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EXIR PHARMACEUTICAL CO.

“Dexmedetomidine”

Exir Marketing Department

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Pharmacologic Category: Alpha2

-Adrenergic Agonist, Sedative

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INDICATIONS AND CLINICAL USE (Adult)

General anesthesia, maintenance:

May reduce sedative-hypnotic and/or opioid requirements of general anesthesia; may reduce postoperative opioid requirements.

Continuous IV infusion: Usual dosage range: 0.1 to 0.8 mcg/kg/hour; titrate to desired effect.

Mechanically ventilated patients in the ICU, sedation:

Loading dose (optional):

Generally not recommended due to concerns for hemodynamic compromise.

Initial: 1 mcg/kg over 10 minutes, followed by a continuous infusion.

Continuous infusion:

Usual dosage range: 0.2 to 1.5 mcg/kg/hour; titrate by 0.2 mcg/kg/hour every 30 minutes to sedation goal or clinical effect. Although infusion rates as high as 2.5 mcg/kg/hour have been used, doses >1.5 mcg/kg/hour do not provide additional clinical efficacy.

Manufacturer recommends that infusion duration not exceed 24 hours.

Procedural sedation or monitored anesthesia care:

Initial: Loading dose of 0.5 to 1 mcg/kg over 10 minutes (use lower range for less invasive procedures [eg, ophthalmic])

followed by a **continuous infusion** of 0.2 to 1 mcg/kg/hour; titrate to desired level of sedation.

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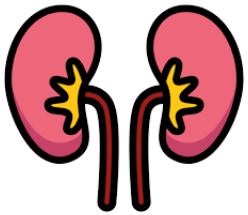
Dosing in Renal or Hepatic impairment

There are no dosage adjustments provided in the manufacturer's labeling; however, pharmacokinetics were not significantly differentin patients with severe renal impairment (CrCl <30 mL/minute).

There are no specific dosage adjustments provided in the manufacturer's labeling; however, consider a dose reduction. Clearance is reduced in varying degrees based on the level of impairment.



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INDICATIONS AND CLINICAL USE (Pediatric)

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ICU sedation:

Loading dose (Optional):

0.5 to 1 mcg/kg/dose over 10 minutes use of loading dose is dependent upon concomitant sedation agents and patient's current and desired level of sedation.

Maintenance dose:

(Continuous IV infusion) Initial: 0.2 to 0.5 mcg/kg/hour; adjust dose to desired level of sedation. Most reported increasing by 0.1 to 0.3 mcg/kg/hour as needed. Reported maintenance dose variable, usual reported range was 0.4 to 0.7 mcg/kg/hour. Maximum reported doses varied; most utilized doses <1 mcg/kg/hour; however, doses as high as 2.5 mcg/kg/hour in intubated patients have been described.

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Sedation/anesthesia, noninvasive procedures:

Loading dose:

Infants, Children, and Adolescents: (IV) 0.5 to 2 mcg/kg/dose over 10 minutes; may be repeated if sedation is not adequate.

Maintenance dose:

Infants, Children, and Adolescents: (Continuous IV infusion) 0.5 to 1 mcg/kg/hour. Hypotension and bradycardia were noted to be age related; risk of hypotension increased by 25% with each 5 year age increment increase and bradycardia occurred more often in children 3 to 12 years than any other age group.

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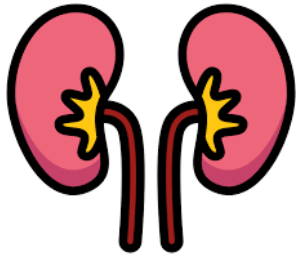

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INDICATIONS AND CLINICAL USE (Geriatric)

Mechanically ventilated patients in the ICU, sedation:

Refer to adult dosing. Consider dosage reduction. No specific guidelines available. Dose selections should be cautious, at the low end of dosage range; titration should be slower, allowing adequate time to evaluate response.

Procedural sedation or monitored anesthesia care (including flexible scope intubation [awake]):

Refer to adult dosing. Initial: Loading dose of 0.5 mcg/kg over 10 minutes; Maintenance infusion: Dosage reduction should be considered.

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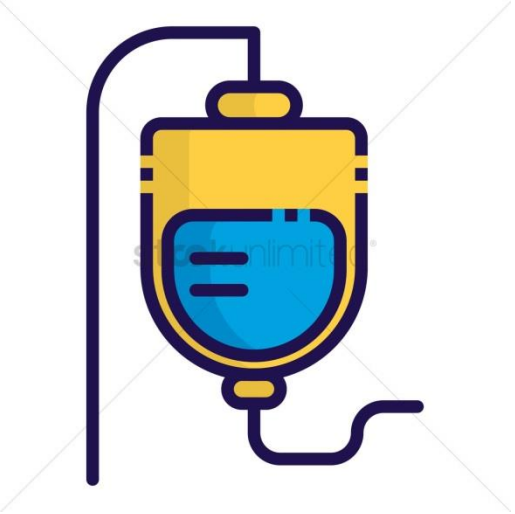
Administration



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Adult

Administer using a controlled infusion device. If loading dose used, administer over 10 minutes; may extend to 20 minutes to further reduce vasoconstrictive effects. Titration no more frequently than every 30 minutes may reduce the incidence of hypotension when used for ICU sedation.

