Package leaflet: Information for the user

Navirel 10 mg/ml concentrate for solution for infusion

vinorelbine

Read all of this leaflet carefully before you start using 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.
- 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 Navirel is and what it is used for

Navirel is a concentrate for solution for infusion. The active substance vinorelbine belongs to a group of medicines used to treat cancer. These medicines are called cytostatic, because they slow or prevent the growth of cancer cells. Navirel is used to treat certain types of lung cancer (so-called non-small cell lung cancer, NSCLC) and breast cancer.

2. What you need to know before you use Navirel

Do not use Navirel, if you
- are allergic to vinorelbine, any of the related family of medicines for the treatment of cancer called vinca alkaloids or any of the other ingredients of this medicine (listed in section 6).
- have a low count of certain white blood cells or a severe current or recent infection (within the last 2 weeks).
- have a low platelet count.
- have a severe liver disease unrelated to the cancer which is treated by vinorelbine.
- are receiving or recently have received yellow fever vaccine.
- are pregnant.
- are breast-feeding.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Navirel if
- you have received radiotherapy where the treatment field includes the liver.
- your liver function is impaired.
- you receive or recently have received certain forms of vaccines with living virus particles (called live attenuated vaccines).
- you receive an antiepileptic medicine called phenytoin or an antifungal medicine called itraconazole at the same time.
- you have a history of heart attack or severe chest pain.

- you show signs or symptoms of infection (fever, chills, etc.). Let your doctor know immediately, so that he/she can carry out any tests which may be needed.
- you belong to the Japanese population, because there is an increased risk to develop diseases of the connective tissue of the lung.

All contact with the eyes must be strictly avoided. There is a risk of severe irritation and even sores of the eye (corneal ulceration). If any contact with the eyes occurs, they must be rinsed with sodium chloride solution immediately.

Tell your doctor immediately if there is a burning sensation in the area of the infusion during or after the infusion. This can be a sign of an injection error and the infusion must be stopped immediately.

Children and adolescents
It is not recommended to give this medicine to children, as not enough data on the effect and safety in children is available.

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

Your doctor should pay special attention if you are taking the following medicines:
- medicines used to thin your blood (anticoagulants),
- antiepileptic medicines like phenytoin, phenobarbital and carbamazepine,
- antibacterial medicines like rifampicin, clarithromycin, erythromycin,
- antiviral medicines like ritonavir,
- antifungal medicines such as itraconazole and ketaconazole,
- an anticancer medicine called mitomycin C,
- medicines that impair your immune system such as ciclosporin and tacrolimus,
- medicines for the treatment of heart diseases like verapamil and quinidine,
- a herbal medicine called St. John's wort (*Hypericum perforatum*).

Live attenuated vaccines (vaccines containing living virus particles e.g. measles vaccine, mumps vaccine, rubella vaccine) are not recommended with Navirel as they may increase the risk of life-threatening vaccine disease. As yellow fever vaccine also contains living virus particles, you must not be given yellow fever vaccines in combination with Navirel.

Pregnancy, breast-feeding and fertility
You must not be given Navirel if you are pregnant unless clearly indicated by your doctor.

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 using this medicine.

You must not be given Navirel if you are breast-feeding. If treatment is necessary, you must stop breast-feeding.

Women should take measures to avoid pregnancy during treatment and for at least three months after the end of the treatment by using effective contraception.

Men receiving treatment should ensure that their partner will not become pregnant during treatment and up to six months afterwards by using effective contraception.
Prior to treatment advice should be sought for conserving sperm due to the risk of irreversible infertility as a consequence of treatment with vinorelbine.

Driving and using machines
Side effects which may impair your ability to drive and/or operate machines may occur after treatment with vinorelbine. If you feel unwell you should not perform tasks that require mental concentration such as driving a car or operating machinery.

3. How to use Navirel

The preparation and administration of Navirel must only be carried out by a trained healthcare professional specialised in cancer treatment. Navirel is intended as single dose only.

Before each treatment a blood sample will be taken for analysis of its components in order to check if you have enough blood cells to receive Navirel. If the results of this analysis are not satisfactory, your treatment may be delayed and further checks made until these values return to normal.

Navirel is normally administered once a week. The usual dose for adults is 25 – 30 mg/m^2. Always follow your doctor's instructions.

Dose adjustment
- In the case of significant liver insufficiency the dose may be changed by your doctor. Please follow your doctor's instructions.
- In the case of renal insufficiency it is not necessary to adjust the dose. Please follow your doctor's instructions.

