

PACKAGE LEAFLET: INFORMATION FOR THE USER

Remifentanyl 1 mg powder for concentrate for solution for injection or infusion
Remifentanyl 2 mg powder for concentrate for solution for injection or infusion
Remifentanyl 5 mg powder for concentrate for solution for injection or infusion

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.
- 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 of the side effects talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Remifentanyl is and what it is used for
2. What you need to know before you are given Remifentanyl
3. How Remifentanyl is given
4. Possible side effects
5. How to store Remifentanyl
6. Contents of the pack and any other information

1. WHAT REMIFENTANIL IS AND WHAT IT IS USED FOR

Remifentanyl belongs to a group of medicines known as opioids. These medicines are used widely to cause anaesthesia and/or to relieve pain during an operation.

Remifentanyl is used:

- as an analgesic, which helps to relieve pain, for use at the onset or during anaesthesia in conjunction with anaesthetic agents
- as an analgesic for patients 18 years of age or older who are mechanically ventilated in the intensive care unit.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN REMIFENTANIL

Remifentanyl must not be given

- if you are allergic to Remifentanyl or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to any medicine used in operations or if you had a side effect during an operation.
- Remifentanyl must not be administered by epidural or intrathecal injection, because this medicine contains glycine.
- as sole medicine to initiate anaesthesia.

Warnings and precautions

Tell your doctor before you are given Remifentanyl:

- If you are allergic to any other opioid medicines, such as morphine or codeine
- If you are over 65 years of age
- If you are dehydrated or have lost a lot of blood
- If you are feeling weak or unwell
- If you are overweight

If you are not sure if any of the above apply to you, talk to your doctor, pharmacist or nurse before you are given Remifentanyl.

Other medicines and Remifentanyl

Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. This includes herbal medicines. This is because Remifentanyl can work with other medicines to cause side effects.

In particular tell your doctor or pharmacist if you are taking:

- medicines for your heart or blood pressure, such as beta-blockers (these include atenolol, metoprolol, carvedilol, propranolol and bisoprolol) or calcium channel blockers (these include amlodipine, diltiazem and nifedipine)

Concomitant use of Remifentanyl 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 Remifentanyl 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.

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 for advice before taking this medicine.

Your doctor will assess if having this medicine is necessary during pregnancy or breastfeeding.

In case of having this medicine, breast-feeding must be stopped during the following 24 hours.

Driving and using machines

After anaesthesia with Remifentanyl you should not drive or operate machinery. The physician should decide when these activities may be resumed. It is advisable that you are accompanied when returning home and that alcoholic drink is avoided.

This medicine can affect your ability to drive.

Do not drive whilst taking this medicine until you know how this medicine affects you.

It may be an offence to drive if your ability to drive safely is affected.

There is further information for patients who are intending to drive in Great Britain - go to <http://www.gov.uk/drug-driving-law>

3. HOW REMIFENTANIL IS GIVEN

This medicine will always be given to you by a person who is qualified to do so. You will never be expected to give yourself this medicine.

Remifentanyl can be given:

- as a single injection into your vein
- as a continuous infusion into your vein. This is where the drug is slowly given to you over a longer period of time.

The way you are given the drug and the dose you receive will depend on:

- your weight
- the operation you have
- how much pain you will be in
- how sleepy the medical staff want you to be in the Intensive Care Unit

The dose varies from one patient to another

If you are given too much

The effects of Remifentanyl are carefully monitored throughout your operation and in intensive care, and appropriate action will be taken promptly if you receive too much.

After your operation

Tell your doctor or nurse if you are in pain. If you are in pain after your procedure, they will be able to give you other painkillers.

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. These effects are normally mild to moderate.

Some people can be allergic to medicines. **You must tell your doctor or nurse immediately if you have:**

- Rare:** may affect up to 1 in 1,000 people
- sudden wheeze and chest pain or chest tightness
- swelling of your eyelids, face, lips, mouth or tongue
- a lumpy skin rash or 'hives' anywhere on the body
- collapse.

For the Medical Profession

Refer to the Summary of Product Characteristics for the complete prescribing information.

