Package Leaflet: Information for the patient

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 hydrochloride

The name of your medicine are “Remifentanil 1 mg powder for concentrate for solution for injection/infusion”, “Remifentanil 2 mg powder for concentrate for solution for injection/infusion” and “Remifentanil 5 mg powder for concentrate for solution for injection/infusion” but in the rest of the leaflet it will be called “Remifentanil”.

Read all of this leaflet carefully before you are given 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 Remifentanil is and what it is used for

Remifentanil powder for concentrate for solution for injection/infusion contains a medicine called remifentanil. This belongs to a group of medicines known as opioids.

Remifentanil is used together with other medicines called anaesthetics
- to help put you to sleep **before** an operation
- to keep you asleep and stop you feeling pain **during** an operation
- to make you feel sleepy and stop you feeling pain while you receive treatment in an Intensive Care Unit.

2 What you need to know before you are given Remifentanil

Do not have remifentanil if:
- you are allergic (hypersensitive) to remifentanil or any of the other ingredients of Remifentanil (listed in section 6)
- you are allergic (hypersensitive) to any other pain-relieving medicines which are similar to fentanyl and which are related to the class of medicines known as opioids.

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

Tell your doctor before using remifentanil if:

- You or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs (“addiction”).
- You are a smoker.
- You have ever had problems with your mood (depression, anxiety or a personality
disorder) or have been treated by a psychiatrist for other mental illnesses.

This medicine contains remifentanil which is an opioid medicine. Repeated use of opioid painkillers may result in the drug being less effective (you become accustomed to it). It may also lead to dependence and abuse which may result in life-threatening overdose. If you have concern that you may become dependent on this medicine, it is important that you consult your doctor.

Withdrawal reactions including rapid heartbeat, high blood pressure and restlessness have occasionally been reported when treatment with this medicine is stopped suddenly, particularly when treatment has lasted more than 3 days (see also section 4. Possible side effects). If you experience these symptoms, your doctor may re-introduce the medicine and gradually reduce the dose.

Warnings and precautions
Check with your doctor or pharmacist before you are given remifentanil if:
- you are allergic (hypersensitive) to any other opioid medicines, such as morphine or codeine
- you are over 65 years of age
- you are dehydrated or have lost a lot of blood
- you have been 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 remifentanil.

Other medicines and Remifentanil
Please tell your doctor or pharmacist if you are taking or have recently taken or might take other medicines, including medicines obtained without a prescription. This includes herbal medicines. This is because remifentanil 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, propanolol and bisoprolol) or calcium channel blockers (these include amlodipine, diltiazem and nifedipine).
- medicines for the treatment of depression such as Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) and Monoamine Oxidase Inhibitors (MAOIs). It is not recommended to use these medicines at the same time as this medicine as they may increase the risk of serotonin syndrome, a potentially life-threatening condition.

Concomitant use of remifentanil 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. The concomitant use of opioids and drugs used to treat epilepsy, nerve pain or anxiety (gabapentin and pregabalin) increases the risk of opioid overdose, respiratory depression and may be life-threatening.

However if your doctor does prescribe remifentanil 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.

This medicine with alcohol
After receiving this medicine, you should not drink alcohol until you have 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 for advice before you are given this medicine.

If you are given this medicine during labour or close to childbirth, it can affect your baby's breathing. You and your baby will be monitored for signs of excessive sleepiness and difficulty breathing.

Driving and using machines
If you are only staying in hospital for the day, your doctor will tell you how long to wait before leaving the hospital or driving a car. It can be dangerous to drive too soon after having an operation.

The medicine can affect your ability to drive as it may make you sleepy or dizzy.
- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
    - The medicine has been prescribed to treat a medical or dental problem and
    - You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
    - It was not affecting your ability to drive safely

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

This medicine contains Sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium free'.

3 How to use Remifentanil

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

Remifentanil 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 remifentanil 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.

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine.

Some people can be allergic to remifentanil. **You must tell your doctor or nurse immediately if you have**:
Rare (may affect up to 1 in 1,000 people)
- sudden wheeziness 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.

Severe allergic reactions can progress to life-threatening anaphylactic shock; Frequency not known (cannot be estimated from the available data) which include worsening of allergic signs, severe drop in blood pressure, heart beats quickly and/or fainting.

Tell your doctor **as soon as possible** if you notice any of the following:
Very common (may affect more than 1 in 10 people)
- muscle stiffness
- low blood pressure
- feeling sick or being sick

Common (may affect up to 1 in 10 people)
- slow heartbeat
- shallow breathing or temporarily stop breathing
- itching
- Cough

Uncommon (may affect up to 1 in 100 people)
- problems breathing (hypoxia)
- constipation

Rare (may affect up to 1 in 1,000 people)
- allergic reactions
- heart stops beating

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

- physical need for remifentanil *(drug dependency)* or the need for increasing doses over time to get the same effect *(drug tolerance)*
- fits (seizures)
- a type of irregular heartbeat *(atrioventricular block)*
- Irregular heartbeat (arrhythmia)
- Withdrawal syndrome (may manifest by the occurrence of the following side effects: increased heart rate, high blood pressure, feeling restless or agitated, nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating)

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)

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. 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 Remifentanil after the expiry date which is stated on the vial and carton after "EXP". The expiry date refers to the last day of that month.
- Do not store above 25°C.
- When Remifentanil is made up it should be used straight away. Any unused solution should not be disposed of via wastewater or household waste. Your doctor or nurse will throw away any medicine that is no longer required. This will help protect the environment.
- Store in the original package with this leaflet.

