

Package leaflet: Information for the patient

- ▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Belvo 250 mg gastro-resistant tablets

Belvo 500 mg gastro-resistant tablets

valproate semisodium

WARNING

Belvo, valproate semisodium can seriously harm an unborn child when taken during pregnancy. If you are a female able to have a baby you must use effective method of birth control (contraception) without interruptions during your entire treatment with Belvo. Your doctor will discuss this with you but you must also follow the advice in section 2 of this leaflet.

Schedule an urgent appointment with your doctor if you want to become pregnant or if you think you are pregnant.

Do not stop taking Belvo unless your doctor tells you to as your condition may become worse.

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 Belvo is and what it is used for
2. What you need to know before you take Belvo
3. How to take Belvo
4. Possible side effects
5. How to store Belvo
6. Contents of the pack and other information

1. WHAT BELVO IS AND WHAT IT IS USED FOR

Belvo is used to treat the manic phase of bipolar disorders (manic-depressive illness) when lithium cannot be used or is not tolerated. Exactly how it works to treat bipolar disorder is not known.

Mania occurs in an illness called “bipolar disorder” and you may feel very excited, elated, agitated, enthusiastic or hyperactive.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE BELVO

Do not take Belvo

- If you are allergic to valproate semisodium, other medicines containing valproic acid or any of the other ingredients of this medicine (listed in section 6).
- If you have a liver disease or acute or chronic hepatitis (inflammation of the liver).
- If you have a genetic problem causing a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome).
- For bipolar disorder, you must not use Belvo if you are pregnant.
- For bipolar disorder, if you are a woman able to have a baby, you must not take Belvo, unless you use effective method of birth control (contraception) during your entire treatment with Belvo. Do not stop taking Belvo or your contraception, until you have discussed this with your doctor. Your doctor will advise you further (see below under “Pregnancy, breast-feeding and fertility – Important advice for women”).

Warnings and precautions

Talk to your doctor or pharmacist before taking Belvo:

- If you are taking anticoagulants (e.g. acetylsalicylic acid and warfarin).
- If you start bruising or bleeding, please inform your doctor immediately because a change in the dosage may be required.
- If you have a history of liver disease. Your doctor will need to carry out some blood tests before and during treatment.
- If you suffer from disseminated lupus erythematosus (an inflammatory disease of connective tissue with symptoms including fever and weakness and fatigability and joint pains and skin lesions on the face or neck or arms).
- If you have kidney problems.
- If you know that there is a genetic problem causing a mitochondrial disorder in your family.

You may find it useful to ask a friend or family to read this leaflet if you are depressed or anxious. You may ask them what they think about your symptoms and if you are becoming worse or if they are concerned about your behaviour.

Children and adolescents

Children and adolescents under 18 years of age: Belvo should not be used in children and adolescents under 18 years of age for the treatment of manic episodes in bipolar disorder.

Other medicines and Belvo

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

Certain drugs can interact with Belvo increasing or decreasing its therapeutic effect. This is especially important if you are taking:

- anticoagulants such as acetylsalicylic acid, warfarin or dicumarol;
- antiepileptic medicines such as phenytoin, phenobarbital, carbamazepine or clonazepam;
- carbapenem agents (antibiotic used to treat bacterial infections). The combination of valproic acid and carbapenems should be avoided because it may decrease the effect of sodium valproate.

Belvo with food, drink and alcohol

You should not drink alcohol whilst taking Belvo. Valproate semisodium may also potentiate the depressant effect of alcohol on the central nervous system, therefore alcoholic drinks should be avoided.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Important advice for women

- For bipolar disorder, you must not use Belvo if you are pregnant.
- For bipolar disorder, if you are a woman able to have a baby, you must not take Belvo, unless you use effective method of birth control (contraception) during your entire treatment with Belvo. Do not stop taking Belvo or your contraception, until you have discussed this with your doctor. Your doctor will advise you further.

The risks of valproate when taken during pregnancy (irrespective of the disease for which valproate is used)

- Talk to your doctor immediately if you are planning to have a baby or are pregnant.
- Valproate carries a risk if taken during pregnancy. The higher

the dose, the higher the risks but all doses carry a risk.

