**Package leaflet: information for the user**

**Remifentanil 1 mg powder for concentrate for solution for injection/infusion**
**Remifentanil 2 mg powder for concentrate for solution for injection/infusion**
**Remifentanil 5 mg powder for concentrate for solution for injection/infusion**

remifentanil

**Read all of this leaflet carefully before you start using this medicine because it containes 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.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**:


## 1. What Remifentanil is and what it is used for

Remifentanil contains the active substance remifentanil. Remifentanil belongs to a group called opioids. It differs from other medicines in this group by its very quick onset and very short duration of action.

Remifentanil may be used to stop you feeling pain before or while you are having an operation.

Remifentanil may be used to relieve pain while you are under controlled mechanical ventilation in an Intensive Care Unit (for patients 18 years of age and over).

## 2. What you need to know before you take Remifentanil

**Do not use Remifentanil**
- if you are allergic to remifentanil or any of the other ingredients of this medicine (listed in section 6)
- if you are allergic to any other fentanyl derivates (such as alfentanil, fentanyl, sufentanil). An allergic reaction may include rash, itching, difficulty of breathing or swelling of the face, lips, throat or tongue. You may know this from earlier experience
- as injection into the spinal canal
- as sole medicine to initiate anaesthesia

**Warnings and precautions**
Talk to your doctor or pharmacist before using Remifentanil. Tell your doctor if you:
- ever had any adverse reactions during an operation
- ever had any allergic reactions or if you have been told that you are allergic to:
  - any medicines used during an operation
  - opioid medicines (e.g., morphine, fentanyl, pethidine, codeine) , see also section above **„Do not use Remifentanil”**

- suffer from impaired lung and/or liver function (you may be more sensitive for breathing difficulties)

- Elderly or weak patients (caused by decreased blood volume and/or low blood pressure) are more sensitive to suffer from cardiac or circulatory disturbances.

- As with other opioids, remifentanil may produce dependency.
- Following anesthesia with Remifentanil, you should leave home only accompanied and you should not drink alcohol.
- Remifentanil should be administered only in a setting fully equipped for the monitoring and support of respiratory and cardiovascular function, and by persons specifically trained in the use of anaesthetic medicines and the recognition and management of the expected adverse effects of potent opioids, including respiratory and cardiac resuscitation.
- In ventilated intensive care patients the use of Remifentanil for more than 3 days is not recommended.
- Due to the rapid offset of action of remifentanil, patients may emerge rapidly from anaesthesia and no residual opioid activity will be present within 5-10 minutes after the discontinuation of Remifentanil. For those patients undergoing surgical procedures where post-operative pain is anticipated, analgesics should be administered prior to discontinuation of Remifentanil.
- At the doses recommended muscle rigidity may occur. As with other opioids, the incidence of muscle rigidity is related to the dose and rate of administration. Therefore, bolus injections should be administered over not less than 30 seconds.

Hypotension and bradycardia may be managed by reducing the rate of infusion of Remifentanil or the dose of concurrent anaesthetics or by using intravenous fluids, vasopressor or anticholinergic agents.

**Children**
Remifentanil is not recommended in neonates and infants (children under the age of one year). There is little experience of use of Remifentanil to treat children in intensive care units.

**Elderly**
If used for an operation under general anaesthesia, the initial dose of Remifentanil should be appropriately reduced in elderly patients.

**Other medicines and Remifentanil**
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Also including medicines obtained without a prescription.

This is especially important with the following medicines as they may interact with your Remifentanil:
- medicines for blood pressure or heart problems (known as beta-blockers or calcium channel blockers). These medicines may increase the effect of Remifentanil on your heart (lowering of your blood pressure and your heart beat).
- other sedative medicines, such as benzodiazepines or related drugs. Concomitant use with Remifentanil 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. Your doctor or pharmacist will alter the dose of these medicines and limit the duration of treatment when you are being given Remifentanil. 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.

It may still be all right for you to receive Remifentanil and your doctor will be able to decide what is suitable for you.

Remifentanil is not metabolized by plasmacholinesterase, therefore, interactions with medicines metabolized by this enzyme are not anticipated.

