Dexmedetomidine HCl Injection

DOSAGE MODIFICATIONS IN PATIENTS WITH RENAL IMPAIRMENT

Dosage Modifications in Patients With Renal Impairment

In patients with renal impairment, Dexmedetomidine HCl Injection is generally well tolerated. In clinical trials, renal impairment did not affect the safety, tolerability, or efficacy of Dexmedetomidine HCl Injection. A dosage adjustment of Dexmedetomidine HCl Injection is not generally recommended for patients with severe renal impairment (CrCl < 30 mL/min) due to its highly protein-bound nature and relatively small volume of distribution. In patients with moderate renal impairment (CrCl 30 to 50 mL/min), the dosage of Dexmedetomidine HCl Injection should be reduced to 1 mcg/kg/hour, and in patients with severe renal impairment (CrCl < 30 mL/min), the dosage of Dexmedetomidine HCl Injection should be reduced to 0.5 mcg/kg/hour. Patients with severe renal impairment should be closely monitored and titration should be based on clinical response.

Dosage Modifications in Patients With Hepatic Impairment

In patients with hepatic impairment, consider dosage reduction of Dexmedetomidine HCl Injection. Generally, reductions of 50% of the MRHD in patients with mild hepatic impairment (Child-Pugh Class A or B) and reductions of 75% of the MRHD in patients with severe hepatic impairment (Child-Pugh Class C) are recommended. In patients with moderate hepatic impairment (Child-Pugh Class B), the dosage of Dexmedetomidine HCl Injection should be reduced to 1 mcg/kg/hour.

Dosage Modifications in Geriatric Patients

The use of Dexmedetomidine HCl Injection in elderly patients (75 years of age or older) has not been adequately studied. In the procedure sedation population, 62% of patients were 65 years or older and 74% were 75 years or older. In the ICU sedation population, 72% of patients were 65 years or older and 74% were 75 years or older. In the sedation population following major orthopedic surgery, 53% of patients were 65 years or older. Dosage reduction is recommended in elderly patients due to age-related decreases in hepatic and renal function. Use caution in administering Dexmedetomidine HCl Injection to elderly patients.

Dosage Modifications in Patients With Opioid Tolerance

Do not make any dosage change in patients with morphine tolerance. The dosage of Dexmedetomidine HCl Injection may be increased for patients with moderate, severe, or unknown opioid tolerance, based on clinical response. In patients with moderate or severe opioid tolerance, the initial loading infusion dose may be increased to 100 mcg/kg over 10 minutes. For patients with unknown opioid tolerance, the initial loading infusion dose may be increased to 100 mcg/kg over 10 minutes.

Dosage Modifications in Patients With Severe Hypotension

In patients with severely compromised cardiovascular status, such as hypotension, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Relative Hypovolemia

In patients with relative hypovolemia, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Bradycardia

In patients with bradycardia, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Cardiac Arrhythmia

In patients with a history of cardiac arrhythmia, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Sleep Apnea

In patients with sleep apnea, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With History of Prolonged QT Interval

In patients with a history of prolonged QT interval, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Pneumonia

In patients with pneumonia, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Asthma

In patients with asthma, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Hypoxia

In patients with hypoxia, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Seizure Disorder

In patients with a history of seizure disorder, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Acute Cardiac Failure

In patients with acute cardiac failure, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Pre-existing Intracranial Hypertension

In patients with pre-existing intracranial hypertension, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With Pre-existing Cerebral Edema

In patients with pre-existing cerebral edema, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dexmedetomidine HCl Injection is generally well tolerated in patients with coronary artery disease, stroke, hypertension, malignancy, and chronic obstructive pulmonary disease. The initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With History of Alcohol Abuse

In patients with a history of alcohol abuse, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.

