Remifentanil

REPAXIR®

REPAXIR® lyophilized powder vial contains Remifentanil hydrochloride in 3 doses: 1, 2 and 5 mg produced by Exir pharmaceutical company

Category:[1] Analgesic, Opioid; Anilidopiperidine Opioid

Indications:[1]

Anesthesia: Analgesic for use during the induction and maintenance of general anesthesia; continued analgesia into the immediate postoperative period in adults; analgesic component of monitored anesthesia in adults

Contraindication:[1]

Hypersensitivity (eg, anaphylaxis) to remifentanil or any component of the formulation; intrathecal or epidural administration.

Pregnancy and lactation:[1]

Remifentanil crosses the placenta; fetal and maternal concentrations may be similar.

Prolonged use of opioids during pregnancy can cause neonatal withdrawal syndrome, which may be life-threatening if not recognized and treated according to protocols developed by neonatology expertsBreast-Feeding Considerations

It is not known if remifentanil is present in breast milk.

The decision to continue or discontinue breastfeeding during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother; monitor infants for excess sedation and respiratory depression. Remifentanil has a limited duration of action; use may be appropriate for breastfeeding women undergoing short procedures

Warnings and Precautions:[1]

For hospital use only

Hypotension: May cause hypotension; use with caution in patients with hypovolemia, cardiovascular disease (including acute MI), or drugs which may exaggerate hypotensive effects (including phenothiazine or general anesthetics). Monitor for symptoms of hypotension following initiation or dose titration.

Intraoperative awareness: Intraoperative awareness has been reported when used with propofol.

Respiratory depression: Serious, life-threatening, or fatal respiratory depression, even when used as recommended may occur. Monitor closely for respiratory depression, especially during initiation or dose escalation. Carbon dioxide retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

Use with caution and monitor for respiratory depression in patients with significant chronic obstructive pulmonary disease, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression, particularly when initiating and titrating therapy; critical respiratory depression may occur, even at therapeutic dosages.

Serotonin syndrome: Potentially life-threatening serotonin syndrome (SS) has occurred with concomitant use of remifentanil and serotonergic agents (e.g., SSRIs, SNRIs, triptans, TCAs, 5-HT3 receptor antagonists, mirtazapine, trazodone, tramadol) and agents that impair metabolism of serotonin (eg, MAO inhibitors). Monitor patients closely for signs of SS such as mental status changes (eg, agitation, hallucinations, delirium, coma); autonomic instability (eg, tachycardia, labile blood pressure, diaphoresis); neuromuscular changes (eg, tremor, rigidity, myoclonus); GI symptoms (eg, nausea, vomiting, diarrhea); and/or seizures. Discontinue remifentanil if serotonin syndrome is suspected.

Bradycardia: Use with caution when administering to patients with bradycardia.

Obesity: Use with caution in patients who are morbidly obese.

Psychosis: Use with caution in patients with toxic psychosis.

Elderly: Use with caution in the elderly; may be more sensitive to adverse effects. Decrease initial dose.

Abuse/misuse/diversion: Remifentanil exposes users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing remifentanil.

Inadequate clearing of IV tubing following administration has been associated with muscle rigidity, respiratory depression, and apnea when another fluid is administered through the same line. Do not administer into the same IV tubing with blood due to potential inactivation by nonspecific esterase's in blood products.

General anesthesia use: Not recommended as the sole agent for induction of anesthesia, because the loss of consciousness cannot be assured.

Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Drug Interaction:

Benzodiazepines or other CNS depressants: Concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may result in hypotension, profound sedation, respiratory depression, coma, and death. Alcohol should be avoided.

Alfuzosin, Alizapride, Alvimopan, Amifostine, Amphetamines, Amifostine, Amphetamines, Antipsychotic Agents, Azelastine, Beta-Blockers, Bionanserin, Blood Pressure Lowering Agents, Brimonidine, Bromopride, Calcium Channel Blockers, Opioids, Chlormethiazole, Chlorphenesin Carbamate, CNS Depressants (May enhance the adverse/toxic effect of other CNS Depressants. Risk C: Monitor therapy), Desmopressin, Diazoxide, Dronabino, Droperidol, Duloxetine, Lofexidine, Methotrimeprazine, Nicorandil, Orphenadrine, Pegvisomant. MAO Inhibitors.

