PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

NEVRINE CODEINE tablets

Paracetamol 500mg
Caffeine 50mg
Codeïne phosphate hemihydrate 30mg

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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What NEVRINE CODEINE is and what it is used for
2. What you need to know before you take NEVRINE CODEINE
3. How to take NEVRINE CODEINE
4. Possible side effects
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1. WHAT NEVRINE CODEINE IS AND WHAT IT IS USED FOR

NEVRINE CODEINE can be used in adults and adolescents over 12 years of age for a short period of time for acute pain of moderate intensity that is not relieved by other analgesics such as paracetamol or ibuprofen used alone.

This medicine contains codeine, caffeine and paracetamol.
Codeine belongs to a group of medicines called opioid analgesics, which act to relieve pain. It is used in combination with another analgesic called paracetamol.
Paracetamol relieves pain and fever.
Caffeine has a double benefit: it increases the pain-killing and fever reducing effect of paracetamol and reduces the side effects of codeine by stimulating the central nervous system.

You must talk to a doctor if you do not feel better or if you feel worse after 3 days.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE NEVRINE CODEINE

Do not take NEVRINE CODEINE
- If you are allergic to the active substances or to any of the other ingredients of this medicine (listed in section 6).
- To relieve pain in children and adolescents up to 18 years of age after removal of tonsils or vegetations as part of an obstructive sleep apnoea syndrome.
- If you are a child under 12 years of age or weighing less than 33kg.

- If you know that you metabolize codeine into morphine very quickly.
- If you are breast-feeding.
- If you have serious respiratory insufficiency.
- If you have acute asthma.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking NEVRINE CODEINE.

- If you regularly take barbiturates or if you take medicines used to treat epilepsy, using NEVRINE CODEINE can increase the risks of liver toxicity.
- If you take regularly NEVRINE CODEINE and for a long period of time, you increase the risk of kidney damage. The presence of caffeine and codeine can promote chronic use.
- In older patients, liver and kidney functions must be tested in order to detect any liver or kidney failure in time.
- In patients with respiratory disorders, a possible worsening of these symptoms should be taken into account.
- The recommended dose of NEVRINE CODEINE cannot in any case be exceeded and the duration of treatment cannot be prolonged. No other medicine containing paracetamol can be taken at the same time.
- Never take at one time a dose of paracetamol equivalent to several times the daily dose, as it could seriously damage the liver (see section 3 " If you take more NEVRINE CODEINE than you should").
- Caution is recommended in case of disease, which can increase the risk of liver damage: a liver disease (including Gilbert's syndrome or an acute hepatitis), a kidney disease, chronic alcoholism and in very thin adults (< 50kg). In these cases, the maximum daily dose must be adjusted (see section 3).
- The risk of liver damage can be increased in patients taking medicines that influence the liver function. The risk of liver damage can also be increased by dehydration and chronic malnutrition. The recommended daily dose must not be exceeded under any circumstances in these patients.
- Codeine is transformed into morphine in the liver by an enzyme. Morphine is the pain-relieving substance. Some people have variable enzyme levels and this can affect them in different ways. For some people, morphine is not produced or is produced in small amounts, and will not sufficiently relieve the pain. For others, a large amount of morphine is produced and can be the source of serious side effects. If you notice any of the following side effects, you must stop taking this medicine and immediately ask your doctor for advice: slow or shallow breathing, confusion, drowsiness, constriction of the pupil, nausea or vomiting, constipation, loss of appetite.
- Caution is recommended in patients with glucose-6-phosphate dehydrogenase deficiency and haemolytic anaemia.
- Do not drink alcohol during treatment with NEVRINE CODEINE.

If you are already using other medicines, please also read the section “Other medicines and NEVRINE CODEINE”.

Children and adolescents up to 18 years of age
- Use in children and adolescents up to 18 years of age after surgery:
  Codeine should not be used after removal of tonsils or vegetations as part of an obstructive sleep apnoea syndrome.

- Use in children with respiratory problems:

Codeine is not recommended in children with respiratory problems as the symptoms of morphine toxicity are worsened in these children.

Other medicines and NEVRINE CODEINE
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

With *paracetamol*:
A liver toxicity can occur during simultaneous administration with alcohol or with medicines that cause the degradation of paracetamol, particularly if it is taken at high doses. This is also the case with barbiturates, carbamazepine, phenytoin, primidone, isoniazid and rifampicin. The maximum daily dose cannot be exceeded in these patients under any circumstances.