Dosage Modifications in Patients With History of Dementia

In patients with dementia, the initial loading infusion dose of Dexmedetomidine HCl Injection should be reduced to 25 mcg/kg/hour. The maintenance infusion dose should be reduced to 0.5 mcg/kg/hour.
Dexmedetomidine HCl is a white or almost white powder that is freely soluble in water. Dexmedetomidine HCl is (+)-4-(S)-[1-(2,3-dimethylphenyl)ethyl]-1H-imidazole monohydrochloride. It is the S-enantiomer of medetomidine and is chemically described as 6-(2-methylphenyl)-3-(1-methylpropyl)-1H-pyrimidin-2(1H)-one, (R)-1-(2-methylpropyl)pyrrolidine-2,5-dicarboxylic acid. Dexmedetomidine HCl is a nonbarbiturate sedative-hypnotic, with centrally mediated sedative, anxiolytic, and antinociceptive properties, as well as sympatholytic effects. It is indicated for the management of sedation in adult patients undergoing procedural sedation and pain management, including procedural sedation in the intensive care unit (ICU). The adverse effects include hypotension, bradycardia, respiratory depression, dizziness, somnolence, and other hypotension-related events.

1. OVERVIEW

1.1. Mechanism of Action

Dexmedetomidine HCl is a centrally acting alpha2-adrenoreceptor agonist which binds to the alpha2A-adrenoreceptors within the CNS. Alpha2-adrenoceptors are found within the brainstem, limbic system, and other CNS structures. This binding leads to inhibition of sympathetic outflow, a decrease in mean arterial pressure, and a reduction in heart rate. The effects of dexmedetomidine are mediated through a complex interaction of alpha2-adrenoceptors with other neurotransmitter systems, including the opioid and GABAergic systems.

1.2. Pharmacodynamics

1.2.1. Monitoring of Sedation

Sedative-hypnotic effects are variable among patients. The sedative effect can be evaluated using a 1 to 6 scale, where 1 is no sedation and 6 is deep sedation. A sedation score of ≥3 without receiving any midazolam rescue compared to the placebo group (see Table 10).

1.2.2. Monitoring of Hypotension

Hypotension is a potential adverse effect of dexmedetomidine HCl. Hypotension may be monitored using a 1 to 6 scale, where 1 is no hypotension and 6 is severe hypotension. Hypotension may be monitored using a 1 to 6 scale, where 1 is no hypotension and 6 is severe hypotension. Hypotension may be monitored using a 1 to 6 scale, where 1 is no hypotension and 6 is severe hypotension.

1.2.3. Monitoring of Bradycardia

Bradycardia is a potential adverse effect of dexmedetomidine HCl. Bradycardia may be monitored using a 1 to 6 scale, where 1 is no bradycardia and 6 is severe bradycardia. Bradycardia may be monitored using a 1 to 6 scale, where 1 is no bradycardia and 6 is severe bradycardia.

1.3. Absorption

Dexmedetomidine HCl is rapidly metabolized in humans, with a mean terminal elimination half-life of approximately 8 hours. The plasma concentration of 0.6 ng/mL) for 24 hours, and 0.70 mcg/kg/hr (target concentration of 0.3 ng/mL) for 12 and 24 hours, 0.33 mcg/kg/hr (target concentration of 0.1 ng/mL) for 12 to 24 hours.

1.4. Distribution

Dexmedetomidine HCl is extensively distributed in body tissues. The volume of distribution (Vss) of dexmedetomidine HCl is 46.3 ± 8.3 liters in normal subjects, respectively. Mean clearances for free drug were 74%, 64% and 53% of those observed in the normal subjects.

1.5. Metabolism and Excretion

Dexmedetomidine HCl is metabolized in the liver and excreted in the urine and feces. The metabolism of dexmedetomidine HCl is mediated by CYP3A4 and CYP2D6. The pharmacokinetics of dexmedetomidine HCl are affected by hepatic and renal function. In subjects with varying degrees of hepatic impairment were 74%, 64% and 53% of those observed in the normal subjects. In subjects with varying degrees of renal function, the mean clearance (CL) of dexmedetomidine HCl was 46.3 ± 8.3 liters/hour in normal subjects, respectively. Mean clearances for free drug were 74%, 64% and 53% of those observed in the normal subjects.

1.6. Special Populations

1.6.1. Pediatric Population

The safety and effectiveness of dexmedetomidine HCl have been evaluated in pediatric patients 3 months to 16 years of age. In Study 2, the sedative properties of dexmedetidine HCl were compared with the use of propofol in children undergoing surgical procedures. Efficacy results showed that dexmedetidine HCl-treated patients achieved a sedation score of ≥3 without receiving any midazolam rescue compared to the placebo group (see Table 10).