- It can cause serious birth defects and can affect the way in which the child develops as it grows. Birth defects which have been reported include spina bifida (where the bones of the spine are not properly developed); facial and skull malformations; heart, kidney, urinary tract and sexual organ malformations; limb defects.
- If you take valproate during pregnancy you have a higher risk than other women of having a child with birth defects that require medical treatment. Because valproate has been used for many years we know that in women who take valproate around 10 babies in every 100 will have birth defects. This compares to 2 to 3 babies in every 100 born to women who don't have epilepsy.
- It is estimated that up to 30-40% of preschool children whose mothers took valproate during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, intellectually less able than other children, and have difficulty with language and memory.
- Autistic spectrum disorders are more often diagnosed in children exposed to valproate and there is some evidence children may be more likely to develop symptoms of Attention Deficit Hyperactivity Disorder (ADHD).
- Before prescribing this medicine to you, your doctor will have explained what might happen to your baby if you become pregnant whilst taking valproate. If you decide later you want to have a baby you must not stop taking your medicine or your method of contraception until you have discussed this with your doctor.
- If you are a parent or a caregiver of a female child treated with valproate, you should contact the doctor once your child using valproate experiences menarche.
- Ask your doctor about taking folic acid when trying for a baby. Folic acid can lower the general risk of spina bifida and early miscarriage that exists with all pregnancies. However, it is unlikely that it will reduce the risk of birth defects associated with valproate use.

Please choose and read the situations which apply to you from the situations described below:

- I AM STARTING TREATMENT WITH BELVO
- I AM TAKING BELVO AND NOT PLANNING TO HAVE A BABY
- I AM TAKING BELVO AND PLANNING TO HAVE A BABY
- I AM PREGNANT AND I AM TAKING BELVO

I AM STARTING TREATMENT WITH BELVO

If this is the first time you have been prescribed Belvo your doctor will have explained the risks to an unborn child if you become pregnant. Once you are able to have a baby, you will need to make sure you use an effective method of contraception without interruption throughout your treatment with Belvo. Talk to your doctor or family planning clinic if you need advice on contraception.

Key messages:

- Pregnancy must be excluded before start of treatment with Belvo with the result of a pregnancy test, confirmed by your doctor.
- You must use an effective method of birth control (contraception) during your entire treatment with Belvo.
- You must discuss the appropriate methods of birth control (contraception) with your doctor. Your doctor will give you information on preventing pregnancy, and may refer you to a specialist for advice on birth control.
- You must get regular (at least annual) appointments with a specialist experienced in the management of bipolar disorder. During this visit your doctor will make sure you are well aware and have understood all the risks and advices related to the use of valproate during pregnancy.
- Tell your doctor if you want to have a baby.
- Tell your doctor immediately if you are pregnant or think you might be pregnant.

I AM TAKING BELVO AND NOT PLANNING TO HAVE A BABY

If you are continuing treatment with Belvo but you are not planning to have a baby make sure you are using an effective method of contraception without interruption during your entire treatment with Belvo. Talk to your doctor or family planning clinic if you need advice on contraception.

Key messages:

- You must use an effective method of birth control (contraception) during your entire treatment with Belvo.
- You must discuss contraception (birth control) with your doctor. Your doctor will give you information on preventing pregnancy, and may refer you to a specialist for advice on birth control.
- You must get regular (at least annual) appointments with a specialist experienced in the management of bipolar disorder. During this visit your doctor will make sure you are well aware and have understood all the risks and advices related to the use of valproate during pregnancy.
- Tell your doctor if you want to have a baby.
- Tell your doctor immediately if you are pregnant or think you might be pregnant.

I AM TAKING BELVO AND PLANNING TO HAVE A BABY

If you are planning to have a baby, first schedule an appointment with your doctor.

Do not stop taking Belvo or your contraception, until you have discussed this with your doctor. Your doctor will advise you further.

Babies born to mothers who have been on valproate are at serious risk of birth defects and problems with development which can be seriously debilitating. Your doctor will refer you to a specialist experienced in the management of bipolar disorder, so that alternative treatment options can be evaluated early on. Your specialist can put several actions in place so that your pregnancy goes as smoothly as possible and any risks to you and your unborn child are reduced as much as possible.

Your specialist may decide to change the dose of Belvo or switch you to another medicine, or stop treatment with Belvo, a long time before you become pregnant – this is to make sure your illness is stable.

