Ebixa 5mg/pump actuation oral solution

Summary of Product Characteristics Updated 26-Feb-2021 | Lundbeck Limited

1. Name of the medicinal product

Ebixa 5 mg/pump actuation oral solution.

2. Qualitative and quantitative composition

Each pump actuation delivers 0.5 ml of solution which contains 5 mg of memantine hydrochloride which is equivalent to 4.16 mg memantine

Excipients with known effect*:*

Each millilitre of solution contains 100 mg sorbitol (E420) and 0.5 mg potassium, see section 4.4.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Oral solution.

The solution is clear and colourless to light yellowish.

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

Week 1 (day 1-7)

The patient should take 0.5 ml solution (5 mg) equivalent to one pump actuation per day for 7 days.

Week 2 (day 8-14)

The patient should take 1 ml solution (10 mg) equivalent to two pump actuations per day for 7 days.

Week 3 (day 15-21)

The patient should take 1.5 ml solution (15 mg) equivalent to three pump actuations per day for 7 days.

From Week 4 on

The patient should take 2 ml solution (20 mg) equivalent to four pump actuations once a 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 (2 ml solution, equivalent to four pump actuations) 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 (1 ml solution, equivalent to two pump actuations). 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 (1 ml solution, equivalent to two pump actuations) 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 Ebixa is not recommended in patients with severe hepatic impairment.

Paediatric population

No data are available.

Method of administration

Ebixa should be taken orally once daily at the same time each day. The solution can be taken with or without food. The solution must not be poured or pumped into the mouth directly from the bottle or the pump, but should be dosed onto a spoon or into a glass of water using the pump.

For detailed instructions on the preparation and handling of the product see section 6.6.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

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

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

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

In most clinical trials, patients with recent myocardial infarction, uncompensated congestive heart failure (NYHA III-IV), or uncontrolled hypertension were excluded. As a consequence, only limited data are available and patients with these conditions should be closely supervised.

Ebixa contains Sorbitol and Potassium

This medicine contains 100 mg sorbitol in each gram which is equivalent to 200 mg /4 pump actuation. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Furthermore, this medicine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially potassium-free.

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.