NERVEN DRAGEE

PRESCRIBING INFORMATION

1. NAME OF THE MEDICINAL PRODUCT

Nerven

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One film coated tablet contains:

Valerian native extract	67.5 mg
Hop native extract	29.4 mg
Passion flower Hawthorn berries (2.8:1) native extract	81.0 mg
Hawthorn leaf and flower native extract	81.0 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dragee (film coated tablet)

Round, white, biconvex film coated tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Sedative, anxiety and tension states, insomnia.

4.2 Posology and method of administration

Posology

Adults
For sedative, anxiety and tension states: 1-2 film coated tablet 3 times daily with some water.
For insomnia: single dose of 2 film coated tablets one hour before bed time.

Not for use in children below the age of 12 years (see section 4.4).

Method of administration

Oral use.

4.3 Contraindication

Hypersensitivity to the active substances or to any of the excipients of Nerven.

4.4 Special warnings and precautions for use

The use of Nerven is not recommended in children below the age of 12 years due to a lack of data on safety and efficacy. Combination with other sedatives requires medical diagnosis and supervision. If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.In the case that irregular heart rate, strong palpitations, acute pain in the cardiac region, and shortage of breath are common or of longer duration, it is necessary to determine whether the heart or blood vessels are physically diseased or if the complaints are due to a nervous condition.

When used as intended, special precautionary measures are not necessary.

4.5 Interaction with other medicinal products and other forms of interaction

No data on pharmacological interactions with other medicinal products is available.

4.6 Fertility, pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, use during pregnancy and lactation is not recommended.

No fertility data available.

4.7 Effects on ability to drive and use machines

No studies were conducted with Nerven film coated tablets. However, impaired ability to drive machines was reported for combination products of Valerian and Hops as well as for products containing Passiflora. This medicinal product may therefore impair the ability to drive and use machines. Affected patients should not drive or operate machinery.

4.8 Undesirable effects

Gastrointestinal symptoms (e.g. nausea, abdominal cramps) may occur after ingestion of valerian root preparations. The frequency is not known.

However, for Nerven film coated tablets no undesirable effects with certain causal relationship have been observed when used as intended.

If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.

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.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

and emailed to the Registration Holder's Patient Safety Unit at: drugsafety@neopharmgroup.com

4.9 Overdose

Valerian root at a dose of approximately 20 g (equivalent to approx. 60 Nerven film coated tablets) caused benign symptoms (fatigue, abdominal cramp, chest tightness, lightheadedness, hand tremor and mydriasis), which disappeared within 24 hours. If symptoms arise, treatment should be supportive. For all other herbal ingredients no cases of overdose have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other hypnotics and sedatives.

ATC code: N05CM

No pharmacological studies were conducted with Nerven film coated tablets or the fixed combination of Hawthorn leaf and flower, Hawthorn berries, Passion flower, Valerian root and Hop strobile dry extract.

However, the sedative effects of preparations of Valerian root and Hop strobile have been long recognised empirically and have been confirmed for Valerian root preparations in preclinical tests and controlled clinical studies. So far no clinical studies have been conducted with hop extracts alone as active drug for insomnia, but at least four randomized, placebo- or reference-controlled prospective clinical studies have been carried out with fixed combinations of dry extracts prepared from valerian root and hop strobilies with methanol 45% (m/m).

Orally administrated fixed combinations of these extracts in the recommended dosage have been shown to improve sleep latency and sleep quality. These effects cannot be attributed with certainty to any known constituents. Several mechanisms of action possibly contributing to the clinical effect have been identified for diverse constituents of Valerian root (sesqulterpenols, lignans, flavonoids) and include interactions with the GABA-system, agonism at the A_1 adenosine receptor and binding to the 5-HT_{1A} receptor. Also several mechanisms of action have been identified for diverse constituents of Hops with the GABA-system, agonism at the melatonin receptors (ML_1 and ML_2) and binding to serotonin receptor subtypes (5-HT_{4e}, 5-HT_6 and 5-HT_7). Whether hop strobile extract

acts either as a mild sedative independently or as a synergist for valerian root extract, is not yet known.

For Passionflower pharmacodynamic data implies that the anxiolytic effects may be mediated via modulation of the GABA system.

No conclusive data exists for Hawthorn preparations.

The active pharmaceutical ingredient is represented by the fixed extract combination as the clinical effect cannot be attributed to single constituents.

5.2 Pharmacokinetic properties

No data are available.

5.3 Preclinical safety data

No preclinical studies were conducted with Nerven film coated tablets or the fixed combination of Hawthorn leaf and flower, Hawthorn berries, Passion flower, Valerian root and Hop strobile dry extract.
Ethanol extracts of valerian root have shown low toxicity in rodents during acute tests and from repeated dose toxicity over periods of 4-8 weeks.
For the other herbal ingredients tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Corn starch, microcrystalline cellulose, maltodextrin, hypromellose, colloidal anhydrous silica, titanium dioxide, hydrogenated castor oil, , magnesium stearate, macrogol 400, propylene glycol, macrogol 20,000,.

This product contains approx. 235 mg digestible carbohydrates per single dose (1 film coated tablet).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials,

6.4 Special precautions for storage

Store below 25°C. Store in the original package.

6.5 Nature and contents of container, pack sizes

PVC/PE/PVdC-Al-blisters in a carton box.

Pack sizes: 4, 20, 30, 60 and 120 film coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MANUFACTURER

Max Zeller Söhne AG
CH-8590 Romanshorn
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8. REGISTRATION HOLDER

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9. REGISTRATION NUMBER

067-74-28081-00

The content of this leaflet was approved by the Ministry of Health in 11/2018 and updated according to the guidelines of the Ministry of Health in 07/2019.