Navirel should always be injected into a vein.
This may be by injection over a 6 to 10 minute period or by a short infusion over 20 to 30 minutes. After administration, sodium chloride solution will be infused into the same vein so that the medicine is dispersed.

If more Navirel was used than described in the package leaflet
Your doctor will ensure that the correct dose for your condition is given. However, contact your doctor, emergency services or pharmacist if you have any concerns or show symptoms of a potential overdose like fever, signs of infection or constipation.

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.

Tell your doctor immediately if you experience any of the following symptoms, as these may indicate serious side effects:

Uncommon (may affect up to 1 in 100 people)
- Cough, fever and chills which may be signs of a severe infection which can lead to organ failure and blood poisoning.
- Difficulty in breathing (dyspnoea) or difficulty in breathing caused by constriction of the airways (bronchospasm).

Rare (may affect up to 1 in 1,000 people)
- Severe chest pain which may spread to your neck and arm. It may occur due to lack of blood to your heart (angina pectoris or heart attack).

- Signs of very low blood pressure such as severe dizziness and light-headedness when you stand up.
- Severe constipation with abdominal pain when you have not had a bowel movement for several days (paralytic ileus).

Not known (frequency cannot be estimated from the available data)
- Signs of a serious allergic reaction which may include wheezing, swelling of your lips, tongue and throat or body, difficulties to swallow, rash, light-headedness and fainting (anaphylactic reaction or shock, anaphylactoid reaction).
- A chest pain, breathlessness and fainting, which can be a symptom of a clot in a blood vessel in the lungs (pulmonary embolism).
- Headaches, changed mental state which may lead to confusion and coma, convulsions, blurred vision and high blood pressure, which could be sign of a neurological disorder such as posterior reversible encephalopathy syndrome.

In the following, please find a list of all other side effects which may occur:

Very common (may affect more than 1 in 10 people)
- Inhibition of bone marrow function with decrease in the number of red blood cells which can make the skin pale and cause weakness or breathlessness and certain type of white blood cells (neutrophils), reversible within 5 to 7 days.
- Constipation, vomiting, inflammation of the mucous membrane of the mouth, inflammation of the oesophagus.
- Loss of some reflex reactions (deep tendon reflex); weakness of legs has been reported after a prolonged chemotherapy.
- Transient elevations of blood tests which show changes in the way the liver is working, without symptoms.
- Hair loss, usually mild.
- Reactions at the injection site like redness of the skin, burning pain, changes of the colour of the vein and local inflammation of the vein (phlebitis)
- Feeling of weakness, fatigue, fever, pain in different locations including chest pain and pain at the tumour site.

Common (may affect up to 1 in 10 people)
- Decreased number of platelets (particles in the blood which help to stop bleedings), seldom severe.
- Bacterial, viral or fungal infections at different parts of the body like in the respiratory, urinary or gastrointestinal tract, mild to moderate and usually reversible with an appropriate treatment.
- Breathing difficulties or skin reactions as a result of a hypersensitivity reaction to vinorelbine.
- Diarrhoea, usually mild to moderate.
- Muscle pain, joint pain, jaw pain.
- An increase of creatinine in the blood, a substance that reflects kidney function.

Uncommon (may affect up to 1 in 100 people)
- Problems with the nerves like feeling of tingling or prickling and increased or decreased muscle tension (paraesthesia).
- Low blood pressure.
- High blood pressure.
- A sudden feeling of heat and skin redness of the face and neck (flushing).
- Feeling cold in hands and feet.

Rare (may affect up to 1 in 1,000 people)
- Severe low blood levels of sodium which can cause tiredness and confusion, muscle twitching, fits or coma.
- Inflammation of the pancreas (organ which regulates glucose in the blood) which causes severe pain

in the abdomen and back (pancreatitis).
- Transitory changes in a graph showing the electrical activity of the heart, including the heartbeat (transitory electrocardiogram changes).
- Problems with breathing due to diseases of the connective tissue of the lung (interstitial lung disease).
- Fainting (collapse).
- Generalised skin reactions.
- Severe disorders of the skin at the injection site like death of tissue (injection site-necrosis).

Very rare (may affect up to 1 in 10,000 people)
- Blood poisoning with complications and blood poisoning leading to death.
- Disorders of the heart like rapid heart rate (tachycardia), feeling your heartbeat (palpitations) and irregular heartbeats (heart rhythm disorders).
- Impaired lung function (respiratory insufficiency).
- Guillain-Barré syndrome (symptoms of this include e.g. weakness or paralysis of legs and arms, problems with breathing and blood pressure).