The information provided in this section are the instructions for the preparation of Remifentanyl powder for concentrate for solution for injection or infusion prior to administration and the guidelines for infusion rates for manually-controlled infusion.

Preparation guide for:

Remifentanyl 1 mg powder for concentrate for solution for injection or infusion
Remifentanyl 2 mg powder for concentrate for solution for injection or infusion
Remifentanyl 5 mg powder for concentrate for solution for injection or infusion

Remifentanyl Injection is a white to off-white powder, to be reconstituted before use. Remifentanyl Injection is available in glass vials containing 1mg, 2mg or 5mg of remifentanyl base.

Do not store above 25°C.

When reconstituted as directed, solutions of Remifentanyl Injection are clear, colourless and practically free from particulate material and contain 1mg/ml of remifentanyl base as remifentanyl hydrochloride. Remifentanyl Injection should not be administered without further dilution after reconstitution of the lyophilised powder.

It is important that you read this guide prior to the preparation of Remifentanyl Injection. This information can also be found under sections 6.4 and 6.6 of the Summary of Product Characteristics.

Reconstitution of the lyophilised powder

Remifentanyl Injection should be prepared for intravenous use by adding, as appropriate 1, 2 or 5ml of diluent (see list of diluents under 'Further Dilution') to give a reconstituted solution with a concentration of approximately 1 mg/ml remifentanyl. The reconstituted solution is clear, colourless and practically free from particulate material. After reconstitution the solution should be visually inspected on contaminations, colour or a defective container. The solution should be discarded, if any of these modifications should appear. The reconstituted solution should be used immediately and is for single use only.

Further Dilution

After reconstitution, Remifentanyl Injection should not be administered by manually-controlled infusion without further dilution to concentrations of 20 to 250 micrograms/ml (50 micrograms/ml is the recommended dilution for adults and 20 to 25 micrograms/ml in paediatric patients aged 1 year and over when used in maintenance of anaesthesia).

After reconstitution, Remifentanyl Injection should not be administered by target-controlled infusion (TCI) without further dilution (20 to 50 micrograms/ml is the recommended dilution for TCI).

The dilution is dependent upon the technical capability of the infusion device and the anticipated requirements of the patient.

One of the following intravenous fluids listed below should be used for dilution

- 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

After dilution, the solution should be inspected visually to ensure it is clear, colourless, practically free from particulate matter and the container is undamaged. Any solution where such defects are observed must be discarded.

The reconstituted and further diluted solution of Remifentanyl Injection should be used immediately.

Remifentanyl Injection has been shown to be compatible with the following intravenous 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

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

Guidelines for Infusion Rates

The tables below give guidelines for infusion rates of Remifentanyl Injection for manually-controlled infusion:

Table 1: Remifentanyl Injection Infusion Rates (ml/kg/h)

Drug Delivery Rate (µg/kg/min)	Infusion Rate (ml/kg/h) for Solution Concentrations of			
	20µg/ml 1mg/50ml	25µg/ml 1mg/40ml	50µg/ml 1mg/20ml	250µg/ml 10 mg/40ml
0.0125	0.038	0.03	0.015	Not recommended
0.025	0.075	0.06	0.03	Not recommended
0.05	0.15	0.12	0.06	0.012
0.075	0.23	0.18	0.09	0.018
0.1	0.3	0.24	0.12	0.024
0.15	0.45	0.36	0.18	0.036
0.2	0.6	0.48	0.24	0.048
0.25	0.75	0.6	0.3	0.06
0.5	1.5	1.2	0.6	0.12
0.75	2.25	1.8	0.9	0.18
1.0	3.0	2.4	1.2	0.24
1.25	3.75	3.0	1.5	0.3
1.5	4.5	3.6	1.8	0.36
1.75	5.25	4.2	2.1	0.42
2.0	6.0	4.8	2.4	0.48

