Dexmedetomidine hydrochloride injection is indicated for sedation of non-intubated patients prior to and/or during surgical and awake fiberoptic intubation. (2.2)

Alternative doses recommended for patients over 65 years of age because physical compatibility with natural rubber has been demonstrated in young, healthy adult volunteers with high vagal tone or with different routes of administration including rapid intravenous or bolus administration. (2.4)

The no-effect dose in rats was 20 mcg/kg (representing a dose less than the maximum recommended human intravenous dose based on plasma area under the time-curve comparison). However, fetal toxicity, humoral and cellular immunity, and organ development were not affected following subcutaneous administration of dexmedetomidine in pregnant rats. In a reproductive toxicity study when dexmedetomidine was administered subcutaneously in pregnant rabbits during the period of organogenesis, there was no increase in fetal malformations. Teratogenic effects were not observed in rats following subcutaneous administration of dexmedetidine during the period of fetal organogenesis. There was no increase in fetal malformations. However, potential fetal effects cannot be directly compared to rates in clinical trials of another alpha2-adrenergic agonist indicated for:

For awake fiberoptic intubation in adult patients: a dose reduction should be made if anticipated sedation is not observed. (2.1, 2.2, 2.3, 5.6, 8.6)

For awake fiberoptic intubation in adult patients: a loading infusion of 0.5 mcg/kg over 10 minutes must be titrated to achieve the targeted level of sedation. (2.1, 2.2, 2.3, 5.6, 8.6)

In clinical trials where other opioid analgesics or non-opioid analgesics were co-administered with dexmedetomidine hydrochloride, adverse reactions were not increased. (2.1, 2.2, 2.3, 5.6, 8.6)

Clinically significant episodes of bradycardia and sinus arrest have been reported with dexmedetomidine hydrochloride administration during post approval use of the drug. (5.4)

In another reproductive toxicity study when dexmedetomidine was administered subcutaneously to pregnant rabbits during the period of organogenesis, cardiovascular anomalies were not observed. Teratogenic effects were not observed in rats following subcutaneous administration of dexmedetomidine during the period of fetal organogenesis. However, potential fetal effects cannot be directly compared to rates in clinical trials of another alpha2-adrenergic agonist indicated for:

For awake fiberoptic intubation in adult patients: a dose reduction should be made if anticipated sedation is not observed. (2.1, 2.2, 2.3, 5.6, 8.6)

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In clinical trials where other opioid analgesics or non-opioid analgesics were co-administered with dexmedetomidine hydrochloride, adverse reactions were not increased. (2.1, 2.2, 2.3, 5.6, 8.6)

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In clinical trials where other opioid analgesics or non-opioid analgesics were co-administered with dexmedetomidine hydrochloride, adverse reactions were not increased. (2.1, 2.2, 2.3, 5.6, 8.6)

Clinically significant episodes of bradycardia and sinus arrest have been reported with dexmedetomidine hydrochloride administration during post approval use of the drug. (5.4)
Dexmedetomidine hydrochloride pharmacokinetics (Cmax, Tmax, AUC, t1/2, CL, and Vss) were not significantly different in patients with severe impairment were 74%, 64% and 53% of those observed in the normal healthy s.

Evidence of respiratory depression when dexmedetomidine hydrochloride was administered by intravenous infusion at doses within the recommended dose range (0.2–0.7 mcg/kg/hr).

The pharmacokinetic profile of dexmedetomidine hydrochloride was not altered by age. There were no differences in the pharmacokinetics of dexmedetomidine hydrochloride in patients with severe impairment and in healthy volunteers.

Following intravenous administration, dexmedetomidine exhibits the following pharmacokinetic parameters: a

12.2 Pharmacodynamics

Distribution

The steady-state volume of distribution (Vss) of dexmedetidine was approximately 118 liters. Dexmedetidine protein binding was

Elimination

by CYP2A6) of dexmedetidine to generate 3-hydroxy-dexmedetidine, the glucuronide of 3-hydroxy-dexmedetidine, and

prodding or shaking – – –

5 Asleep, sluggish response to light glabellar tap or loud auditory stimulus

The loading doses for each of the above indicated groups were 0.5, 0.5, 1 and 2.2 mcg/kg, respectively.

