Package leaflet: Information for the patient

Sendolor 1 mg/ml, solution for infusion
Sendolor 10 mg/ml, solution for infusion
Sendolor 20 mg/ml, solution for infusion

morphine hydrochloride trihydrate

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

What is in this leaflet

1. What Sendolor is and what it is used for

Sendolor contains morphine, which belongs to a class of medicines called "opiods" and which are strong analgesics or 'painkillers'. Sendolor is used for the treatment of severe acute pain, cancer pain and breakthrough cancer pain.

2. What you need to know before you use Sendolor

Do not use Sendolor
- If you are allergic to morphine hydrochloride or any of the other ingredients of this medicine (listed in section 6).
- Respiratory depression; obstructive airways disease; excessive airways secretions; during a bronchial asthma attack or in heart failure secondary to chronic lung disease.
- Head injury; raised intra-cranial pressure.
- Coma.
- Convulsion disorders.
- Ulcerative colitis.
- Presence of a risk of paralytic ileus.
- Gall bladder and kidney pain or spasm.
- Acute alcoholism or when agitated under the influence of alcohol or medicines to help you sleep.
- Moderate to severe renal impairment (glomerular filtration rate <20 ml/min).
- Severe or acute liver failure.
- Patients receiving monoamine oxidase inhibitors or within two weeks of discontinuing such treatment.

Warnings and precautions
This medicine can cause addiction and you may get withdrawal symptoms if you stop taking it suddenly. Tolerance (getting used to a medicine, resulting in the medicine being less effective) may also develop.

Drug dependence (addiction), tolerance and potential for abuse
For all patients, prolonged use of this product may lead to drug dependence, even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, yawning, perspiration, chills, myalgia and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

However, when doses of morphine are carefully titrated against pain, clinically significant respiratory depression, dependence, rapid tolerance and euphoria rarely develop. Clinically significant tolerance to morphine is unusual in cancer patients with severe pain.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

Talk to your doctor, prescriber or pharmacist before using Sendolor if you have:
- Asthma.
- Cyanosis (blue colour of the skin caused by lack of oxygen in the blood).
- Head injuries.
- Low blood pressure with not enough blood in the blood vessels (decreased blood volume).
- Underactive thyroid.
- Liver problems.
- Kidney problems.
- Inflammatory bowel diseases such as Crohn's disease or ulcerative colitis.
- Inflammation of the pancreas.
- Cramping in the muscles of the bile duct (bile duct spasm).
- Cramping in the muscles of the urinary tract (urinary tract spasm).
- Convulsions (fits).
- Acute chest syndrome (ACS) in patients with sickle cell disease (SCD)
  Due to a possible association between ACS and morphine use in SCD patients treated with morphine during a vaso-occlusive crisis, close monitoring for ACS symptoms is warranted.
- Adrenal insufficiency
  Opioid analgesics may cause reversible adrenal insufficiency requiring monitoring and glucocorticoid replacement therapy. Symptoms of adrenal insufficiency may include e.g. nausea, vomiting, loss of appetite, fatigue, weakness, dizziness, or low blood pressure.

Talk to your doctor or pharmacist if you experience any of the following symptoms while using Sendolor:
- Increased sensitivity to pain despite the fact that you are taking increasing doses (hyperalgesia). Your doctor or prescriber will decide whether you will need a change in dose or a change in strong analgesic ("painkiller") (see section 2).
- Weakness, fatigue, lack of appetite, nausea (feeling sick), vomiting (being sick) or low blood pressure. This may be a symptom of the adrenals producing too little of the hormone cortisol, and you may need to take hormone supplement.
- Loss of libido (sex drive), impotence (inability to have or maintain an erection), or periods stopping. This may be because of decreased sex hormone production.
- Are using drugs or alcohol or have used drugs or alcohol in the past.
- If you feel that you are becoming dependent on Sendolor while you are using it. You may have started to think a lot about when you can take the next dose, even if you do not need it for the pain.
- Withdrawal symptoms. The most common withdrawal symptoms are mentioned in section 3 "If your treatment with Sendolor is stopped". If this occurs, your doctor or prescriber may change the type of medicine or the times between doses.