Dosing:[1]

The amount and method of taking the drug for each patient is recommended by the physician, but the usual dose is as follows:

Adult Anesthesia: IV continuous infusion:

Induction of anesthesia: 0.5 to 1 mcg/kg/minute; if endotracheal intubation is to occur in <8 minutes, an initial dose of 1 mcg/kg may be administered over 30 to 60 seconds

Coronary bypass surgery: 1 mcg/kg/minute

Maintenance of anesthesia: Supplemental bolus dose of 1 mcg/kg may be administered every 2 to 5 minutes. Consider increasing concomitant anesthetics with infusion rate >1 mcg/kg/minute. Infusion rate can be titrated upward in increments of 25% to 100% or downward in decrements of 25% to 50% every 2 to 5 minutes.

With nitrous oxide (66%): 0.4 mcg/kg/minute (range: 0.1 to 2 mcg/kg/minute)

With isoflurane: 0.25 mcg/kg/minute (range: 0.05 to 2 mcg/kg/minute)

With propofol: 0.25 mcg/kg/minute (range: 0.05 to 2 mcg/kg/minute)

Coronary bypass surgery: 1 mcg/kg/minute (range: 0.125 to 4 mcg/kg/minute); supplemental dose: 0.5 to 1 mcg/kg

Continuation as an analgesic in immediate postoperative period: 0.1 mcg/kg/ minute (range: 0.025 to 0.2 mcg/kg/ minute). Infusion rate may be adjusted every 5 minutes in increments of 0.025 mcg/kg/ minute. Bolus doses are not recommended. Infusion rates >0.2 mcg/kg/minute are associated with respiratory depression.

Coronary bypass surgery, continuation as an analgesic into the ICU: 1 mcg/kg/minute (range: 0.05 to 1 mcg/kg/minute)

Analgesic component of monitored anesthesia care:

Note: Supplemental oxygen is recommended:

Single IV dose administered 90 seconds prior to local anesthetic:

Remifentanil alone: 1 mcg/kg over 30 to 60 seconds

With midazolam: 0.5 mcg/kg over 30 to 60 seconds

Continuous infusion beginning 5 minutes prior to local anesthetic:

Remifentanil alone: 0.1 mcg/kg minute With midazolam: 0.05 mcg/kg/minute

Continuous infusion administered after local anesthetic:

Remifentanil alone: 0.05 mcg/kg/ minute (range: 0.025 to 0.2 mcg/kg/minute)

With midazolam: 0.025 mcg/kg/minute (range: 0.025 to 0.2 mcg/kg/minute)

Note: Following local or anesthetic block, infusion rate should be decreased to 0.05 mcg/kg/minute; rate adjustments of 0.025 mcg/kg/minute may be done at 5-minute intervals. Infusion rates >0.2 mcg/kg/minute are associated with respiratory depression.

Pediatric

Note: For use of continuous IV infusion in obese patients, dose should be based on ideal body weight (IBW) in obese patients (>30% over IBW).

Anesthesia, maintenance of anesthesia:

Infants 1-2 months: Maintenance of anesthesia with nitrous oxide (70%): 0.4 mcg/kg/minute (range: 0.4-1 mcg/kg/minute); supplemental bolus dose of 1 mcg/kg may be administered, smaller bolus dose may be required with potent inhalation agents, potent neuraxial anesthesia, significant comorbidities, significant fluid shifts, or without atropine pretreatment

Infants ≥3 months, Children, and Adolescents:

Maintenance of anesthesia with halothane, sevoflurane, or isoflurane: 0.25 mcg/kg/minute (range: 0.05-1.3 mcg/kg/minute); supplemental bolus dose of 1 mcg/kg may be administered every 2-5 minutes. Consider increasing concomitant anesthetics with infusion rate >1 mcg/kg/minute. Infusion rate can be titrated upward in increments up to 50% or titrated downward in decrements of 25% to 50%. May titrate every 2-5 minutes.