Not known (frequency cannot be estimated from the available data)
- Low level of certain white blood cells accompanied by fever (febrile neutropenia).
- Severe reduction in all blood cells which can cause weakness, bruising or make infections more likely.
- Systemic infection with fever and an unusually low count of certain white blood cells with potentially fatal outcome (neutropenic sepsis).
- SIADH-syndrome (symptoms of this include e.g. weight gain, nausea, muscle cramps).
- Loss/lack of appetite.
- Palmar-plantar erythrodysesthesia syndrome (symptoms of this include e.g. numbness, tingling, burning, or itching sensation, redness [resembling a sunburn], swelling, discomfort, tenderness, rash).
- Darker colour of skin that follows the path of veins.

Burning pain and redness in the area of the infusion may occur during or after the infusion. As this can be a sign of an injection error, you should inform the doctor or nurse, and the infusion must be stopped immediately.

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

5. How to store Navirel

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

This medicine should not be used after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C-8 °C). Do not freeze. Store in the original package in order to protect from light.

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 to protect the environment.

6. Contents of the pack and other information

What Navirel contains
The active substance is vinorelbine (as tartrate), 10 mg/ml.
Each 1 ml vial contains a total content of vinorelbine (as tartrate) of 10 mg.
Each 5 ml vial contains a total content of vinorelbine (as tartrate) of 50 mg.

The other ingredient is water for injections.

What Navirel looks like and contents of the pack
Navirel is a clear, colourless to slightly yellow concentrate for solution for infusion (sterile concentrate) which is supplied in glass vials.

Pack sizes: 1 ml or 5 ml concentrate in packs of 1 or 10 vials. Also available as multipacks of 10 packs each containing 1 vial.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
medac
Gesellschaft für klinische
Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany

This medicinal product is authorised in the Member States of the EEA under the following names:

Cyprus	Navirel 10 mg/ml πυκνό διάλυμα για ιαπυκνό διάλυμα koncentráéγχυση
Czech Republic	Navirel 10 mg/ml koncentrát pro infuzní roztok
Denmark	Navirel 10 mg/ml koncentrat til infusionsvæske, opløsning
Finland	Navirel 10 mg/ml infuusiokonsentraatti, liuosta varten
Germany	Navirel 10 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Netherlands	Navirel 10 mg/ml concentraat voor oplossing voor infusie
Norway	Navirel 10 mg/ml konsentrat til infusjonsvæske
Poland	Navirel
Portugal	Vinorelbina Navirel 10 mg/ml concentrado para solução para perfusão
Slovakia	Navirel 10 mg/ml infúzny koncentrát
Sweden	Navirel 10 mg/ml koncentrat till infusionsvätska, lösning

This leaflet was last revised in 02/2023.

The following information is intended for healthcare professionals only:

How to use Navirel
The preparation and administration of vinorelbine should be carried out only by trained personnel. Suitable protective goggles, disposable gloves, face mask and disposable clothing must be worn. Spills and leakages must be wiped up.
Any contact with the eyes must be strictly avoided. If the solution does come into contact with the eyes they must be rinsed immediately with plenty of sodium chloride 9 mg/ml (0.9 %) solution.

After preparation, any exposed surface must be thoroughly cleaned and hands and face washed.

There is no incompatibility between the contents and container for Navirel 10 mg/ml concentrate for solution for infusion and a neutral glass bottle, PVC bag, vinylacetate bag or infusion set with PVC tubes.

Vinorelbine may be administered
- by slow bolus (6-10 minutes) after dilution in 20-50 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection or in 5 % (w/v) glucose solution for injection or
- by a short infusion (20 -30 minutes) after dilution in 125 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection or in 5 % (w/v) glucose solution for injection.

Administration should always be followed by a sodium chloride 9 mg/ml (0.9 %) infusion with at least 250 ml to flush the vein.

How to store Navirel
After opening and dilution:
The product has to be used immediately after opening and dilution. It is intended as single dose only.

Reconstituted solutions: 24 hours when stored at 25 ºC or in a refrigerator (2 °C -8 °C).

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not normally be longer than 24 hours at 2 °C -8 °C, unless opening and dilution has taken place in controlled and validated aseptic conditions.

Do not use Navirel if you notice that the concentrate is not a clear, colourless to pale yellow solution free from visible particles.