1.6.2. Elderly Population

The safety and effectiveness of dexmedetidine HCl have been evaluated in elderly patients (≥65 years) subjects. In Study 2, the sedative properties of dexmedetidine HCl were compared with the use of propofol in elderly patients undergoing surgical procedures. Efficacy results showed that dexmedetidine HCl-treated patients achieved a sedation score of ≥3 without receiving any midazolam rescue compared to the placebo group (see Table 10).

1.7. Concurrent Use of Other Drugs

Concurrent use of other drugs may affect the pharmacokinetics and pharmacodynamics of dexmedetidine HCl. The use of other drugs, such as benzodiazepines, opioids, and sedatives, may modify the effects of dexmedetidine HCl. The use of other drugs, such as benzodiazepines, opioids, and sedatives, may modify the effects of dexmedetidine HCl.

1.8. Pregnancy

The safety and effectiveness of dexmedetidine HCl have been evaluated in pregnant women. In Study 2, the sedative properties of dexmedetidine HCl were compared with the use of propofol in pregnant women undergoing surgical procedures. Efficacy results showed that dexmedetidine HCl-treated patients achieved a sedation score of ≥3 without receiving any midazolam rescue compared to the placebo group (see Table 10).

1.9. Nursing Mothers

Dexmedetidine HCl is excreted in human milk. The use of dexmedetidine HCl in breastfeeding mothers is not recommended. The use of dexmedetidine HCl in breastfeeding mothers is not recommended.

1.10. Reversal of Effects

The effects of dexmedetidine HCl can be reversed using naloxone. Naloxone is a selective opioid receptor antagonist that can be used to reverse the sedative effects of dexmedetidine HCl. Naloxone is a selective opioid receptor antagonist that can be used to reverse the sedative effects of dexmedetidine HCl.

1.11. Storage

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature] and protect from light. Protect from light. It is recommended that the infusion bags be kept in the overwrap as follows: NDC No. 0099-9569-04 (50 mg/mL), 0099-9569-07 (100 mg/mL), and 0099-9569-08 (200 mg/mL).

1.12. OVERDOSAGE

The effects of overdose of dexmedetidine HCl are managed as necessary based on the severity of the overdose. The effects of overdose of dexmedetidine HCl are managed as necessary based on the severity of the overdose.

1.13. ADVERSE REACTIONS

Adverse reactions associated with the use of dexmedetidine HCl include hypotension, bradycardia, sedation, and sedation-related events. Adverse reactions associated with the use of dexmedetidine HCl include hypotension, bradycardia, sedation, and sedation-related events.

1.14. CLINICAL STUDIES

Studies in human liver microsomes demonstrated that the glucuronide of 3-hydroxy-dexmedetidine, the glucuronide of 3-hydroxy-dexmedetidine. The glucuronide of 3-hydroxy-dexmedetidine. The glucuronide of 3-hydroxy-dexmedetidine is a major metabolite of dexmedetidine HCl in human beings. The glucuronide of 3-hydroxy-dexmedetidine is a major metabolite of dexmedetidine HCl in human beings.

1.15. DOSAGE AND ADMINISTRATION

Dexmedetidine HCl is intended for administration by intravenous infusion only. Dexmedetidine HCl is intended for administration by intravenous infusion only. Dexmedetidine HCl is intended for administration by intravenous infusion only.

1.16. HOW SUPPLIED/STORAGE AND HANDLING

Dexmedetidine HCl Injection is a clear and colorless solution and is supplied in 50 mg/mL, 100 mg/mL, and 200 mg/mL strengths. In a second study, 198 adult patients were randomized to receive placebo or dexmedetidine HCl. The sedative properties of dexmedetidine HCl were compared with the use of propofol in adult patients undergoing surgical procedures. Efficacy results showed that dexmedetidine HCl-treated patients achieved a sedation score of ≥3 without receiving any midazolam rescue compared to the placebo group (see Table 10).