Addressing anesthesia challenges in specific patient populations

- Obese
- Obstructive sleep apnea
- Elderly
- Pediatric
- Renally impaired
- Hepatically impaired

INDICATIONS AND IMPORTANT RISK INFORMATION

INDICATIONS
ULTIVA® (remifentanil HCl) for Injection is indicated for intravenous administration:
- As an analgesic agent for use during the induction and maintenance of general anesthesia for inpatient and outpatient procedures
- For continuation as an analgesic into the immediate postoperative period in adult patients under the direct supervision of an anesthesia practitioner in a postoperative anesthesia care unit or intensive care setting
- As an analgesic component of monitored anesthesia care in adult patients

IMPORTANT RISK INFORMATION
Due to the presence of glycine in the formulation, ULTIVA is contraindicated for epidural or intrathecal administration. ULTIVA is also contraindicated in patients with known hypersensitivity to fentanyl analogs.

Please see Important Risk Information continued on pages 14-15, and accompanying full Prescribing Information in pocket for all precautions, warnings, contraindications, and adverse events.
**Obese**

**Situation**

- More than one-third of US adults are obese, creating a rapidly growing subset of high-risk surgical patients.\(^1,2\)
- Approximately 113,000 bariatric surgeries are performed in the US each year.\(^3\)

**Common considerations**

- Short-acting anesthetic agents that allow for rapid awakening and help reduce risk of postoperative respiratory depression may be advantageous.\(^4\)
- Opioids tend to accumulate in corporal tissues, especially adipose tissue, which may delay awakening and limit their use.\(^5\)
- Morbidly obese patients (BMI >35 kg/m\(^2\)) have impaired respiratory mechanics during anesthesia.\(^4,6\)

\(^1\)Remifentanil is commonly referred to as Remi by anesthesia providers.

\(^2\)During the first 4 hours of recovery, pain was reported higher in Remi group. Duration of stay in the postanesthesia care unit was comparable between sufentanil and Remi.\(^4\)

\(^3\)Within 5 to 10 minutes after discontinuation of Remi, no residual analgesic activity will be present. However, respiratory depression may occur in some patients up to 30 minutes after termination of infusion due to residual effects of concomitant anesthetics. Other analgesics should be administered prior to discontinuation of Remi where postoperative pain is anticipated.\(^7\)

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**Characteristics of Remi**

**Remi should be used with caution in obese patients.** Clearance of Remi generally correlates with total body weight and may vary in pediatric, geriatric, and morbidly obese patients due to variation in physiology and pharmacodynamics. Remi should be dosed to ideal body weight.

- A potent ultra–short-acting IV opioid.\(^7\)
- Helps facilitate early extubation in morbidly obese patients.\(^4\)
- Recovery of respiratory drive after 3-hour infusions was more rapid and less variable with Remi than alfentanil.\(^7\)
- No accumulation in adipose tissue.\(^7,8\)
- Pharmacokinetics unaltered in obese patients.\(^7,9\)
- Maintains intraoperative hemodynamic stability in morbidly obese surgical patients.\(^10\)

**Remi produces adverse events that are characteristic of μ-opioids, such as respiratory depression, apnea, tachycardia, bradycardia, hypotension, hypertension, and skeletal muscle (including chest wall) rigidity.**

\(^1\)In patients greater than 30\% over body weight when normalized to ideal body weight (IBW).\(^7\)

\(^2\)Recovery and respiratory function were similar to sufentanil.\(^10\)

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Remifentanil in specific patient populations

Obstructive sleep apnea

Situation

Studies have shown that ≈20% of the general and surgical populations have obstructive sleep apnea (OSA).11,12

Studies have shown that >30% of neurosurgical patients and up to 91% of patients undergoing bariatric surgery have OSA.13*,14-16

Common considerations

- Anesthesia and sleep reduce pharyngeal dilator muscle activation and lung volume, thereby predisposing to upper airway obstruction.17,18
- Sleep-disordered breathing can increase emergent intubation and mechanical ventilation in patients undergoing orthopedic, prostate, abdominal, and cardiac surgeries.17,19

Characteristics of Remi†

Remi should be used with caution in obese patients. Clearance of Remi generally correlates with total body weight and may vary in pediatric, geriatric, and morbidly obese patients due to variation in physiology and pharmacodynamics. Remi should be dosed to ideal body weight.

Rapid response for rapid titration to the desired depth of anesthesia/analgesia.17

Rapid recovery from the effects of Remi (5 to 10 minutes) independent of duration of drug administration.57

Recovery of respiratory drive after 3-hour infusions was more rapid and less variable with Remi than alfentanil.7

No accumulation in adipose tissue.7,8

Pharmacokinetics unaltered in obese patients.7*,9

Remi produces adverse events that are characteristic of μ-opioids, such as respiratory depression, apnea, tachycardia, bradycardia, hypotension, hypertension, and skeletal muscle (including chest wall) rigidity.

*Continuous infusions of Remi should be administered only by an infusion device and continuous monitoring is necessary. Interruption of infusion will result in rapid offset of effect.7

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†Presented for education purposes only. Retrospective data show only an association and do not establish cause and effect.