Colestyramine (an anti-cholesterol agent) can reduce the absorption of paracetamol. If simultaneous administration of paracetamol and colestyramine is necessary, the paracetamol must be taken at least 1 hour before or 4 hours after administration of colestyramine.

A reduction in the dose of paracetamol should be considered during simultaneous treatment with probenecid.

The simultaneous administration of paracetamol and vitamin K antagonist anticoagulants could reduce the metabolism of the latter and increase its effect.

Simultaneous administration of paracetamol and zidovudine (an antiretroviral agent) can lead to a degeneration of the blood and a liver toxicity. If chronic use of paracetamol and zidovudine is necessary, white blood cells and the liver function must be monitored, particularly in patients with malnutrition.

A reduction in the therapeutic effect of lamotrigine (an anti-epileptic agent) can occur when lamotrigine is taken at the same time as paracetamol.

Metoclopramide and domperidone (medicines used to treat nausea and vomiting) cause increased absorption of paracetamol.

Consult your doctor if you are prescribed some laboratory tests (uric acid or levels of sugar in your blood), as the results may be modified.

With *codeine*:
- Interactions with Central Nervous System depressants: increased sedative effect and respiratory depression.
- Interactions with MAO inhibitors: increased sedative effect and respiratory depression.
- Concomitant use of NEVRINE CODEINE and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible.
  However if your doctor does prescribe NEVRINE CODEINE together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor.
  Please tell your doctor about all sedative medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

NEVRINE CODEINE with food and alcohol
The risk of liver toxicity associated with this medicine is higher if you regularly consume alcohol. The presence of codeine increases the sedative effect of alcohol when they are taken together.

Pregnancy and breast-feeding
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.

Do not take NEVRINE CODEINE if you are pregnant. Codeine crosses the placental barrier.
Do not take NEVRINE CODEINE if you are breast-feeding. Codeine and morphine pass into breast milk.

Driving and using machines
Codeine phosphate has a major influence on the ability to drive and use machines: taking NEVRINE CODEINE can cause drowsiness and even light-headedness during the day. Your ability to drive or use machines can therefore be affected. Extreme caution is strongly recommended.

NEVRINE CODEINE contains 0.06mg of cochineal red A (E124) per tablet that can cause allergic reactions, and contains less than 1 mmol sodium (23mg) per tablet, that is to say essentially 'sodium-free'.

3. HOW TO TAKE NEVRINE CODEINE

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

Swallow the tablets with a large glass of water.

The medicine must only be used when symptoms occur.

The medicine should be used only during periods where symptoms appear.

This medicine should not be taken for more than 3 days. If the pain is not relieved after 3 days, consult your doctor.

NEVRINE CODEINE should not be given to children under 12 years of age or weighing less than 33kg due to the risk of severe breathing problems.

Adults and adolescents (body weight > 50kg)
The recommended dose is 1 to 2 tablets per administration up to 3 times per day. Allow an interval of at least 6 hours between 2 administrations.

- The maximum daily dose that must not be exceeded is 8 tablets in any 24 hour period.
- For adults weighing less than 50kg, the maximum daily dose that must not be exceeded is 60 mg of paracetamol/kg/24 hours.
- In patients with reduced liver function, the dose should be reduced or the interval between two doses should be prolonged. The daily dose must not exceed 4 tablets in patients with liver insufficiency, Gilbert's syndrome or chronic alcoholism.

Children over 12 years of age and adolescents weighing between 33 and 50kg

The recommended dose is 1 tablet per administration up to 4 times per day. Allow an interval of at least 6 hours between 2 administrations.
The maximum daily dose that must not be exceeded is 60mg paracetamol/kg and 240mg codeine phosphate per 24 hours.

No other medicines containing paracetamol or codeine can be used at the same time.

Patient with poor kidney function
In patients with moderate and acute renal insufficiency, the dose of paracetamol must be reduced. Your doctor will establish the dose that you can take based on your kidney function.

Elderly patients
Due to the presence of codeine, the treatment is recommended to be initiated with caution in elderly patients, particularly with liver and/or kidney failure, by starting with the lowest possible effective dose and by increasing this dose with caution if necessary.

If you take more NEVRINE CODEINE than you should
If you take too much NEVRINE CODEINE, immediately contact your doctor, your pharmacist or the Anti-poison Centre (070/245.245).

a) For acute toxicity

Paracetamol
In case of overdose, there is a risk of serious liver toxicity, particularly in elderly patients, young children, patients with liver or kidney failure, in case of chronic alcoholism, chronic malnutrition, in patients receiving enzyme inducers and in very thin adults (< 50kg).