Table 2: Remifentanyl Injection Infusion Rates (ml/h) for a 20ug/ml Solution

Infusion Rate (µg/kg/min)	Patient Weight (kg)						
	5	10	20	30	40	50	60
0.0125	0.188	0.375	0.75	1.125	1.5	1.875	2.25
0.025	0.375	0.75	1.5	2.25	3.0	3.75	4.5
0.05	0.75	1.5	3.0	4.5	6.0	7.5	9.0
0.075	1.125	2.25	4.5	6.75	9.0	11.25	13.5
0.1	1.5	3.0	6.0	9.0	12.0	15.0	18.0
0.15	2.25	4.5	9.0	13.5	18.0	22.5	27.0
0.2	3.0	6.0	12.0	18.0	24.0	30.0	36.0
0.25	3.75	7.5	15.0	22.5	30.0	37.5	45.0
0.3	4.5	9.0	18.0	27.0	36.0	45.0	54.0
0.35	5.25	10.5	21.0	31.5	42.0	52.5	63.0
0.4	6.0	12.0	24.0	36.0	48.0	60.0	72.0

Table 3: Remifentanyl Injection Infusion Rates (ml/h) for a 25 µg/ml Solution

Infusion Rate (µg/kg/min)	Patient Weight (kg)									
	10	20	30	40	50	60	70	80	90	100
0.125	0.3	0.6	0.9	1.2	1.5	1.8	2.1	2.4	2.7	3.0
0.025	0.6	1.2	1.8	2.4	3.0	3.6	4.2	4.8	5.4	6.0
0.05	1.2	2.4	3.6	4.8	6.0	7.2	8.4	9.6	10.8	12.0
0.075	1.8	3.6	5.4	7.2	9.0	10.8	12.6	14.4	16.2	18.0
0.1	2.4	4.8	7.2	9.6	12.0	14.4	16.8	19.2	21.6	24.0
0.15	3.6	7.2	10.8	14.4	18.0	21.6	25.2	28.8	32.4	36.0
0.2	4.8	9.6	14.4	19.2	24.0	28.8	33.6	38.4	43.2	48.0

Table 4: Remifentanyl Injection Infusion Rates (ml/h) for a 50 µg/ml Solution

Infusion Rate (µg/kg/min)	Patient Weight (kg)								
	30	40	50	60	70	80	90	100	
0.25	0.9	1.2	1.5	1.8	2.1	2.4	2.7	3.0	
0.05	1.8	2.4	3.0	3.6	4.2	4.8	5.4	6.0	
0.075	2.7	3.6	4.5	5.4	6.3	7.2	8.1	9.0	
0.1	3.6	4.8	6.0	7.2	8.4	9.6	10.8	12.0	
0.15	5.4	7.2	9.0	10.8	12.6	14.4	16.2	18.0	
0.2	7.2	9.6	12.0	14.4	16.8	19.2	21.6	24.0	
0.25	9.0	12.0	15.0	18.0	21.0	24.0	27.0	30.0	
0.5	18.0	24.0	30.0	36.0	42.0	48.0	54.0	60.0	
0.75	27.0	36.0	45.0	54.0	63.0	72.0	81.0	90.0	
1.0	36.0	48.0	60.0	72.0	84.0	96.0	108.0	120.0	
1.25	45.0	60.0	75.0	90.0	105.0	120.0	135.0	150.0	
1.5	54.0	72.0	90.0	108.0	126.0	144.0	162.0	180.0	
1.75	63.0	84.0	105.0	126.0	147.0	168.0	189.0	210.0	
2.0	72.0	96.0	120.0	144.0	168.0	192.0	216.0	240.0	

Table 5: Remifentanyl Injection Infusion Rates (ml/h) for a 250 µg/ml Solution

Infusion Rate (µg/kg/min)	Patient Weight (kg)							
	30	40	50	60	70	80	90	100
0.1	0.72	0.96	1.20	1.44	1.68	1.92	2.16	2.40
0.15	1.08	1.44	1.80	2.16	2.52	2.88	3.24	3.60
0.2	1.44	1.92	2.40	2.88	3.36	3.84	4.32	4.80
0.25	1.80	2.40	3.00	3.60	4.20	4.80	5.40	6.00
0.5	3.60	4.80	6.00	7.20	8.40	9.60	10.80	12.00
0.75	5.40	7.20	9.00	10.80	12.60	14.40	16.20	18.00
1.0	7.20	9.60	12.00	14.40	16.80	19.20	21.60	24.00
1.25	9.00	12.00	15.00	18.00	21.00	24.00	27.00	30.00
1.5	10.80	14.4	18.00	21.60	25.20	28.80	32.40	36.00
1.75	12.60	16.80	21.00	25.20	29.40	33.60	37.80	42.00
2.0	14.40	19.20	24.00	28.80	33.60	38.40	43.20	48.00

