REMIFENTANIL MEDIS 1 mg – REMIFENTANIL MEDIS 5 mg

Powder for solution for injection or infusion
Remifentanil Hydrochloride

Read all of this leaflet carefully before you start using this medicine.
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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT REMIFENTANIL MEDIS 1 MG– 5 MG IS AND WHAT IT IS USED FOR

Remifentanil is an anesthetic used for induction and or maintenance of general anesthesia under close supervision
Remifentanil is indicated to relieve pain and sedation in patient under controlled mechanical ventilation in an Intensive Care Unit for patients 18 years of age and over.

2. WHAT YOU SHOULD KNOW BEFORE YOU HAVE REMIFENTANIL MEDIS 1 mg – 5 mg

You should not be given REMIFENTANIL-MÉDIS 1 mg - 5 mg in the following cases:
- If you are allergic to the active substance, or Fentanyl derivates or any of the other ingredients.
- Administration epidurally or intrathecally, because it contains glycine.
- Use as a single treatment during induction of anesthesia
- Use during the work period before delivery
- Use during caesarean section.
- This medicine SHOULD NOT BE USED GENERALLY, unless otherwise directed by your doctor during pregnancy.

Take special care with REMIFENTANIL MEDIS 1 mg – 5 mg:
This drug will be administered only by specially trained persons to the use of anesthetics and drugs in facilities entirely equipped for the monitoring and support of respiratory and cardiovascular functions.
A perfusion technique will be used specifically to prevent inadvertent administration, particularly at the end of anesthesia.
In ventilated patients, the use of this drug is not recommended for periods longer than 3 days.
As with all powerful opioids, the administration of this product is accompanied by respiratory depression.
The occurrence of respiratory depression requires a proper management, including a 50% reduction in the infusion rate or temporary interruption of the infusion.
Your doctor will ensure that you have fully regained consciousness and recovered a satisfactory respiration before letting you leave the recovery room.
At recommended doses, muscle rigidity may occur. As with other opioids, the incidence of muscle rigidity depends on the dose and rate of administration. This is why intravenous slow in bolus form should not be performed in less than 30 seconds. Modalities of care depend on the intensity of muscle stiffness, your general condition and phase of anesthesia during which the rigidity appears.
Similarly, in case of a decrease in blood pressure or heart rate, a specific treatment will be performed.
The duration of action of Remifentanil is very short; the residual analgesic activity does not persist more than 5 to 10 minutes after stopping the administration. During surgery known painful awakening or during use in Intensive Care Unit, analgesics should be administered prior to discontinuation of the infusion of Remifentanil. Sufficient time must be respected for the long-term analgesic actions are effective. These analgesics should be chosen depending on the type of surgery and the level of postoperative monitoring.

Like other opioids, this drug can induce dependence.
During a sudden stop of the administration of Remifentanil and particularly after prolonged administration of more than 3 days, symptoms such as tachycardia (rapid heartbeat), hypertension (increased blood pressure) or agitation may occur infrequently.

Precautions
Before you receive Remifentanil tell your doctor if you:
- A history of adverse and / or unexpected during anesthesia;
- Are allergic to any drugs that have been used in a previous transaction;
- Respiratory problems (shortness of breath ...)
- Heart problems: slow or irregular heartbeat, low blood pressure;
- Severe hepatic impairment;
- Pregnant or breastfeeding.

Using other medicines
Please tell your doctor or pharmacist if you are taking, or have recently taken, any other medicines, including medicines you can get without a prescription.

Pregnancy and breast-feeding
Tell your anesthetist if you are pregnant or breastfeeding.
Remifentanil should not be given to pregnant or breastfeeding women.
It is recommended that you stop breast-feeding for 24 hours after Remifentanil has been given to you.
Ask your doctor or pharmacist for advice before taking any medicine.

Sports
The attention of athletes is drawn to the fact that this drug contains an active ingredient that can cause a positive reaction to tests performed during doping controls.

Driving and using machines
After anesthesia with this drug, you should not drive or operate machinery until your doctor has decided the time of resumption of these activities. It is prudent that you are accompanied when you return home and don't consuming any alcoholic beverage

3. HOW TO USE REMIFENTANIL MEDIS 1 mg – 5 mg?

Remifentanil MEDIS must only be given under carefully controlled conditions and emergency equipment has to be available. Remifentanil MédiS will be given by or under the supervision of an experienced doctor who is familiar with the use and action of the type of medicine.
It will always be given to you by a person who is qualified to do so, as well as in the diagnosis and management of expected adverse effects of opioids powerful, including respiratory and cardiac resuscitation.