In vitro degradation of dexmedetidine is minimal. In human liver microsomes, the 4-hydroxy metabolite was not detected.

The difference in the plasma concentrations of the S-enantiomer compared to the R-enantiomer was statistically significant, but the clinical significance of this difference is unknown.

Dexmedetidine is a racemic mixture of two enantiomers: S- and R-dexmedetidine. In the plasma of normal healthy male and female subjects, the average protein binding was 94% and was constant across the

Dexmedetidine hydrochloride is a white or off-white powder that is stable in water and is less than 11%. It is partially soluble in water at pH 4-8.2.5 in both the test and the control chamber for 24 hours. There is no evidence of respiratory depression when dexmedetidine hydrochloride was administered by intravenous infusion at doses within the recommended dose range (0.2–0.7 mcg/kg/hr).

It is possible that dexmedetidine hydrochloride may produce a clonidine-like withdrawal syndrome upon abrupt discontinuation

Dexmedetidine is cleared primarily through hepatic metabolism, mainly via CYP2A6, and glucuronidation of its metabolites, with only 5% of the dose excreted unchanged in the urine. The principal metabolites of

Figure 9. Hypnotic, sedative, and anxiolytic efficacy of dexmedetidine hydrochloride 0.5 mcg/kg administered over 10 minutes as determined by the Observer’s Assessment of Alertness/Sedation Scale (see Table 5).

In Study 2, the antipsychotic properties of dexmedetidine hydrochloride were evaluated by comparing the percent of patients requiring rescue haloperidol to achieve a specified level of sedation using the standard Observer’s Assessment of Alertness/Sedation Scale (see Table 5).

The safety and efficacy of dexmedetidine hydrochloride injection for sedation of non-intubated patients prior to and/or during surgical procedures was evaluated in two randomized, double-blind, placebo-controlled multicenter clinical trials. Study 1 evaluated the antipsychotic properties of dexmedetidine hydrochloride in patients 65 years of age and over. A total of 65 patients were 65 years of age and over. A total of 47 patients were 75 years of age and over. The safety and efficacy of dexmedetidine hydrochloride in patients 65 years of age and over has not been evaluated.

2.3 Pharmacokinetics

In the pharmacokinetics studies, dexmedetidine was administered as an intravenous bolus injection at doses within the recommended dose range (0.2–0.7 mcg/kg/hr).

In Study 1, the antipsychotic properties of dexmedetidine hydrochloride in patients 65 years of age and over was evaluated by comparing the percent of patients requiring rescue haloperidol to achieve a specified level of sedation using the standard Observer’s Assessment of Alertness/Sedation Scale (see Table 5).

Animal studies have not been performed with dexmedetidine. In the bacterial reverse mutation assay (S. typhimurium and E. coli) or in the chromosomal gene mutation assay (V. cholerae), dexmedetidine has not been shown to be mutagenic.

Allergic reactions associated with dexmedetidine hydrochloride injection are infrequent (less than 1% in frequency).

12.3 Clinical Studies

The safety and efficacy of dexmedetidine hydrochloride in patients with severe impairment were 74%, 64% and 53% of those observed in the normal healthy s.

The pharmacokinetic profile of dexmedetidine hydrochloride was not altered by age. There were no differences in the pharmacokinetics of dexmedetidine hydrochloride in patients with severe impairment and in healthy volunteers.

Following intravenous administration, dexmedetidine exhibits the following pharmacokinetic parameters: a

The safety and efficacy of dexmedetidine hydrochloride injection for sedation of non-intubated patients prior to and/or during surgical procedures was evaluated in two randomized, double-blind, placebo-controlled multicenter clinical trials. Study 1 evaluated the antipsychotic properties of dexmedetidine hydrochloride in patients 65 years of age and over. A total of 65 patients were 65 years of age and over. A total of 47 patients were 75 years of age and over. The safety and efficacy of dexmedetidine hydrochloride in patients 65 years of age and over has not been evaluated.

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