Children and adolescents

All children have a risk of breathing problems with this medicine. Your doctor or prescriber will give morphine very carefully to children under one year old.

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

- Sedative medicines such as benzodiazepines increase the risk of drowsiness, low blood pressure, difficulties in breathing (respiratory depression) or coma and may be life-threatening. Because of this, accompanying use should only be considered when other treatment options are not possible. However if your doctor does prescribe Sendolor together with sedative medicines the dose and duration of accompanying treatment should be limited. Please tell your doctor or prescriber 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 or prescriber when experiencing such symptoms.
- Rifampicin (an antibiotic used to treat tuberculosis).
- Cimetidine (used in the treatment of heartburn and peptic ulcers).
- Nimodipine (a calcium channel blocker used to prevent changes in brain function after bleeding around the brain).
- Monoamine oxidase inhibitors (MAOI) such as moclobemide or phenelzine used in the treatment of depression.
- Combined morphine stimulants/depressants (buprenorphine, nalbuphine, pentazocine (opioid pain killers)).

Sendolor with alcohol
Sendolor may cause difficulty in breathing which can be made worse if combined with alcohol. Avoid alcohol (even small amounts) during treatment with this medicine.

Pregnancy, breast-feeding and fertility
Do not take Sendolor if you are pregnant or think you might be pregnant unless you have discussed this with your prescriber and the benefits of treatment are considered to outweigh the potential harm to the baby.

If you use Sendolor during pregnancy, your baby may become dependent and experience withdrawal symptoms after the birth which may need to be treated.

Do not take Sendolor while you are breastfeeding as morphine sulfate passes into breast milk and will affect your baby.

Morphine could harm an unborn baby. Both men and women of childbearing age should use an effective method of birth control (contraception) during your treatment with this product.

Driving and using machines
Morphine has influence on the ability to drive and use machines. This should be considered when alertness is required e.g. when driving.

Sendolor contains sodium
Sendolor 1 mg/ml, solution for infusion contains 354.5 mg sodium (the main component of cooking/table salt) in each 100 ml bag. This is equivalent to 17.7% of the recommended maximum daily dietary intake of sodium for an adult.
Sendolor 10 mg/ml, solution for infusion contains 295.4 mg sodium (the main component of cooking/table salt) in each 100 ml bag. This is equivalent to 14.8% of the recommended maximum daily dietary intake of sodium for an adult.
Sendolor 20 mg/ml, solution for infusion contains 236.3 mg sodium (the main component of cooking/table salt) in each 100 ml bag. This is equivalent to 11.8% of the recommended maximum dailty dietary intake of sodium for an adult.

3. How Sendolor should be given

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

Your doctor or prescriber will decide the dose that is best for you. If you do not understand what you are being given, or are in any doubt, ask your doctor or nurse. The dose and how it is given will depend on your age, weight, pain severity and previous medication and pain. If your are elderly or have impaired liver or kidney function your doctor or prescriber may prescribe a lower dose.

If you are given more Sendolor than you should
People who have taken an overdose may get pneumonia from inhaling vomit or foreign matter, symptomes may include breathlessness, cough and fever. People who have taken an overdose may also have breathing difficulties leading to unconsciousness or even death.

If you miss a dose of Sendolor
If you think that a dose has been missed, speak to your doctor, nurse or prescriber.

If your treatment with Sendolor is stopped
Do not suddenly stop taking this medicine. If you want to stop taking this medicine, discuss this with your prescriber first. They will tell you how to do this, usually by reducing the dose gradually so that any unpleasant withdrawal effects are kept to a minimum. Withdrawal symptoms may include body aches, tremors (shaking), diarrhoea, stomach pain, feeling sick, flu-like symptoms, fast heartbeat and large pupils, restlessness, anxiety and irritability.