Ask your doctor about taking folic acid when planning to have a baby. Folic acid can lower the general risk of spina bifida and early miscarriage that exists with all pregnancies. However, it is unlikely that it will reduce the risk of birth defects associated with valproate use.

Key messages:

- Do not stop taking Belvo unless your doctor tells you to.
- Do not stop using your methods of birth control (contraception) before you have talked to your doctor and worked together on a plan to ensure your condition is controlled and the risks to your baby are reduced.
- First schedule an appointment with your doctor. During this visit your doctor will make sure you are well aware and have understood all the risks and advices related to the use of valproate during pregnancy.
- Your doctor will try to switch you to another medicine, or stop treatment with Belvo a long time before you become pregnant.
- Schedule an urgent appointment with your doctor if you are pregnant or think you might be pregnant.

I AM PREGNANT AND I AM USING BELVO

Do not stop taking Belvo, unless your doctor tells you to as your condition may become worse. Schedule an urgent appointment with your doctor if you are pregnant or think you might be pregnant. Your doctor will advise you further.

Babies born to mothers who have been on valproate are at serious risk of birth defects and problems with development which can be seriously debilitating.

You will be referred to a specialist experienced in the management of bipolar disorder, so that alternative treatment options can be evaluated.

In the exceptional circumstances when Belvo is the only available treatment option during pregnancy, you will be monitored very closely both for the management of your underlying condition and to check how your unborn child is developing. You and your partner could receive counselling and support regarding the valproate exposed pregnancy.

Ask your doctor about taking folic acid. Folic acid can lower the general risk of spina bifida and early miscarriage that exists with all pregnancies. However, it is unlikely that it will reduce the risk of birth defects associated with valproate use.

Key messages:

- Schedule an urgent appointment with your doctor if you are pregnant or think you might be pregnant.
- Do not stop taking Belvo unless your doctor tells you to.
- Make sure you are referred to a specialist experienced in the treatment of bipolar disorder to evaluate the need for alternative treatment options.
- You must get thorough counselling on the risks of Belvo during pregnancy, including teratogenicity and developmental effects in children.
- Make sure you are referred to a specialist for prenatal monitoring in order to detect possible occurrences of malformations.

Make sure you read the patient guide that you will receive from your doctor. Your doctor will discuss the Annual Risk Acknowledgement Form and will ask you to sign it and keep it. You will also receive a Patient Card from your pharmacist to remind you of valproate risks in pregnancy.

Driving and using machines

You should not drive a car or operate machines until you know how Belvo affects you. You may feel dizzy, while taking Belvo. This is more likely to happen when you start taking Belvo or start taking a higher dose. If this happens, do not drive or use any tools or machines.

Belvo 250 mg gastro-resistant tablets contains Sunset yellow (E110) and Belvo 500 mg gastro-resistant tablets contains Carmoisine (E122) and Ponceau 4R (E124) that may cause allergic reactions.

Belvo contains sodium

Belvo 250 mg gastro-resistant tablets: this medicine contains less than 1 mmol sodium per tablet, that is to say essentially 'sodium-free'.

Belvo 500 mg gastro-resistant tablets: this medicine contains 69 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 3.5% of the recommended maximum daily dietary intake of sodium for an adult .

3. HOW TO TAKE BELVO

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

Belvo treatment must be started and supervised by a doctor specialised in the treatment of bipolar disorders.

Usual dosage

Average daily dosage is generally established according to the body weight of the patient and should be administered in two to three partial doses.

Acute mania and bipolar disorder

The daily dosage should be established and controlled individually by your doctor.

Initial dose:

The recommended initial daily dose is 750 mg.

Average daily dose:

The recommended daily doses usually range between 1000 mg and 2000 mg.

The minimum effective dose is 250 mg twice daily and treatment should last at least 3 months. The average dose is 1000 mg to 1500 mg/day.

Maximum recommended dose is 60 mg/kg/day. If the daily dose is equal to or higher than 50 mg/kg/day, your doctor may request to perform analysis for a control of the blood levels. Please speak with your doctor or pharmacist if you feel that Belvo is too strong or too weak for you.

Use in elderly

Due to the fact that Belvo is in the form of gastro-resistant tablets and as such must be swallowed whole, alternatively, it is recommended to use oral solution formulations in elderly with difficulty in swallowing.

Patients with liver and kidney problems

Your doctor may need to make an adjustment of the dose.