Liver toxicity often appears 24 to 48 hours after ingestion. Overdose can be fatal. In case of overdose, a doctor must be consulted immediately, even if no symptom is observed.

The symptoms are: nausea, vomiting, lack of appetite, paleness, abdominal pain. They generally occur within the first 24 hours.

Emergency treatment
Massive absorption of paracetamol requires emergency hospitalisation. A blood draw will be performed. Treatment with activated charcoal can be started (during one hour after ingestion), but the main therapeutic measure consists in administering the antidote N-acetylcysteine (if possible within 8 hours after ingestion). Symptoms will also be treated.
This will be done by a doctor.

Codeine
Intoxication results in dry mouth, urinary retention, dizziness, slow heart rate, palpitations, feeling of drowsiness, contraction of the pupils, respiratory depression, too low blood pressure, coma. Emergency treatment of respiratory depression by artificial ventilation: administration of the antidote naloxone.

Caffeine
A dose of more than 1g is toxic. Lethal dose at approximately 10g.
The symptoms are: vomiting, seizures, drowsiness, agitation, tremor, too fast heart rate. The treatment consists in treating these symptoms.

b) For long-term toxicity
It should be kept in mind that chronic use of analgesics such as NEVRINE CODEINE, even at low doses but over a long period of time, can cause kidney damage.
In this case, the use of the medicine should be discontinued, the kidney function should be checked and the necessary measures should be taken to completely re-establish this function.

If you forget to take NEVRINE CODEINE
Take the indicated dose as quickly as possible and the next dose after the recommended interval of 4 hours.

Do not take a double dose to make up for the forgotten tablet(s).

If you stop taking NEVRINE CODEINE
The pain can then come back. You should consult your doctor or pharmacist for further treatment.

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.

Codeine:
- Respiratory depression may occur in the lungs as well as bronchospasm.
- Patients with a sensitive digestive system may have constipation, nausea or dyspepsia.
- The risk of addiction and/or withdrawal symptoms in case of sudden treatment discontinuation have been observed at dosages that are too high.

Caffeine:
- The presence of caffeine can cause palpitations, a heart rate that is too fast and nausea.

Paracetamol:
The frequency of the possible side effects is defined as following:
- Very common: affects more than one patient out of 10
- Common: affects 1 to 10 patients out of 100
- Uncommon: affects 1 to 10 patients out of 1 000
- Rare: affects 1 to 10 patients out of 10 000
- Very rare: affects less than 1 patient out of 10 000
- Not known: the frequency cannot be estimated from the available data.

Rare:
- Allergic reactions
- Headache
- Abdominal pain, diarrhoea, nausea, vomiting, constipation
- Liver function disorders, poor liver function, liver necrosis, jaundice
- Itching, redness, sweating, hives on the skin
- Light-headedness, malaise
- Overdose, intoxication

Very rare:
- Degeneration of the blood: decrease in thrombocytes, in white blood cells, in all of the blood

cells and granulocytes, haemolytic anaemia.
- Serious allergic reactions that require treatment discontinuation
- Severe liver toxicity, due to prolonged use of high doses
- Serious skin reactions
- Uninfected cloudy urine

Not known:
- Anaemia
- Allergic shock
- Inflammation of the liver
- Kidney disease after prolonged use of high doses

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system:
Federal Agency for Medicines and Health Products.
Vigilance division
EUROSTATION II
Place Victor Horta, 40/ 40
B-1060 Brussels
Website: www.famhp.be
e-mail: patientinfo@fagg-afmps.be

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE NEVRINE CODEINE

Keep this medicine out of the sight and reach of children.

Keep the blisters in the outer carton.

Do not use this medicine after the expiry date which is stated on the pack after EXP. You will find there a month and a year. The expiry date refers to the last day of that month.

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 NEVRINE CODEINE contains
- The active substances are paracetamol 500mg, caffeine 50mg and codeine phosphate hemihydrate 30mg.
- The other ingredients are povidone, sodium starch glycolate type A, magnesium stearate, microcrystalline cellulose and cochineal red A (E124) (see section 2 *NEVRINE CODEINE contains 0.06mg of cochineal red A (E124)*).

What NEVRINE CODEINE looks like and contents of the pack
Oblong, pink tablets with a score line on one side.

Tablets are packaged in PVC-PVDC/Aluminium blisters containing 10 tablets. Box of 20 tablets.

Marketing Authorisation Holder and Manufacturer
LABORATOIRES STEROP NV, Scheutlaan 46-50, 1070 Brussels.

Delivery status
Medicinal product subject to medical prescription.

Marketing Authorisation number
BE163256

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