REPAXIR® Dosing Guidelines-General Anesthesia and continuing as an Analgesic into the Postoperative Care Unit or Intensive care Setting

Phase	Continuous I.V. Infusion (mcg/kg/min)	Infusion Dose range (mg/kg/min)	Supplemental I.V. bolus dose
Induction of anesthesia (through intubation)	0.5 to 1	NA	NA
Maintenance of anesthesia with: Nitrous oxide (66%) Isoflurane (0.4 to 1.5 MAC*) Propofol (100 to 200 mcg/kg/min)	0.4 0.25 0.25	0.1 to 2 0.05 to 2 0.05 to 2	1 1 1
Continuation as an analgesic in to the immediate postoperative period	0.1	0.025 to 0.2	Not recommended

Renal Impairment: There is no dosage adjustments required; however, remifentanil pharmacokinetics is unchanged in patients with end stage renal disease.

Hepatic Impairment: There is no dosage adjustments required; however, remifentanil pharmacokinetics is unchanged in patients with severe hepatic impairment.

Geriatric Decrease initial dose by 50% and cautiously titrate to effect. Refer to adult dosing.

Administration:[1,2]

For IV use only. An infusion device should be used to administer continuous infusions. During the maintenance of general anesthesia, IV boluses may be administered over 30 to 60 seconds. Injections should be given into IV tubing close to the venous cannula; tubing should be cleared after treatment to prevent residual effects when other fluids are administered through the same IV line.

To reconstitute solution, add 1 ml of diluent per mg of remifentnil shake well to dissolve, when reconstituted as directed, the solution contains approximately 1 mg/ml, it should be diluted to a recommended final concentration of 20,25, 50, 250 mcg/ml prior to administration, do not inject before dilution.

Compatible solution: sterile water for injection; 0.9% sodium chloride injection; 0.45% sodium chloride injection; dextrose 5%; dextrose 5% and 0.9% sodium chloride injection.

Rapid IV infusion (over 30 to 60 minute) should only be used during maintenance of general anesthesia.

Rapid infusion may result in skeletal muscle and chest wall rigidity. So it's not recommended use for sedation and pain management after surgery. Chest wall rigidity may resolve by decreasing the infusion rate, discontinuing the infusion, or by administering a neuromuscular blocking agent.

Remifentanil should only be administered by health care providers specifically trained in the use of anesthetic agents. Should not be used in diagnostic or therapeutic procedures outside the monitored anesthesia setting; resuscitative and intubation equipment should be readily available.

Dilution of remifentanyl

Final concentration	dosage	Total volume after dilution
20 mcg / ml	1 mg 2 mg 5 mg	50 ml 100 ml 250 ml
25 mcg / ml	1 mg 2 mg 5 mg	40 ml 80 ml 200 ml
50 mcg / ml	1 mg 2 mg 5 mg	20 ml 40 ml 100ml
250 mcg / ml	5 mg	20 ml

Adverse effects:[1]

Each drug, along with the desired therapeutic effects, may also cause unwanted side effects.

Adverse Reactions Frequency of adverse events may vary based on surgical procedures and rate of infusion.

Dermatologic: Pruritus

Gastrointestinal: Nausea, vomiting

Neuromuscular & skeletal: Muscle rigidity (; includes chest wall rigidity)

Cardiovascular: Bradycardia (; dose-dependent), shivering, hypertension (; dose-dependent), flushing, flushing sensation, tachycardia (; dose-dependent)

Central nervous system: Dizziness, chills, agitation, Headache

Dermatologic: Diaphoresis

Local: Pain at injection site

Respiratory: Respiratory depression, apnea, hypoxia

Miscellaneous: Fever, postoperative pain

Poisoning:[1]

If you accidentally use more than recommended, refer to the treatment center immediately.

Storage condition:[1]

Store intact vial at the temperature below 25°C, Protect from light and freezing

Keep products in original box.

Keep out of the reach of children.

It's for single use only, dispose the remained amounts.

The prepared solution should be diluted immediately, after reconstitution is stable for 24 hours at room temperature

The content is clear, colorless, particle free solution; avoid using otherwise crystal or turbid drugs.

References:

1. Lexicomp Drug information handbook, 2017, 26th edition, Pages: 1989-1991
2. Handbook of injectable drugs 19th edition, Pages: 849-857

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