†Remifentanil is commonly referred to as Remi by anesthesia providers.

‡Continuous infusions of Remi should be administered only by an infusion device and continuous monitoring is necessary. Interruption of infusion will result in rapid offset of effect.7

§Within 5 to 10 minutes after discontinuation of Remi, no residual analgesic activity will be present. However, respiratory depression may occur in some patients up to 30 minutes after termination of infusion due to residual effects of concomitant anesthetics. Other analgesics should be administered prior to discontinuation of Remi where postoperative pain is anticipated.7

¶In patients greater than 30% over body weight when normalized to IBW.7
**Elderly**

**Situation**

*Patients age ≥65 years undergo about one-third of the inpatient and outpatient surgical procedures.*

**Common considerations**

- Elderly patients often have comorbidities and respond differently to anesthetic agents due to altered pharmacokinetics and pharmacodynamics.\(^1\)
- Postoperative confusion is common in elderly patients,\(^2\) but early cognitive recovery is desirable if early neurologic evaluation is required.\(^3\)
- Inhaled anesthetics may increase the risk of transient postoperative cognitive dysfunction in elderly patients.\(^4\)

**Characteristics of Remi**

Remi should be used with caution in elderly patients (>65 years). The starting dose of Remi should be decreased by 50% in these patients. Remi should then be cautiously titrated to effect.

| **Short elimination half-life** of approximately 3 to 10 minutes.\(^7\) |
| **Rapid metabolism** by hydrolysis via nonspecific blood and tissue esterases (unlike other opioids).\(^7\) |
| **Shorter time to recovery of cognitive function** in elderly patients with Remi-N\(_2\)O vs isoflurane-N\(_2\)O-fentanyl.\(^6,7\) |
| **Rapid recovery** from the effects of Remi (5 to 10 minutes) independent of duration of drug administration.\(^7\) |
| **Established use** in elderly patients.\(^7\) |
| **Synergistic effect** may reduce the dosage of other anesthesia drugs.\(^7,28,29\) |

Remi produces adverse events that are characteristic of μ-opioids, such as respiratory depression, apnea, tachycardia, bradycardia, hypotension, hypertension, and skeletal muscle (including chest wall) rigidity.

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\(^1\) Remifentanil is commonly referred to as Remi by anesthesia providers.

\(^2\) Study evaluated 60 patients age >65 years undergoing lumbar laminectomy. Postsurgical pain and perioperative use of vasoactive drugs were similar in both groups. More Remi patients were treated with antiemetics (difference did not reach statistical significance). Remi-based anesthesia did not shorten PACU length of stay, which depends on multiple administrative issues.\(^6\)

\(^3\) Within 5 to 10 minutes after discontinuation of Remi, no residual analgesic activity will be present. However, respiratory depression may occur in some patients up to 30 minutes after termination of infusion due to residual effects of concomitant anesthetics. Other analgesics should be administered prior to discontinuation of Remi where postoperative pain is anticipated.\(^7\)

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Remifentanil in specific patient populations

Pediatric

Situation

Approximately 450,000 US children <18 years of age are admitted for inpatient surgery annually and one-fourth of these are <3 years of age.

Common considerations

- Opioids that don't accumulate or cause unpredictable extubation times are desired.
- Advances in surgical techniques and the availability of short-acting intravenous agents help make TIVA an attractive option for pediatric anesthesia.

Characteristics of Remi

Remi should be used with caution in pediatric patients. Clearance of Remi generally correlates with total body weight and may vary in pediatric, geriatric, and morbidly obese patients due to variation in physiology and pharmacodynamics.

- A potent ultra–short-acting IV opioid.
- Established safety and efficacy profiles as part of general anesthesia in a range of pediatric studies.
- No accumulation in adipose tissue.
- Rapid response for rapid titration to the desired depth of anesthesia/analgesia.
- Rapid time to extubation (median) in pediatric clinical trials:
  - Study 1: 10 minutes (range, 1 to 24 minutes; n = 68)
  - Study 2: 9 minutes (range, 2 to 19 minutes; n = 119)
  - Study 3: 13 minutes (range, 4 to 31 minutes; n = 185)
  - Study 4: 8.5 minutes (range, 1 to 14 minutes; n = 38)

Remi produces adverse events that are characteristic of μ-opioids, such as respiratory depression, apnea, tachycardia, bradycardia, hypotension, hypertension, and skeletal muscle (including chest wall) rigidity.

Remifentanil is commonly referred to as Remi by anesthesia providers.

Remi has been studied in 342 pediatric patients in controlled clinical trials for maintenance of general anesthesia. In the pediatric population (birth to 12 years), the most commonly reported events were nausea, vomiting, and shivering.

Remi has not been studied in pediatric patients for use as a postoperative analgesic or as an analgesic component of monitored anesthesia care.

Continuous infusions of Remi should be administered only by an infusion device and continuous monitoring is necessary. Interruption of infusion will result in rapid offset of effect.