The following table provides the equivalent blood remifentanyl concentration using a TCI approach for various manually-controlled infusion rates at steady state:

Table 6: Remifentanyl Blood Concentrations (nanograms/ml) estimated using the Minto (1997) Pharmacokinetic Model in a 70 kg, 170 cm, 40 Year Old Male Patient for Various Manually-Controlled Infusion rates (micrograms/kg/min) at Steady State.

Remifentanyl Infusion Rate (micrograms/kg/min)	Remifentanyl Blood Concentration (nanograms/ml)
0.05	1.3
0.10	2.6
0.25	6.3
0.40	10.4
0.50	12.6
1.0	25.2
2.0	50.5

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Tell your doctor immediately if you notice some of the following symptoms:

Very common: may affect more than 1 in 10 people

- Muscle stiffness
- Nausea
- Vomiting
- Decreased blood pressure

Common: may affect up to 1 in 10 people

- Slow heart rate
- Problems breathing
- Itching

Uncommon: may affect up to 1 in 100 people

- Constipation
- Problems breathing (hypoxia)

Rare: may affect up to 1 in 1,000 people

- Allergic reaction, including anaphylaxis (allergic general reaction)
- Heart function disorders (cardiac arrest)

Not known: frequency cannot be estimated from the available data

- Drug dependence (physical need for Remifentanil)
- Convulsions (fits)
- Atrioventricular block (heart block)
- Drug tolerance (the need for increasing doses over time to get the same effect (drug tolerance)

Other side effects that can happen when you wake up after having an anaesthetic include:

Common: may affect up to 1 in 10 people

- shivering
- increases in blood pressure

Uncommon: may affect up to 1 in 100 people

- aches

Rare: may affect up to 1 in 1,000 people

- feeling very calm or drowsy (sedation)

Other side effects which occurred particularly upon abrupt cessation of Remifentanil after prolonged administration of more than 3 days

- heart beating faster (*tachycardia*)
- high blood pressure (*hypertension*)
- restlessness (*agitation*)

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 Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. HOW TO STORE REMIFENTANIL

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial and on the carton. The expiry date refers to the last day of the month.

Do not store above 25°C.

Shelf life after reconstitution:

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.

Shelf life after dilution:

All mixtures with infusion fluids should be used immediately.

After reconstitution the solution must not be used, if it is not clear, colourless and free of visible particles.

Do not throw away any medicines via wastewater. 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 Remifentanil contains

The active substance is Remifentanil. Each vial contains 1 mg, 2 mg or 5 mg of Remifentanil (as hydrochloride).

After reconstitution the solution contains 1 mg/ml if prepared as recommended.

The other ingredients are: glycine and hydrochloric acid 37% (for pH-adjustment).

What Remifentanil looks like and contents of the pack

Remifentanil is a white to off-white powder for concentration for solution for injection or infusion.

Each carton of Remifentanil 1 mg contains 5 vials of 3 ml.

Each carton of Remifentanil 2 mg contains 5 vials of 3 ml.

Each carton of Remifentanil 5 mg contains 5 vials of 6 ml.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Wockhardt UK Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

Manufacturer: Laboratorio Reig Jofre, S.A., Gran Capitán, 10, 08970 Sant Joan Despí, Barcelona, Spain.

Other formats:

To listen or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000

Please be ready to give the following information:

Product Name	Reference Number
Remifentanil 1 mg powder for concentrate for solution for injection or infusion	PL29831/0482
Remifentanil 2 mg powder for concentrate for solution for injection or infusion	PL29831/0483
Remifentanil 5 mg powder for concentrate for solution for injection or infusion	PL29831/0484

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