6 Contents of the pack and other information

What Remifentanil contains
The active substance is remifentanil hydrochloride.
The other ingredients are glycine, hydrochloric acid (for pH adjustment), and sodium hydroxide (for pH adjustment if needed).

What Remifentanil looks like and contents of the pack
Remifentanil for injection is a sterile, non-pyrogenic, preservative-free, white to off-white, lyophilised powder and is available in the following strengths:
- 1 mg Remifentanil for injection, in 3 ml glass vials
- 2 mg Remifentanil for injection, in 5 ml glass vials
- 5 mg Remifentanil for injection, in 10 ml glass vials

The powder will be mixed with an appropriate fluid before being injected. When mixed to form a solution, Remifentanil is clear and colourless.
Each strength of Remifentanil is supplied in cartons containing 5 vials.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Aspen Pharma Trading Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland
Tel: + 44 1748 828 391
Manufacturer:
GlaxoSmithKline Manufacturing S.p.A., San Polo di Torrile, Parma, Italy
or
Aspen Pharma Ireland Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland
or
Avara Liscate Pharmaceutical Services S.p.A., Via Fosse Ardeatine, 2, 20050 Liscate (MI), Italy

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

0800 198 5000 (UK Only)

Please be ready to give the following information:

Product name	**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
Reference number	PL 39699/0095
	PL 39699/0096
	PL 39699/0097

This is a service provided by the Royal National Institute of Blind People.

This leaflet was last revised in November 2023.

Package Leaflet: Information for the Medical Profession

Remifentanil powder for concentrate for solution for injection/infusion
remifentanil hydrochloride

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 Remifentanil prior to administration and the guidelines for infusion rates of Remifentanil for manually-controlled infusion.

PREPARATION GUIDE for
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 is a sterile, non-pyrogenic, preservative-free, white to off white, lyophilised powder, to be reconstituted before use. Remifentanil injection is available in glass vials containing 1 mg, 2 mg or 5 mg of remifentanil base. The vials should be stored at or below 25°C.

When reconstituted as directed, solutions of remifentanil are clear and colourless and contain 1 mg/ml of remifentanil base as remifentanil hydrochloride. Remifentanil 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 Remifentanil. This information can also be found under sections 6.4 and 6.6 of the Summary of Product Characteristics.

Reconstitution of the lyophilised powder
Remifentanil should be prepared for intravenous use by adding, as appropriate 1, 2, or 5 ml of diluent (see list of diluents under "Further Dilution") to give a reconstituted solution with a concentration of 1 mg/ml remifentanil. The reconstituted solution is clear, colourless, and practically free from particulate material. After reconstitution, visually inspect the product for particulate material, discolouration or damage of container. Discard any solution where such defects are observed. Reconstituted product is for single use only. Any unused material should be discarded.

Further Dilution
After reconstitution, Remifentanil 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 for paediatric patients aged 1 year and over when used in maintenance of anaesthesia). Use of Remifentanil in paediatric patients aged under 18 is not recommended for provision of analgesia in mechanically ventilated intensive care patients.

After reconstitution, Remifentanil 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 IV fluids listed below should be used for dilution:

Water for Injections
Glucose 5% solution for injection
Glucose 5% and Sodium Chloride 0.9% solution for injection
Sodium Chloride 0.9% solution for injection
Sodium Chloride 0.45% solution for injection

After dilution, visually inspect the product to ensure it is clear, colourless, practically free from particulate matter and the container is undamaged. Discard any solution where such defects are observed.

The reconstituted and further diluted solution of Remifentanil is chemically and physically stable for 24 hours at room temperature (25°C). However, Remifentanil does not contain an antimicrobial preservative and thus care must be taken to assure the sterility of prepared solutions, reconstituted product should be used promptly, and any unused material discarded.

Remifentanil 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 5% solution for injection

Remifentanil 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 Remifentanil for manually-controlled infusion:

Table 1. Remifentanil injection Infusion Rates (ml/kg/h)

Drug Delivery Rate (micrograms/kg/min)	Infusion Delivery Rate (ml/kg/h) for Solution Concentrations of			
	20 micrograms/ml 1 mg/50 ml	25 micrograms/ml 1 mg/40 ml	50 micrograms/ml 1 mg/20 ml	250 micrograms/ml 10 mg/40 ml
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. Remifentanil injection Infusion Rates (ml/h) for a 20 micrograms/ml Solution

Infusion Rate (micrograms/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. Remifentanil injection Infusion Rates (ml/h) for a 25 micrograms/ml Solution

Infusion Rate (micrograms/kg/min)	Patient Weight (kg)									
	10	20	30	40	50	60	70	80	90	100

0.0125	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. Remifentanil injection Infusion Rates (ml/h) for a 50 micrograms/ml Solution

Infusion Rate (micrograms/kg/min)	**Patient Weight (kg)**							
	30	**40**	**50**	**60**	**70**	**80**	**90**	**100**
0.025	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. Remifentanil injection Infusion Rates (ml/h) for a 250 micrograms/ml Solution

Infusion Rate (micrograms/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	14.40	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

This leaflet was last revised in November 2023.