**Remifentanil with alcohol**
After having received Remifentanil you should not drink alcohol until fully recovered.

**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 this medicine is given to you.

Remifentanil should not be given to pregnant women unless medically justified. Remifentanil is not recommended during labour or a Caesarian section.

It is recommended that you stop breast-feeding for 24 hours after Remifentanil has been given to you.

**Driving and using machines**
This medicine is only used in hospitalized patients.
If you are discharged early, after you have been given Remifentanil, you must not drive, operate machinery, or work in dangerous situations. You should not go home alone.

**Remifentanil contains sodium**
This medicinal product contains less than 1 mmol sodium (23 mg) per ml, i.e. essentially 'sodium-free'.

## 3. How to use Remifentanil

Remifentanil is always used by healthcare professionals and only in a setting fully equipped for the monitoring and support of respiratory and cardiovascular function and by persons specifically trained in the use of anaesthetic medicines and the recognition and management of the expected adverse effects of potent opioids, including respiratory and cardiac resuscitation.

The recommended dosage is always determined by the doctor dependent on the patient's individual condition and his response to the drug.

Remifentanil is for intravenous use only and must not be administered by epidural or intrathecal injection.

Dilution should be adjusted to the technical equipment of the infusion system and the expected patient requirements.

Remifentanil should not be mixed with other therapeutic agents prior to administration and for intravenous use it should only be admixed with one of the following fluids:
- Glucose 50 mg/ml (5%) solution for injection
- Glucose 50 mg/ml (5%) solution for injection and sodium chloride 9 mg/ml (0.9 %) solution for injection
- Sodium chloride 9 mg/ml (0.9 %) solution for injection
- Sodium chloride 4.5 mg/ml (0.45 %) solution for injection

<u>Newborns and infants</u>
There are no data available on administration to newborns and infants younger than 1 year.

<u>Dosage in special patient groups</u>
In obese or critically ill patients the initial dose will be appropriately reduced and enhanced due to the response.

In patients with impaired liver or kidney function and in patients undergoing neurosurgery a dose reduction will not be necessary.

**If you receive more Remifentanil than you should**

If you have received too much of Remifentanil, or if it is suspected, that you may have received too much, appropriate action will be taken promptly by your healthcare specialist team.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
The following side effects have been reported:

Very common (may affect more than 1 in 10 people)
- muscle stiffness
- feeling sick (nausea)
- being sick (vomiting)
- low blood pressure (hypotension)

Common (may affect up to 1 in 10 people)
- slow heart beat (bradycardia)
- shallow breathing (respiratory depression)
- breathing stops (apnoea)
- itching
- shivering after the operation
- high blood pressure (hypertension) after the operation

Uncommon (may affect up to 1 in 100 people)
- constipation
- pain after the operation
- oxygen deficiency (hypoxia)

Rare (may affect up to 1 in 1,000 people)
- slow heart beat followed by heart block in patients receiving remifentanil with one or more anaesthetic medicines
- sleepiness (during recovering from the operation)
- severe allergic reactions including shock, circulatory failure and heart attack in patients receiving remifentanil with one or more anaesthetic medicines

Not known (frequency cannot be estimated from the available data)
- cough

As with other medicines of this class (opioids), long-term use of Remifentanil can lead to dependence (frequency cannot be estimated from the available data). Please ask your doctor for advise.

**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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie; E-mail: medsafety@hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Remifentanil

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 carton**.** The expiry date refers to the last day of that month.

1 mg
Do not store above 25°C.
Do not refrigerate or freeze.
Keep the vial in the outer carton in order to protect from light.

2 and 5 mg
Do not store above 30°C.
Do not refrigerate or freeze.

After reconstitution and dilution, chemical and physical in-use stability has been demonstrated for 24 hours at 25°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 normally not be longer than 24 hours at 2 to 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Following dilution, the solution has to be inspected visually to ensure that it is clear, colourless and virtually free from solids, and that there is no damage to the vials. If such changes are detected, the solution has to be discarded.

The diluted solution is for single use only.