Dosage
The dosage should be adjusted according to your operation and effects obtained during anesthesia.
As a guide, the recommended dosages are:
ADULTS
*** Administration by infusion in manual mode:**

Indication	IV Injection (bolus) (micrograms/kg)	Continuous infusion (micrograms / kg / min)	
		Starting Rate	Range
Induction of anesthesia	1 (injected over 30 seconds)	0,5 to 1	-
Maintenance of anesthesia in ventilated patients :			
- Nitrous Oxide (66 %)	0,5 to 1	0,40	0,10 to 2
- Isoflurane (Starting dose: 0,5 MAC)	0,5 to 1	0,25	0,05 to 2
- Propofol (satrting dose: 100 micrograms/kg/min)	0,5 to 1	0,25	0,05 to 2

Depending on your response to treatment, your doctor may adjust the dosage anesthetist during maintenance of anesthesia, every 2 to 5 minutes.

*** Administration mode «TCI» (Intra Venous Anaesthesia at Target Concentration):**
- Induction and maintenance of anesthesia in ventilated patients:
Remifentanil MEDIS 1 mg - 5 mg should be used in combination with a hypnotic agent inhaled or intravenous ventilated adult patients. In association with these agents, adequate analgesia for induction of anesthesia and surgery can usually be obtained with Remifentanil target plasma concentrations from March to August nanograms / ml.
The dose of Remifentanil MEDIS 1 mg - 5 mg should be adapted (titration) depending on your response. Some particularly painful surgical procedures may require target blood concentrations up to 15 nanograms / ml.
There are insufficient data to make recommendations on the use of Remifentanil MEDIS 1 mg - 5 mg mode «TCI» for anesthesia in spontaneously breathing patients.
- Recommendations for continuing / stopping during the immediate post-operative:
Mode «TCI» at the end of surgery, when the Remifentanil infusion MEDIS 1 mg - 5 mg is stopped or when the target concentration is reduced, you must restore spontaneous respiration at concentrations of Remifentanil calculated from 12 in nanograms / ml. As in the case of manual infusion, the postoperative analgesia should be started before the end of surgery with analgesics long duration of action.
There are insufficient data to make recommendations on the use of Remifentanil MEDIS 1 mg - 5 mg mode «TCI» for the control of postoperative analgesia.

CHILDREN (AGES 1 TO 12 YEARS)

Anesthetic agents associated (*)	IV Injection (bolus) (micrograms/kg)	CONTINUOUS INFUSION (microgram per per minute)	
		satrting rate	Range
Halothane (starting dose 0,3 MAC)	1	0,25	0,05 to 1,3
Sevoflurane (starting dose 0,3 MAC)	1	0,25	0,05 to 0,9
Isoflurane (starting dose : 0,5 MAC)	1	0,25	0,06 to 0,9

(*)with concomitant administration of a mixture of nitrous oxide / oxygen in a ratio of 2/1.
- In neonates and infants less than 1 year, the available data are insufficient to recommend a posology.
- In the absence of data, the administration mode «TCI» is not recommended in children and neonates.

GENERAL ANAESTHESIA FOR CARDIAC SURGERY ANESTHESIE
*** Administration by perfusion in manuel mode:**

Associated Indication (*)	INJECTION IV (bolus) (microgram/kg)	CONTINUOUS PERFUSION (microgram/kg/min)	
		satrting rate	Range
Intubation	not recommended	1	-
Maintenance of anesthesia: - Isoflurane (starting dose: 0.4 MAC) - Propofol (starting dose: 50 microgram / kg / min)	0,5 to 1 0,5 to 1	1 1	0,003 to 4 0,01 to 4,3
continuation of postoperative analgesia prior to extubation	not recommended	1	0 to 1

*** Administration in mode «TCI»**
- Induction and maintenance of anesthesia in ventilated patients:
REMIFENTANIL MEDIS 1 mg - 5 mg should be used in combination with a hypnotic agent inhaled or intravenous ventilated adult patients. In association with these agents, adequate analgesia for induction of anesthesia and surgery can usually be obtained with Remifentanil target plasma concentrations higher than those used in acts of general surgery.
- The dose of REMIFENTANIL MEDIS 1 mg - 5 mg should be adapted (titration) depending on your response. Blood concentrations up to 20 nanograms / ml were used in the clinical studies with titration according to individual patient response.
There are insufficient data to make recommendations on the use of REMIFENTANIL MEDIS 1 mg - 5 mg mode «TCI» for anesthesia in spontaneously breathing patients.
***Recommendations for continuing / stopping during the immediate post-operative:**
Mode «TCI» at the end of surgery, when REMIFENTANIL MEDIS 1 mg – 5 mg is stopped or when the target concentration is reduced, you must restore spontaneous respiration at concentrations of remifentanil calculated from 1 2 in nanograms / ml. As in the case of manual infusion, the postoperative analgesia should be started before the end of surgery with analgesics long duration of action.
There are insufficient data to make recommendations on the use of Remifentanil MEDIS 1 mg - 5 mg mode «TCI» for the control of postoperative analgesia.

