

PACKAGE LEAFLET: INFORMATION FOR THE USER

Remifentanil Noridem 1 mg powder for concentrate for solution for injection or infusion
Remifentanil Noridem 2 mg powder for concentrate for solution for injection or infusion
Remifentanil Noridem 5 mg powder for concentrate for solution for injection or infusion

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.

The name of your medicine is Remifentanil Noridem 1 mg, 2 mg, 5 mg Powder for Concentrate for Solution for Injection or Infusion

In the rest of this leaflet Remifentanil Noridem 1 mg, 2 mg, 5 mg powder for concentrate for solution for injection or infusion is called Remifentanil.

What is in this leaflet:

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

1. What Remifentanil is and what it is used for

Remifentanil 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.

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, propranolol and bisoprolol) or calcium channel blockers (these include amlodipine, diltiazem and nifedipine).

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

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:
 - o The medicine has been prescribed to treat a medical or dental problem and
 - o You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
 - o 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.

3. How Remifentanil is given

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.

The following information is intended for medical or healthcare professionals only:

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 Noridem 1 mg powder for concentrate for solution for injection or infusion

Remifentanil Noridem 2 mg powder for concentrate for solution for injection or infusion

Remifentanil Noridem 5 mg powder for concentrate for solution for injection or infusion

Remifentanil is a sterile, endotoxin-free, preservative-free, white to off white, lyophilised powder, to be reconstituted before use. Remifentanil is available in glass vials containing 1 mg, 2 mg or 5 mg of remifentanil base. The vials should not be stored above 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 (where the container permits) 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.

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/dilution has taken place in controlled and validated aseptic conditions.

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 Noridem Powder for Concentrate for Solution for Injection or Infusion

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

4. Possible side effects

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

Some people can be allergic to Remifentanyl. **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
- a collapse

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

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 remifentanyl (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)

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 remifentanyl 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

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

For IE: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971;

Fax: +353 1 6762517, Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

5. How to store Remifentanyl

Keep this medicine out of the sight and reach of children. Do not use Remifentanyl 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 use the reconstituted product unless it is clear, colourless and practically free from particulate material. Do not store above 25°C. Keep the vial in the outer carton in order to protect from light. When Remifentanyl 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.

6. Contents of the pack and other information

What Remifentanyl contains

- The active substance is remifentanyl hydrochloride.
- The other ingredients are glycine and hydrochloric acid. (*for pH adjustment*).

What Remifentanyl looks like and contents of the pack

Remifentanyl is a sterile, bacteria-free, freeze-dried white to off-white powder. The powder will be mixed with an appropriate fluid before being injected. When mixed to form a solution, Remifentanyl is clear and colourless. Remifentanyl Noridem Powder for Concentrate for Solution for Injection or Infusion is available in glass vials with bromobutyl rubber stoppers, each containing 1 mg, 2 mg or 5 mg of remifentanyl (as remifentanyl hydrochloride). Each strength of Remifentanyl is supplied in cartons containing 5 and 10 vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Noridem Enterprises Ltd., Evagorou & Makariou, Mitsi Building 3, Office 115, 1065 Nicosia, Cyprus.

Manufacturer: DEMO S.A., 21st km National Road Athens-Lamia, 14568 Krioneri, Attiki, Greece.

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

United Kingdom:	Remifentanyl Noridem 1 mg, 2 mg & 5 mg powder for concentrate for solution for injection or infusion
Ireland:	Remifentanyl Noridem 1 mg, 2 mg & 5 mg powder for concentrate for solution for injection or infusion
Austria:	Remifentanyl Noridem 1 mg, 2 mg & 5 mg Pulver für ein Konzentrat zur Herstellung einer Injektions- oder Infusionslösung
Greece:	Remifentanyl/Noridem Κόνις για πυκνό σκεύασμα για Παρασκευή Διαλύματος προς Ένεση ή Έγχυση, 1 mg/vial, 2 mg/vial & 5 mg/vial
Spain:	Remifentnilo Noridem 1 mg, 2 mg & 5 mg polvo para concentrado para solución inyectable y para perfusión EFG

This leaflet was last revised in 11/2017.

If this leaflet is difficult to see or read please contact the following address for help: Athlone Laboratories, Ballymurray, Co. Roscommon, Ireland, Tel +353-9066-61109, Email medical@athlone-laboratories.com.

Table 2. Remifentanyl Noridem powder for concentrate for solution for injection or infusion 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. Remifentanyl Noridem powder for concentrate for solution for injection or infusion 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. Remifentanyl Noridem powder for concentrate for solution for injection or infusion 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. Remifentanyl Noridem Powder for concentrate for solution for injection or infusion 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	

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