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, prescriber or nurse immediately if you experience the following serious side effects:
- A severe allergic reaction, such as dizziness, breathing difficulties, shock or low blood pressure. If you suffer such a reaction, you should not be given any more morphine. Your doctor will decide on the appropriate treatment for allergic reactions.
- Difficulty in breathing and physical and psychological dependence are possible serious side effects. It is possible that you could become dependent on morphine (for symptoms see section 3: “If your treatment with Sendolor is stopped”).

Very common: may affect more than 1 in 10 people
- Drowsiness.

Common: may affect up to 1 in 10 people
- Confusion.
- Sleeplessness.
- Dizziness.
- Head ache.
- Sleepiness.
- Small pupils in the eye, blurred vision.
- Losing weight.
- Dry mouth.
- Feeling sick or being sick.
- Constipation.
- A lumpy, itchy rash on your skin.
- Sweating.

- Difficulty or pain in passing urine.

Uncommon: may affect up to 1 in 100 people
- Allergic reaction.
- Agitation (feeling nervous, exited, or restless).
- Mood changes, feeling extremely happy for no particular reason or a feeling of emotional and mental unease (dysphoria).
- Hallucinations (seeing things that are not real).
- Convulsions (fits).
- Stiff and cramped muscles.
- Abnormal heartbeat.
- Facial flushing.
- Breathing difficulties.
- Injection, site pain and irritation.

Rare: may affect up to 1 in 1000 people
- Feeling faint on standing up.

Unknown: frequency cannot be estimated from the available data
- Drug dependence.
- Increased sensitivity to pain.
- Slow heartbeat.
- Fast heartbeat.
- Alteration in liver enzymes.
- Reduced sexual drive.
- Impotence (less able to have an erect penis).
- Drug withdrawal syndrome (abstinence syndrome) or dependence (for symptoms see section 3: "If your treatment with Sendolor is stopped").
- Drug tolerance (the body gets used to the drug).
- Muscle rigidity (stiffness).

Drug withdrawal
When you stop taking Sendolor, you may experience drug withdrawal symptoms, which include restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhoea, shaking, shivering or sweating.

How do I know if I am addicted?
If you notice any of the following signs whilst taking Sendolor, it could be a sign that you have become addicted.
- You need to take the medicine for longer than advised by your prescriber.
- You feel you need to use more than the recommended dose.
- You are using the medicine for reasons other than prescribed.
- When you stop taking the medicine you feel unwell, and you feel better once taking the medicine again.

If you notice any of these signs, it is important you talk to your prescriber.

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:
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 Sendolor

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

Keep the bag in the outer pouch and 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 protect the environment.

6. Contents of the pack and other information

What Sendolor contains
- The active substance is morphine hydrochloride trihydrate.
- The other ingredients are sodium chloride, hydrochloric acid and water for injection.

What Sendolor looks like and contents of the pack
The solution for infusion is clear and (almost) colourless.
The colourless bags contain 100 ml solution. The bags are overwrapped in outer pouches. Between the bag and the overwrapping there is an oxygen absorbing sachet. One outer carton contains 1, 5 or 10 pouches.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Eurocept International BV
Trapgans 5
1244 RL Ankeveen
The Netherlands

This medicinal product is authorised in United Kingdom (Northern Ireland) under the following names:
- Sendolor 1 mg/ml, solution for infusion: PL 35068/0006
- Sendolor 10 mg/ml, solution for infusion: PL 35068/0007
- Sendolor 20 mg/ml, solution for infusion: PL 35068/0008

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The following information is intended for healthcare professionals only:

The recommended dose is

Adults
Intravenous (in the vein): 2.5 to 15 mg administered over 4-5 minutes.
Subcutaneous (under the skin), *intramuscular* (in the muscle): 5-20 mg, usually 10 mg per time, if necessary, up to every 4 hours.
Epidural (outside the meninges and in the spinal cord): initially 5 mg, if necessary after one hour 1-2 mg, repeated if necessary, usually to a total of 10 mg per day.
Epidural infusion: initially 3.5 to 7.5 mg per day (=24 hours), if necessary increased by 1-2 mg per day.
Intrathecal (within the meninges): 0.2-1 mg one time, preferably not repeat; with an implanted micro-infusion system, the daily dose can gradually increase to 25 mg (after 40 weeks of continuous treatment).