Within 5 to 10 minutes after discontinuation of Remi, no residual analgesic activity will be present. However, respiratory depression may occur in some patients up to 30 minutes after termination of infusion due to residual effects of concomitant anesthetics. Other analgesics should be administered prior to discontinuation of Remi where postoperative pain is anticipated.
Remifentanil in specific patient populations

Renally impaired

**Situation**

- *Remifentanil is commonly referred to as Remi by anesthesia providers.*
- *Within 5 to 10 minutes after discontinuation of Remi, no residual analgesic activity will be present. However, respiratory depression may occur in some patients up to 30 minutes after termination of infusion due to residual effects of concomitant anesthetics. Other analgesics should be administered prior to discontinuation of Remi where postoperative pain is anticipated.*

**Characteristics of Remi**

Remi produces adverse events that are characteristic of μ-opioids, such as respiratory depression, apnea, tachycardia, bradycardia, hypotension, hypertension, and skeletal muscle (including chest wall) rigidity.

<table>
<thead>
<tr>
<th>Characteristic</th>
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<tbody>
<tr>
<td><em>Rapid metabolism</em> by hydrolysis via nonspecific blood and tissue esterases (unlike other opioids).*</td>
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<tr>
<td><em>Pharmacokinetics and pharmacodynamics unaltered in patients with renal impairment.</em></td>
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<td><em>No clinically significant increased offset time following longer duration in patients with renal impairment.</em></td>
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<td><em>End-stage renal failure does not prolong recovery from TIVA with Remi and propofol.</em></td>
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**Common considerations**

Elimination of traditional opioids is dependent on organ function, which may be impaired in many patients, leading to prolonged offset of effects.

*One in 10 American adults (>20 million) have chronic kidney disease (CKD).*

*CKD incidence is increasing most rapidly in people age ≥65 years, more than doubling between 2000 and 2008.*

*Remifentanil is commonly referred to as Remi by anesthesia providers.*

*Within 5 to 10 minutes after discontinuation of Remi, no residual analgesic activity will be present. However, respiratory depression may occur in some patients up to 30 minutes after termination of infusion due to residual effects of concomitant anesthetics. Other analgesics should be administered prior to discontinuation of Remi where postoperative pain is anticipated.*

*In 40 adults, Remi time to offset during scheduled down-titrations of the infusion was more variable and statistically significantly longer in the moderate/severe renal impairment group than in the normal/mild group at 24 hours and 72 hours. These observed differences were not clinically significant (the difference in mean offset at 72 hours was only 16.5 min).*

*Study compared total intravenous anesthesia (TIVA) with Remi and propofol in 22 end-stage renal failure patients and 22 normal renal function patients. No differences were found in the time to maintenance of adequate respiration, date of birth recollection, and first analgesic administration between the two groups.*

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Remifentanil in specific patient populations

**Hepatically impaired**

**Situation**

In 2010, about 101,000 hospital discharges had chronic liver disease and cirrhosis as the first-listed diagnosis.40

**Common considerations**

Elimination of traditional opioids is dependent on organ function, which may be impaired in many patients, leading to prolonged offset of effects.7

*Remifentanil is commonly referred to as Remi by anesthesia providers.

**Characteristics of Remi* 

Remi produces adverse events that are characteristic of μ-opioids, such as respiratory depression, apnea, tachycardia, bradycardia, hypotension, hypertension, and skeletal muscle (including chest wall) rigidity.

- **Rapid metabolism** by hydrolysis via nonspecific blood and tissue esterases (unlike other opioids).7
- **Pharmacokinetics and pharmacodynamics unaltered** in patients with hepatic impairment.7
- **Rapid recovery** from the effects of Remi (5 to 10 minutes) independent of duration of drug administration.†7
- **Recovery of respiratory drive** after 3-hour infusions was more rapid and less variable with Remi than alfentanil.7

*Within 5 to 10 minutes after discontinuation of Remi, no residual analgesic activity will be present. However, respiratory depression may occur in some patients up to 30 minutes after termination of infusion due to residual effects of concomitant anesthetics. Other analgesics should be administered prior to discontinuation of Remi where postoperative pain is anticipated.7

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ULTIVA SHOULD BE USED IN CAREFULLY MONITORED SETTINGS BY SPECIFICALLY TRAINED PERSONS NOT INVOLVED IN THE SURGICAL OR DIAGNOSTIC PROCEDURE. OXYGEN SATURATION IS TO BE CONTINUOUSLY MONITORED. RESUSCITATIVE AND INTUBATION EQUIPMENT, OXYGEN, AND AN OPIOID ANTAGONIST MUST BE READILY AVAILABLE.

Please see accompanying full Prescribing Information in pocket for all precautions, warnings, contraindications, and adverse events.

The study by Bekker and colleagues (reference 26) was supported in part by a grant from Glaxo Wellcome Inc.
Addressing anesthesia challenges with Remifentanil

- Rapid response
- Rapid recovery
- Established hemodynamic profile
- Early post-op neurological assessment
- No accumulation

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