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Pediatric

Administer using a controlled infusion device. Infuse loading dose over 10 minutes; may extend up to 20 minutes in neonatal patients or when needed to further reduce vasoconstrictive effect. Rapid infusions are associated with severe side effects.

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Medication Safety Issues

- Sound-alike/look-alike issues:

DexmedeTOMIDine may be confused with dexAMETHasone.

Precedex may be confused with Peridex.

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Adverse Reactions

(>10%)

Cardiovascular: Hypotension (24% to 56%), bradycardia (5% to 42%), systolic hypertension (28%), tachycardia (25%), hypertension (diastolic; 12%), hypertension (11%)

Central nervous system: Agitation (5% to 14%)

Gastrointestinal: Constipation (6% to 14%), nausea (3% to 11%)

Respiratory: Respiratory depression (37%; placebo 32%)

(1% to 10%)

Cardiovascular: Atrial fibrillation (2% to 9%), peripheral edema (3% to 7%), hypovolemia (3%), edema (2%)

Central nervous system: Anxiety (5% to 9%)

Endocrine & metabolic: Hypokalemia (9%), hyperglycemia (7%), hypoglycemia (5%), increased thirst (2%), hypocalcemia (1%), hypomagnesemia (1%)

Gastrointestinal: Xerostomia (3% to 4%)

Genitourinary: Oliguria (2%)

Hematologic & oncologic: Anemia (3%)

Renal: Acute renal failure (2% to 3%), decreased urine output (1%)

Respiratory: Respiratory failure (2% to 10%), adult respiratory distress syndrome (1% to 9%), pleural effusion (2%), wheezing (≤1%)

Miscellaneous: Fever (5% to 7%), withdrawal syndrome (ICU sedation; 3% to 5%)

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Contraindications

There are no contraindications listed in the US manufacturer's labeling.

Canadian labeling: Hypersensitivity to dexmedetomidine or any component of the formulation.

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Precautions

- Patients with heart block, bradycardia, severe ventricular dysfunction, hypovolemia, or chronic hypertension.
- Patients with diabetes mellitus; cardiovascular adverse events (eg, bradycardia, hypotension) may be more pronounced.
- Patients with hepatic impairment; dosage reductions recommended.
- Elderly. cardiovascular events (eg, bradycardia, hypotension) may be more pronounced. Dose reduction may be necessary.
- Should be administered only by persons skilled in management of patients in intensive care setting or operating room.
- Use of infusions >24 hours has been associated with tolerance and tachyphylaxis and dose-related increase in adverse reactions.

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Withdrawal Symptoms

When withdrawn abruptly in patients who have received >24 hours of therapy, withdrawal symptoms may result (eg, hypertension, tachycardia, nervousness, nausea, vomiting, agitation, headaches). Use for >24 hours is not recommended by the manufacturer.

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Drug Interactions

Antipsychotic Agents (Atypical):

(Aripiprazole, Clozapine, olanzapine, quetiapine, risperidone)

enhance the hypotensive effect of Antipsychotic Agents

Barbiturates:

(phenobarbital, primidone)

May enhance the hypotensive effect of Blood Pressure Lowering Agents.

Blood Pressure Lowering Agents:

May enhance the hypotensive effect of Hypotension-Associated Agents.

Levodopa-Containing Products:

Blood Pressure Lowering Agents may enhance the hypotensive effect of Levodopa-Containing Products.

Nicorandil:

May enhance the hypotensive effect of Blood Pressure Lowering Agents.

Pentoxifylline:

May enhance the hypotensive effect of Blood Pressure Lowering Agents.

Phosphodiesterase 5 Inhibitors:

May enhance the hypotensive effect of Blood Pressure Lowering Agents.

Serotonin/Norepinephrine Reuptake Inhibitors:

(duloxetine, venlafaxine)

May diminish the antihypertensive effect of Alpha2-Agonists.

Tricyclic Antidepressants:

May diminish the antihypertensive effect of Alpha2-Agonists.

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Pregnancy & Breastfeeding

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Pregnancy Risk Factor: C

Drug ratings in pregnancy (US Food and Drug Administration)

Category	Interpretation
A	Controlled human studies show no risk
	Controlled studies in pregnant women fail to demonstrate a risk to the fetus in the first trimester with no evidence of risk in later trimesters. The possibility of fetal harm appears remote.
B	No evidence of risk in studies
	Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women or animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester and there is no evidence of a risk in later trimesters.
C	Risk cannot be ruled out
	Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal effects or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefits justify the potential risk to the fetus.
D	Positive evidence of risk
	There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg, if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
X	Contraindicated in pregnancy
	Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

Pregnancy Considerations:

Dexmedetomidine is expected to cross the placenta. Information related to use during pregnancy is limited.

Breast-Feeding Considerations:

It is not known if dexmedetomidine is excreted in breast milk. According to the manufacturer, the decision to continue or discontinue breastfeeding during therapy should take into account the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother.

