

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT

Valocordin®
oral drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml (= 30 drops) contains: Phenobarbital 18.40 mg
Ethylbromisovalerate 18.40 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral drops, solution

- clear colourless solution
- aromatic odour
- bitter flavour

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

As part of complex therapy as a symptomatic remedy for functional disorders of the nervous system (neurasthenia and sleep disturbances).

The drug is intended for short-term use due to the risk of addiction and dependence.

4.2 Posology and method of administration

Doses and duration of treatment should be decided by the doctor individually. Valocordin® is prescribed orally before food intake 3 times a day, 22-30 drops each, previously dissolved in a small amount of water. For sleep disturbances the dose can be increased up to 45 drops.

The drug is intended for short-term use due to the risk of addiction and dependence.

4.3 Contraindications

- hypersensitivity to bromine or any component of the drug;
- renal and / or hepatic impairment;
- porphyria;
- alcoholism, epilepsy, traumatic brain injury and other brain diseases with the seizure in anamnesis;
- pregnancy, lactation period;
- children under 18 years of age.

4.4 Special warnings and precautions for use

The medicinal product contains 56 % ethyl alcohol, the content of ethyl alcohol in the maximum single dose (45 drops) is 663 mg.

The drug should not be taken by patients with alcoholism, pregnant women breastfeeding women, children under 18 years of age, patients with liver disease and epilepsy.

The simultaneous use of alcohol with Valocordin® should be avoided. The simultaneous intake of alcohol increases the toxicity of phenobarbital.

Avoid prescribing the drug to patients with depressive disorders, suicidal tendencies, people with drug addiction.

Elderly and debilitated patients may respond to phenobarbital by developing intense agitation, depression, and confusion.

With prolonged use, the accumulation of bromine in the body and the development of intoxication is possible.

Phenobarbital can cause the development of addiction, mental and physical dependence. When addiction (tolerance) to phenobarbital develops, the dose required to maintain the same level of effect increases. Abrupt discontinuation of phenobarbital after prolonged use in a person with addiction may lead to the development of withdrawal symptoms.

In case of signs of intoxication, addiction (tolerance) or dependence, the patient should immediately consult a doctor. Signs of chronic intoxication include confusion, decreased criticism, irritability, insomnia, and somatic complaints.

Caution should be exercised when prescribing phenobarbital to patients with acute or chronic pain, because paradoxical excitement and important clinical symptoms can be masked.

There have been reports of the development of life-threatening skin reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis) when using drugs containing phenobarbital. The best results in the treatment of Stevens-Johnson syndrome or toxic epidermal necrolysis were obtained with early diagnosis and immediate discontinuation of the suspected drug. In such cases, the patient should never take Valocordin® again.

Use in pediatrics: the drug is contraindicated in children and adolescents under the age of 18.

4.5 Interaction with other medicinal products and other forms of interaction

When taking pharmaceuticals calming the central nervous system together with alcohol, a mutual increase in efficacy must be reckoned with.

Pharmaceuticals containing valproinic acid are increasing the efficacy of the barbiturate.

Phenobarbital induces liver enzymes and may therefore accelerate the metabolism of some drugs which are metabolised through liver enzymes (e.g. coumarin derivatives, antibiotics and sulfonamides).

In combination with coumarin derivatives, lamotrigin, thyroid hormones, doxycycline, chloramphenicol, antimycotics (azol-type), griseofulvin, glucocorticoids or oral contra-ceptives, due to the phenobarbital contained in Valocordin®, an accelerated loss of efficacy to the above-mentioned substances may occur as an unwelcome interaction or reciprocity.

The toxicity of pharmaceuticals containing methotrexate increases.

The effect of phenobarbital on phenytoin metabolism is unpredictable. Blood concentrations of phenytoin and phenobarbital should be monitored if these drugs are administered concomitantly.

Sodium valproate and valproic acid inhibit phenobarbital metabolism.

Interactions associated with the presence of ethyl alcohol in the composition: it is necessary to avoid concomitant administration of drugs that cause disulfiram-like reaction (feeling of heat, redness of the skin, vomiting, tachycardia) when taken together with alcohol (disulfiram, cefamandol, cefoperazone, latamoxef, chloramphenicol, chlorpropamide, glibenclamide, glipizide, tolbutamide, griseofulvin, nitro-5-imidazole derivatives (metronidazole, ornidazole, tinidazole), ketoconazole, procarbazine).

It is necessary to avoid the simultaneous use of other medicines containing ethyl alcohol.

4.6 Fertility, pregnancy and lactation

Pregnancy

Valocordin[®] should not be used during pregnancy.

Breastfeeding

Valocordin[®] should not be taken by breastfeeding mothers during their lactation period.

4.7 Effects on ability to drive and use machines

The medicinal product contains ethyl alcohol, phenobarbital and ethyl bromisovalerianate, therefore, patients taking Valocordin[®] are contraindicated to drive vehicles and engage in other potentially hazardous activities that require increased concentration of attention and speed of psychomotor reactions.

4.8 Undesirable effects

Nervous system: drowsiness, decreased concentration of attention, slowing down of reactions, impaired coordination of movements, dizziness, headache, nervousness, agitation, anxiety, confusion, increased physical activity, ataxia, depression of the central nervous system, sleep disturbances, insomnia, nightmares, mental disorders, hallucinations.

Respiratory system: hypoventilation, apnea.

Digestive system: nausea, vomiting, constipation, with prolonged use - impaired liver function.

Hematopoiesis: agranulocytosis, megaloblastic anemia, thrombocytopenia.

cardiovascular system: bradycardia, low blood pressure, fainting.

musculoskeletal system: with prolonged use of drugs containing phenobarbital, there is a risk of impaired osteogenesis. There have been reports of decreased bone mineral density, the development of osteopenia and osteoporosis, and fractures in patients taking phenobarbital for a long time.