Children and adolescents
Intravenous (in the vein): Only where particularly rapid onset of action is required 0.05-0.1 mg/kg body weight, very slowly administered (dilution with isotonic sodium chloride solution is recommended).
Subcutaneous (under the skin), intramuscular (in the muscle): 0.05-0.2 mg/kg of body weight, if necessary, up to every 4 hours. Single dose should not exceed 10 mg.

Elderly
Subcutaneous (under the skin), *intramuscular* (in the muscle), *intravenous* (in the vein): 2.5-10 mg at a time. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range with incremental titration to the desired effect.

For premedication up to 10 mg may be given by subcutaneous (under the skin) or intramuscular (in the muscle) injection 60 to 90 minutes before surgery.
For continuous intravenous (in the vein) administration maintenance doses have generally ranged from 0.8 to 80 mg/hour.

Method of administration
In case of bad circulation slow intravenous administration should be used, since via subcutaneously or intramuscularly administration the active substance is not sufficiently absorbed.

The recommended initial dose for continuous epidural infusion in opioid-naïve patients ranges from 3.5 to 7.5 mg daily; those who have some degree of opioid tolerance may be given 4.5 to 10 mg daily. However, dosage requirements may increase significantly during treatment and up to 20 to 30 mg daily may be required in some patients.

Patient-controlled analgesia (PCA)**
PCA is used to mean intermittent or continuous parenteral infusion of morphine with patient-controlled administration of rescue doses on an "as needed" basis programmed into a portable pump. Postoperatively the PCA technique may involve intermittent patient-directed rescue boluses and/or a baseline infusion plus patient directed rescue dosing. PCA is given intravenously or subcutaneously.

A PCA device for chronic cancer pain is indicated when:
1. Oral administration is not advisable.
2. When the total dose of oral morphine is large.
3. When PCA is necessary to obtain better compliance.
4. When PCA provides immediate relief from incident pain.

For patients with breakthrough cancer pain despite optimised round the clock opioid use, an intravenous bolus of 20% of the total daily equivalent oral morphine dose of the background opioid therapy is recommended.

Technically, the patient self-administers a rescue dose by pushing a button that activates a program operating a computerized drug injector connected to the infusion pump. The rescue dose is 25-50% of the continuous hourly dose, with a minimum PCA bolus of 1 mg morphine. A lockout interval (the time during which no drug is delivered even if an attempt is made to activate the machine) is programmed in and may be set for intervals of 5 min to hourly or 2 hours intervals for incident or breakthrough. Patients and responsible family members or the principal caregiver should be trained in pump operation, battery changing, and interpretation of pump alarms. A 24 hours telephone contact and a constant home care support system are essential for outpatient PCA.
**Local clinical guidelines could differ from the above.

Impaired renal function
Morphine is one of the opioids whose dosing is greatly affected by renal failure. As a result of decreased renal clearance, accumulation of the metabolites can lead to serious adverse effects. Morphine doses must be carefully titrated in patients with decreased renal function or renal failure.

Hepatic impairment
In patients with severe hepatic impairment a doubling of the dose interval should be considered. Caution is advised when giving morphine to patients with hepatic impairment.

Overdose
Treatment of overdose: Respiratory depression at morphine intoxication can be reversed with naloxone. Support respiration if needed and check the fluid and electrolyte balance. Symptomatic therapy.

Incompatibilities
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.