USE IN INTENSIVE CARE UNITS

Continuous infusion (microgram / kg / h)	
starting rate	Range
0,1 (6) to 0,15 (9)	0,006 (0,38) to 0,74 (44,6)

The administration of REMIFENTANIL MEDIS 1 mg – 5 mg bolus is not recommended for patients in Intensive Care Unit. In the absence of data, the administration mode «TCI» is not recommended in patients in Intensive Care Unit.
When REMIFENTANIL MEDIS 1 mg – 5 mg is administered with other sedative agents, the use of REMIFENTANIL MEDIS 1 mg – 5 mg reduce doses of these agents.
The usual initial dose of sedative agents is given below:

sedative agents	Bolus (mg/kg)	infusion (mg/kg/h)
Propofol	To 0,5	0,5
Midazolam	To 0,03	0,03

Sedative agents are to be administered separately so that their assay is possible.
For ventilated patients undergoing painful stimuli, increased infusion rate of REMIFENTANIL MEDIS 1 mg – 5 mg may be necessary to provide additional analgesic cover.
Patients in Intensive Care Unit, the safety and efficacy of Remifentanil have been established in clinical trials for treatment durations of up to 3 days.
- If you are over 65, the recommended starting dosage in adults should be reduced by half, and adapted to your needs. Mode «TCI» initial target concentration should be 1.5 to 4 nanograms / ml, and tailored to your needs.
- For patients ASA class III / IV, it is recommended to reduce the dose and subsequently adapt the flow until the desired effect.
- In case of obesity, the dosage should be reduced based on the theoretical ideal weight. Mode «TCI» to avoid under-dosing, the dosage should be carefully tailored to the individual response.
- For patients with renal impairment, it is not necessary to adjust the dosage.
- The severe hepatic impairment requires special monitoring.

Method of administration:
This medication will be administered intravenously either by slow bolus (administered over at least 30 seconds) or by infusion.
Continuous infusions of Remifentanil should be administered using an infusion system at a controlled rate and through a pipe fast flow (fine caliber tubing) or tubing reserved for this drug. These pipes must be connected directly or adjacent to the venous catheter to minimize the dead space potential.
Remifentanil can be administered by intravenous anesthesia with target concentration («TCI») using approved equipment including Minto pharmacokinetic model taking into account your age and your body weight.
Care must be taken to avoid these tubes are blocked or disconnected.
A sufficient amount of Remifentanil may be present in the dead space of the tubing or catheter to cause respiratory depression, apnea, and / or muscle rigidity if the tubing is rinsed with a solution or with other injectable drugs.
This can be prevented by administering the drug in a pipe with a rapid rate through a pipe or reserved for this drug to be disconnected to stop its administration.

Incompatibilities
This drug must be reconstituted or diluted only with the recommended injectable solutions.
It should not be reconstituted or mixed with lactated Ringer's injection or lactated Ringer's and glucose 50 mg/ml (5%) solution for injection
This medication should not be mixed with propofol or placed in the same intravenous admixture solution
Administration of Remifentanil into the same intravenous line with blood/serum/plasma is not recommended.
Remifentanil should not be mixed with other therapeutic agents prior to administration

Instructions, instructions for handling:
REMIFENTANIL MEDIS 1 mg – 5 mg must be reconstituted by adding respectively 1 ml or 5 ml solution for injection to obtain a reconstituted solution with a concentration of remifentanil of approximately 1 mg / ml.
After reconstitution, remifentanil should not be administered without further dilution.For infusions made in manual mode, remifentanil can be diluted to concentrations ranging from 20 to 250 micrograms / ml (the recommended dilution is 50 micrograms / ml in adults and 20 to 25 micrograms / ml in children 1 year or more).
For infusion in «TCI», the recommended dilution of remifentanil is from 20 to 50 micrograms / ml.

Reconstitution and dilution of the solution of remifentanil can be performed with one of the following solutions:
• water for injections;
• solution of 5% glucose;
• solution of glucose (5%) sodium (0.9%);
• solution of sodium chloride 0.9%;
• solution of sodium chloride at 0.45%.
Dilution will depend on the technical characteristics of the equipment and infusion needs for the patient.
This drug is compatible with lactated Ringer's injections and lactated Ringer's and glucose 50 mg/ml (5%) solution for injection.
Remifentanil is compatible with propofol when administered into a running IV catheter.