Any unused solution has to be discarded.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. Contents of the pack and other information

**What Remifentanil contains**

- The active substance is: remifentanil (as hydrochloride)
  1 vial contains 1 mg remifentanil (as remifentanil hydrochloride).
  1 vial contains 2 mg remifentanil (as remifentanil hydrochloride).
  1 vial contains 5 mg remifentanil (as remifentanil hydrochloride).
  After reconstitution the solution contains 1 mg/ml remifentanil (as hydrochloride), if prepared as recommended.
- The other ingredients are: glycine; hydrochloric acid 37% (for pH adjustment); sodium hydroxide 17% (for pH adjustment)

**What Remifentanil looks like and contents of the pack**

Remifentanil 1/ 2/ 5 mg is a lyophilized white to slightly yellow cake or powdery mass for concentrate for solution for injection/infusion.

Each carton of Remifentanil 1 mg contains 5 vials of 3.5 ml.
Each carton of Remifentanil 2 mg contains 5 vials of 3.5 ml.
Each carton of Remifentanil 5 mg contains 5 vials of 8 ml.

**Marketing Authorisation Holder**

Actavis Group PTC ehf.,

Reykjavikurvegi 76-78,

220 Hafnarfjordur,

Iceland

**Manufacturer**

Elaiapharma

2881 Route de Crêtes,

BP 205 Valbonne

06904 Sophia Antipolis Cedex

France

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

| | |
|---|---|
| Germany: | Remifentanil-Actavis 1,2,5 mg Pulver für ein Konzentrat zur Herstellung einer Infusions-/Injektionslösung |
| Finland: | Remifentanil Actavis 1,2,5 mg injektio/infuusiokuiva-aine, konsentraatti liuosta varten |
| Ireland: | Remifentanil 1,2,5 mg powder for concentrate for solution for infusion/injection |
| Iceland: | Remifentanil Actavis |
| Poland: | Remifentanyl Actavis |
| Sweden: | Remifentanil Actavis |
| United Kingdom: | Remifentanil 1,2,5 mg, powder for concentrate for solution for injection/infusion |

**This leaflet was last revised in September 2018**.

**Other sources of information**

**The following information is intended for healthcare professionals only:**

**Instructions on use/handling of remifentanil 1, 2 and 5 mg powder for concentrate for solution for infusion/injection**

Remifentanil should be prepared for intravenous use by adding the appropriate volume (as stated in the table below) of one of the below listed diluents to give a reconstituted solution with a concentration of approximately 1mg/ml.

| Presentation | Volume of diluent to be added | Concentration of the reconstituted solution |
|---|---|---|
| Remifentanil 1 mg | 1 ml | 1 mg/ml |
| Remifentanil 2 mg | 2 ml | 1 mg/ml |
| Remifentanil 5 mg | 5 ml | 1 mg/ml |

Following reconstitution, the product has to be inspected visually (as far as supported by the vial) for solids, discoloration or damage to the vials. If such changes are detected, the solution has to be discarded. The finished solution is for single use only. Unused solution has to be discarded.

For manually-controlled infusion, Remifentanil should be administered following further dilution to a concentration of 20 to 250 µg/ml (50 µg/ml is the recommended dilution for adults and 20 to 25 µg/ml for paediatric patients aged 1 year and over).

For target controlled infusion (TCI), Remifentanil should be administered following further dilution to a concentration of 20 to 50 µg/ml.

Dilution should be adjusted to the technical equipment of the infusion system and the expected patient requirements.

For dilution, one of the following IV fluids listed below should be used:
Water for Injections
Glucose 50 mg/ml (5%) solution for Injection
Glucose 50 mg/ml (5%) and sodium chloride 9 mg/ml (0,9 %) solution for injection
Sodium chloride 9 mg/ml (0,9 %) solution for injection
Sodium chloride 4,5 mg/ml (0,45 %) solution for injection

Remifentanil has been shown to be compatible with the following IV fluids when administered into a running IV catheter:

Lactated Ringer's solution for injection
Lactated Ringer's and Glucose 50 mg/ml (5%) solution for injection

Remifentanil has been shown to be compatible with propofol when administered into a running IV catheter.

Any unused product or waste material should be disposed of in accordance with local requirements.

For full prescribing information refer to the Summary of Product Characteristics.