Method and route of administration

Oral route.

The gastro-resistant tablets should be swallowed with a full glass of non-sparkling water, without chewing. Do not divide or crush the tablets.

If you take more Belvo than you should

Talk to your doctor or go to your nearest hospital casualty department straight away.

Do not drive to the hospital, get somebody else to take you or call for an ambulance.

If you took the medicine less than two hours ago, try to induce vomiting.

The symptoms of overdose include severe dizziness, marked drowsiness, intense tremor, miosis (contraction of the pupil), and breathing problems.

If you forget to take Belvo

In case you forget to take a dose, you may take it up to one or two hours after the time of the dose. If there had been over three hours, skip the missed dose and continue to take the next dose at the normal dose. 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, pharmacist or nurse.

4. POSSIBLE SIDE EFFECTS

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

Belvo was formulated so that the active substance is only released in the small intestine, significantly reducing the side effects of the stomach. However, sometimes in the beginning of the treatment gastric disorders (nausea and vomiting) may be experienced that disappear with continued treatment.

These are:

- being sick and feeling sick,
- diarrhoea,
- intestinal colics,
- constipation,
- rarely, a decrease or increase of appetite.

Nail and nail bed disorders (common).

Exceptionally, the following side effects may be observed:

- an involuntary, somewhat rhythmic, muscle movement (tremor),
- sleepiness,
- ataxia (loss of ability to coordinate muscle action),
- headaches,
- confusion,
- nystagmus (rhythmic oscillation of the eyeball),
- loss of hair growing back curly hair,
- skin disorders,
- muscular weakness,
- dysmenorrhoea (difficult and painful menstruation),
- emotional disorder,
- depression,
- psychosis,
- aggression,
- hyperactivity,
- unexpected bruises or hematomas - a collection of blood outside of a blood vessel,
- obesity.

Cases of nausea, sedation, extrapyramidal disorders (disturbances of movement) have also been reported.

There have been reports of bone disorders including osteopenia and osteoporosis (thinning of the bone) and fractures. Check with your doctor or pharmacist if you are on long-term antiepileptic medication, have a history of osteoporosis, or take steroids.

Additional side effects in children

Some side effects of valproate occur more frequently in children or are more severe compared to adults. These include liver damage, inflammation of the pancreas (pancreatitis), bedwetting (enuresis), renal dysfunction (Fanconi Syndrome), overgrowth of gum tissue, aggression, agitation, disturbance in attention, abnormal behaviour, hyperactivity and learning disorder.

Reporting of side effects

If you get any side effects, talk to doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE BELVO

Do not store above 25°C.

Keep the blister in the outer carton in order to protect from light and moisture.

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 blister and carton after "EXP". The expiry date refers to the last day of that month.

Do not take this medicine if you notice visible signs of deterioration in the tablets.

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 Belvo contains

- The active substance is valproate semisodium.
- The other excipients are:

Belvo 250 mg gastro-resistant tablets:

silicon dioxide, pregelatinized starch, povidone, titanium dioxide (E171), talc, hypromellose phthalate, diacetylated monoglycerides, Yellow Aluminium Lake (Sunset yellow (E110) and Aluminium), vanillin.

Belvo 500 mg gastro-resistant tablets:

silicon dioxide, pregelatinized starch, povidone, titanium dioxide (E171), talc, hypromellose phthalate, diacetylated monoglycerides, Carmoisine lake (Carmoisine (E122) and Aluminium), Ponceau 4R lake (Ponceau 4R (E124) and Aluminium), vanillin.

What Belvo looks like and contents of the pack

Belvo 250 mg consists of peach oblong gastro-resistant tablets without inscriptions.

Belvo 500 mg consists of pink oblong gastro-resistant tablets.

The tablets are packed in Aluminium/PVDC+PVC/PE/PVDC. Packs of 20, 30, 60 and 90 tablets.

Not all pack sizes may be marketed.

Marketing Authorization Holder and Manufacturer:

Marketing Authorization Holder:

Consilient Health Limited
5th Floor, Beaux Lane House,
Mercer Street Lower,
Dublin 2, Ireland

Manufacturer:

Lusomedicamenta – Sociedade Técnica Farmacêutica, Lda.
Estrada Consiglieri Pedroso, 69-B – Queluz de Baixo
2730-055 Barcarena, Portugal

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