Frequency of administration:
The administration of REMIFENTANIL MEDIS 1 mg – 5 mg will be adjusted according to your operation and effects obtained during anesthesia.

If you use more REMIFENTANIL MEDIS 1 mg – 5 mg, than you should:
Due to the very short duration of action of remifentanil, the potential for deleterious effects due to overdose is limited to the immediate time period following medicinal product administration. Response to discontinuation of the medicinal product is rapid, with return to baseline within ten minutes.
In the event of overdose, or suspected overdose, take the following actions: discontinue administration of Remifentanil, maintain a patent airway, initiate assisted or controlled ventilation with oxygen, and maintain adequate cardiovascular function. If depressed respiration is associated with muscle rigidity, a neuromuscular blocking agent may be required to facilitate assisted or controlled respiration. Intravenous fluids and vasopressor agents for the treatment of hypotension and other supportive measures may be employed.
Intravenous administration of an opioid antagonist such as naloxone may be given as a specific antidote in addition to ventilatory support to manage severe respiratory depression. The duration of respiratory depression following overdose with Remifentanil is unlikely to exceed the duration of action of the opioid antagonist.
If you stop using remifentanil MEDIS 1 mg - 5 mg:
As with other opioids, this drug may produce dependency.

4. POSSIBLE SIDE EFFECTS

Like all drugs, REMIFENTANIL MEDIS 1 mg – 5 mg can cause side effects, although not everybody gets them.
Very common :
- Muscle stiffness;
- low blood pressure;
- Nausea, vomiting.,Common :
- High blood pressure after the operation;
- A slow heartbeat;
- shivering after the operation
- Respiratory problems;
- Itching.uncommon
- pain after the operation;
- Constipation;
- A feeling of fatigue, drowsiness;
- oxygen deficiency;
- A asystole / cardiac arrest (in combination with other anesthetics).

Very rarely :
severe allergic reactions in patients receiving Remifentanil with one or more anaesthetic medicine
Seizures, heart rhythm disorders, dependence and addiction were also observed following the use of Remifentanil.
If you notice any side effects not listed in this leaflet, or if any of the side effects become serious, please tell your doctor or pharmacist.

5. HOW TO STORE REMIFENTANIL MEDIS 1 mg – REMIFENTANIL MEDIS 5 mg ?

Keep out of the sight and reach of children.
REMIFENTANIL MEDIS 1 mg – 5 mg should not be used after the expiry date which is stated on the carton and label.

Before reconstitution:
Store at a temperature not exceeding 25 ° C
After reconstitution:
The 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.
After dilution:
Any mixture of the reconstituted solution , REMIFENTANIL MEDIS 1 mg – 5 mg with injectable liquids should be used immediately. Any remaining solution should 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. FURTHER INFORMATION

a. What REMIFENTANIL MEDIS 1 mg – 5 mg contains:

Active substance :	REMIFENTANIL MEDIS 1 mg	REMIFENTANIL MEDIS 5 mg
Remifentanil (hydrochloride form)	1 mg	5 mg
Excipients :		
Glycine, sodium hydroxide, hydrochloric acid	..... q.s.	

b. What REMIFENTANIL MEDIS 1 mg – 5 mg looks like and contents of the pack
REMIFENTANIL MEDIS 1 mg is a narcotic ; prescription limited to 7 days
REMIFENTANIL MEDIS 1 mg : vial of a Powder for solution for injection or infusion. Box of 05 vials.
REMIFENTANIL MEDIS 5 mg is a narcotic : prescription limited to 7 days
REMIFENTANIL MEDIS 5 mg vial of a Powder for solution for injection or infusion. Box of 05 vials.
c. MARKETING AUTHORISATION HOLDER AND MANUFACTURER
Marketing authorisation holder: Les Laboratoires MEDIS – route de Tunis Km 7 – BP206 – 8000 Nabeul.
Manufacturer: Les Laboratoires MEDIS – route de Tunis Km 7 – BP206 – 8000 Nabeul.
d. THE LAST DATE THIS LEAFLET WAS APPROVED (MONTH / YEAR):
«August 2012» «version 00».

This is a drug
- A drug is a product but it is different from the other products.
- A drug is a product which acts on your health and its non appropriate consumption can expose you to danger.
- Rigorously respect your doctor's prescription and the mode of administration he prescribed. Follow your pharmacist's advices.
- Your doctor and your pharmacist know drugs, their indications and contra-indications.
- Do not stop on your own initiative the treatment during the prescribed period
- Do not retake, do not increase doses without consulting your doctor.

KEEP ANY DRUG OUT OF THE REACH OF CHILDREN.

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