength only) and 28 or 56 tablets (20 mg strength only).

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

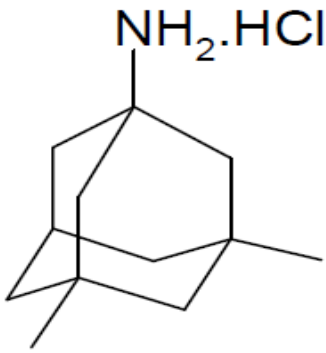
II.2 ACTIVE SUBSTANCE(S)

rINN: memantine hydrochloride

Chemical Name: - 3,5-Dimethyltricyclo-[3.3.1.1.3,7]decan-1-amine hydrochloride
Other names:
- 3,5-Dimethyl-1-adamantanamine hydrochloride
- 1-amino-3,5-dimethyladamantane hydrochloride
- Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-hydrochloride

Molecular Formula: $C_{12}H_{21}N \cdot HCl$

Chemical Structure:



Molecular Weight: 215.76

Appearance: White or almost white crystalline powder

Solubility:

Water	:	50 mg/ml	soluble
Acetone	:	< 10 mg/ml	sparingly soluble
Methanol	:	> 100 mg/ml	freely soluble
DMF	:	20 mg/ml	sparingly soluble

The information related to the active substance was provided in an ASMF.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specification. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging complies with the current regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

II.3 DRUG PRODUCT(S)

Pharmaceutical development

A satisfactory account of the pharmaceutical development was provided.
Comparative *in vitro* dissolution and impurity profiles were provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis were provided for all excipients.

No excipients of animal or human origin are used in the final products.

These products do not contain or consist of genetically modified organisms (GMO).

Manufacture of the product(s)

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability

Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 2 years with no special storage conditions requirments, is acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of marketing authorisations was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of memantine hydrochloride are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology
No new pharmacology data were provided, and none were required for these applications.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided, and none were required for these applications.

III.4 Toxicology
No new toxicology data were provided, and none were required for these applications.

III.5 Ecotoxicity/Environmental Risk Assessment
A suitable justification was provided for non-submission of an Environmental Risk Assessment. As the applications are for generic versions of an already authorised products, an increase in environmental exposure is not anticipated following approval of the marketing authorisations for the proposed products.

III.6 Discussion on the non-clinical aspects
The grant of marketing authorisations was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
The clinical pharmacology, efficacy and safety of memantine hydrochloride is/are well-known. With the exception of data from one bioequivalence study, no new clinical data are provided or are required for this type of application. An overview based on a literature review and a review of this study is, thus, satisfactory.

IV. 2 Pharmacokinetics
In support of the application, the applicant submitted the following bioequivalence study

This study was an open-label, randomised, two-treatment, two-sequence, two-period, single-dose, crossover oral bioequivalence study comparing the test product with the reference product under fasting conditions comparing the test product Memantine 20 mg orodispersible tablets versus the reference product Ebixa 20 mg film-coated tablets in subjects under fasted conditions.

Subjects were administered a single dose of the test or reference products. Blood samples were taken pre-dose and up to 72.00 hours post dose, with a washout period of 28 days between the treatment periods.

A summary of the pharmacokinetic results is presented below:

Table: Pharmacokinetic data – descriptive statistics

Memantine	Memantina Normon		Ebixa®	
	Mean	SD	Mean	SD
AUC_{0-72h} (h*ng/mL)	1380550.59	232022.32	1336718.53	221723.02
C_{max} (ng/mL)	31912.75	6509.01	31355.77	4891.54
T_{max} (h) Mean, SD	5.66	3.58	4.48	3.47
Median (range)	5.00 (1.50 - 12.00)		2.50 (1.00 - 12.00)	

Table: Bioequivalence evaluation

Pharmacokinetic Parameter	Geometric Mean ratio Test/Ref	Confidence Intervals
AUC_{0-72}	103.16	100.74 – 105.63
Cmax	101.15	97.44 – 105.00

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

As the additional 10 mg strengths of the product meet the biowaiver criteria specified in the current bioequivalence guideline, the results and conclusions from the bioequivalence study on the product strength can be extrapolated to the other strengths.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted for these applications and none were required.

IV.4 Clinical efficacy

No new efficacy data were submitted with these applications and none were required.

IV.5 Clinical safety

The safety data from the bioequivalence study showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence study.

No new safety data were submitted with these applications and none were required. The safety profile for these products is considered to be the same as Ebixa 10 and 20 mg film-coated tablets.

IV.6 Risk Management Plan (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects

The grant of marketing authorisations was recommended for these applications.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with memantine hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**