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Monitoring Parameters

- Level of sedation
- heart rate
- respiration rhythm
- blood pressure
- pain control

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Pharmacodynamics and Pharmacokinetics

Onset of action:

IV loading dose: 5 to 10 minutes

Peak effect:

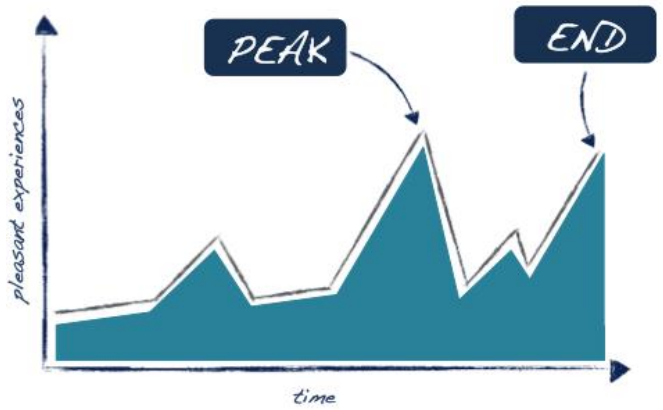
IV loading dose: 15 to 30 minute

Duration (dose dependent):

60 to 120 minutes

Excretion:

Urine (95%); feces (4%)



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Half-life elimination

Preterm Neonates (28 to <36 weeks GA):

Terminal: 7.6 hours (range: 3 to 9.1 hours)

Term Neonates (36 to ≤44 weeks GA):

Terminal: Median: 3.2 hours (range: 1 to 9.4 hours)

Infants and Children <2 years:

Terminal: Median: 2.3 hours (range: 1.5 to 3.3 hours)

Children 2 to 11 years:

Terminal: Median: 1.6 hours (range: 1.2 to 2.3 hours)

Adults:

Distribution: ~6 minutes; Terminal: ~up to 3 hours

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“ Articles”

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Review Article

Korean J Anesthesiol 2012 May 62(5): 405-411
http://dx.doi.org/10.4097/kjae.2012.62.5.405

Dexmedetomidine sedation in ICU

Soo-Bong Yu

Department of Anesthesiology and Pain Medicine, Kosin University Gospel Hospital, Busan, Korea

Conclusion: DEX preserves a natural sleep pattern and induces cooperative sedation in wich patients are easily arousable, leads to less impairment in cognitive function, and has an opiod sparing effect as well. If daily arousal and appropriate assessment for sedation and delirium are performed routinely, DEX decreases duration of ventilatory care, ICU stay, prevalence, and duration of delirium with better adequacy of sedation, and therefore improvement in outcomes. DEX is a promising sedative optimized for ICU care.

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ADIS NEW DRUG PROFILE

Drugs 2000 Feb; 59 (2): 263-268
0012-6667/00/0002-0263/$25.00/0

Dexmedetomidine

Nila Bhana, Karen L. Goa and *Karen J. McClellan*

Adis International Limited, Auckland, New Zealand

Conclusion: Dexmedetomidine is an α2-adrenoceptor agonist that has been approved in the US for use as a sedative for patients in the ICU. It has shown clinical efficacy in providing sedation and analgesia in postsurgical initially intubated and mechanically ventilated patients in an intensive care setting and is well tolerated.

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SciMedCentral

International Journal of Clinical Anesthesiology

Research Article

Dexmedetomidine and Bronchoscopy

Pablo Rubinstein-Aguñin* and Ricardo Leiro-Riera

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Conclusion: Its onset of rapid action and its relatively short duration, make it a suitable agent for performing bronchoscopy sedation because it can be easily titrated. As has been demonstrated in some studies, short-term sedation is a safe procedure, although hypotension and bradycardia are the most significant side effects. It is note worthy that dexmedetomidine appears to have minimal respiratory depression, which makes it a safe agent in patients who are breathing spontaneously. In addition, it offers potential benefits in relation to neuroprotection, cardioprotection and kidney-protection.

World Journal of Anesthesiology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5313/wja.v5.i1.1

World J Anesthesiol 2016 March 27; 5(1): 1-14
ISSN 2218-6182 (online)

EDITORIAL

Dexmedetomidine in gastrointestinal endoscopic procedures

Somchai Amornyotin

Exir Pharmaceutical Co.

Conclusion: several sedative and analgesic drugs are commonly used in GIE procedures. Their safety profile is dependent on their pharmacokinetic and pharmacodynamic profiles,the patient medical condition and the experience of the physician using them. Dexmedetomidine has analgesic, amnesic, sedative and anxiolytic properties. The use of dexmedetomidine as the sole anesthetic agent and as the adjuvant anesthetic agent in various GIE procedures has been published. A distinct advantage of dexmedetomidine is the maintenance of respiratory force and preserved airway patency even in the existence of rising sedation These properties of dexmedetomidine have verified to be beneficial in high-risk patients such as the patients with OSA and COPD patients as well as the patients with extensive tracheomalacia. However, it can produce bradycardia and hypotension. Additionally, the negative results of dexmedetomidine for some GIE procedures have been happened. Therefore, further clinical investigations should to be done.


THANK YOU