Others: visual impairment, allergic reactions (angioedema, skin rash, exfoliative dermatitis), fever, liver damage.

With prolonged use - drug dependences.

With prolonged use of high doses, the development of chronic bromine poisoning is possible, the manifestations of which are: depressive mood, apathy, rhinitis, conjunctivitis, hemorrhagic diathesis, impaired coordination of movements. After prolonged use, megaloblastic anemia may develop. With the use of drugs containing phenobarbital, there have been reports of the development of life-threatening skin reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis).

Extended use of the drug may cause dependence.

[Mandatory statement only for EU countries]

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 [to be completed nationally].

4.9 Overdose

Symptoms of intoxication

Acute light to medium barbiturate intoxication:

Dizziness, tiredness, unintentional deep sleep.

Acute heavy intoxication:

Deep coma, accompanied by tissue hypoxia, shallow respiration, accelerated in the beginning, slowing down later. Increased heartbeat frequency, cardiac arrhythmia, low blood pressure, circulatory collapse, weak or absence of reflexes.

When the intoxication is not treated, death occurs due to circulatory failure, respiratory paralysis or pulmonary oedema.

The prolonged uptake of compounds containing bromine may cause bromine poisoning with the following symptoms: states of confusion, ataxia, apathy, depressive mood, conjunctivitis, common cold, bromide acne or purpura.

Treatment of intoxications

Cases of acute intoxication with Valocordin® should be treated as known from soporifics and barbiturate intoxications in dependence on the severity of the intoxication symptoms. The patient should be transferred to an intensive ward.

Respiration and circulation need stability and normalization. Respiratory insufficiency should be combatted with artificial respiration, shock by infusion of plasma or plasma expanders. Gastric lavage (instill two tablespoonfuls of 10 g of pulverized coal and sodium sulphate) is indicated even if a long time has elapsed since the uptake of the barbiturate. To accelerate the elimination of the barbiturate from the body, forced alkalinising diuresis and haemodialysis and/or haemoperfusion are indicated.

Treatment of bromine poisoning: Abundant quantities of table salt with the simultaneous administration of saluretics accelerate the elimination of bromine ions.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Barbiturates in combination with other drugs
ATC code: N05CB02

Pharmacodynamic effects

Valocordin[®] contains a combination of the active substances phenobarbital and ethylbromine isovalerate (α -bromisoethyl valerate). Depending on the dosage, this will have a sedative, hypnotic and - at high dose - narcotic effect. Like other derivatives of the barbituric acid phenobarbital primarily has an inhibitory effect on the activating parts of the *Formatio reticularis*. At a high, narcotic dose it also paralyses the cerebral cortex and other areas of the central nervous system.

Ethylbromine isovalerate has spasmolytic and sedative action. By incorporating a bromine atom into the ester molecule of the isovaleric acid at α -position the sedative action of the acid is increased in the sense of an additive effect.

At the concentration chosen in Valocordin[®], ethylbromine isovalerate operates as a synergist of phenobarbital in the sense of a quick onset of the efficacy.

5.2 Pharmacokinetic properties

Barbiturates are already resorbed in the stomach. Approximately 35 percent of phenobarbital is bound in plasma albumin. The portion which is not bound to the albumin is ultrafiltered in the kidneys. Reabsorption occurs at low pH. Back-diffusion is prevented by the alkalinity of the urine. The half-life of phenobarbital in plasma is three days. Thirty percent of the phenobarbital is eliminated in unmodified form with the urine while some is oxidized in the liver. When used chronically phenobarbital is accumulated in the plasma and enzyme induction may occur in the liver. This induction accelerates the decomposition of the barbiturate and other drugs.

The bromine bound in ethylbromine isovalerate is being eliminated only very slowly. If the pharmaceutical is used for a longer period of time the bromine will cumulate and be enriched in the central nervous system; bromism will be the result.

5.3 Preclinical safety data

The lethal dose of phenobarbital is approximately 6 g (in individual cases, 1.7 g proved to be lethal). A plasma concentration of 40 ng/l is considered toxic, one of 60 ng/l is lethal.

Phenobarbital proved to be teratogenic in animal experiments. No teratogenic action is known to occur in man at therapeutic doses.

Phenobarbital enters the mother's milk and may cause somnolence. When taken chronically, barbiturate may cause dependence in breast-fed infants.

Acute poisoning by ethylbromine isovalerate is to be expected if single doses of about 20 g and more are taken. If the bromine content of the plasma has become increased to about 150 mg%, toxic phenomena will occur, and a content exceeding 200 mg% is

tantamount to chronic bromism. 300 to 400 mg% are dangerous to life and connected with most serious psychosis and stupor.

In case of prolonged use there is the hazard of addiction and bromism.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mint oil	Ph. Eur. *	* The current version of the monograph is always the valid one, except there is noted something different. ** The drug contains potassium hydroxide to adjust pH
Hops oil	manufact. standard	
Ethanol 96 %	Ph. Eur. *	
Potassium hydroxide**	Ph. Eur. *	
Purified water	Ph. Eur. *	

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

The shelf life of the unopened bottle and also after its first opening is printed as use-before date on the folding box and the label (3 years from production date). The preparation should not be used after that date.

6.4 Special precautions for storage

Do not store above 25 °C.

Store in the original package in order to protect from light.

The drug should be kept out of the reach of children.

6.5 Nature and contents of container

Brown glass bottle with 20 ml and 50 ml solution

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Krewel Meuselbach GmbH
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53783 Eitorf
Germany

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8. MARKETING AUTHORISATION NUMBER

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

July 2023

11. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.