

EXHIBIT I

Medical Rationale

**Medical Rationale for
Midazolam Hydrochloride Injection 5 mg/mL, 10 mL ADD-Vantage® Vial
(Preservative Free)**

Overview

Midazolam hydrochloride is a short-acting benzodiazepine central nervous system depressant utilized in patients for preoperative sedation and to provide conscious sedation prior to diagnostic or radiographic procedures. Midazolam hydrochloride is a white to light yellow crystalline compound insoluble in water. Its molecular weight is 362.24.

The recommended uses and dosages for Midazolam hydrochloride are:

1. Sedation in mechanically intubated patients
 - IV continuous infusion: 0.01-0.05 mg/kg initially and either repeated at 10-15 minute intervals until adequate sedation is achieved or continuous infusion rates of 0.02-0.1 mg/kg/hour (1-7 mg/hour) and titrate to reach desired level of sedation
2. Conscious sedation
 - IV: A dose of 0.5-2 mg slow I.V. over at least 2 minutes should be administered initially. Slowly titrate to effect by repeating doses every 2-3 minutes as needed.
 - Neonates should receive a dose of 0.15-1 mcg/kg/minute continuous intravenous infusion and preterm neonates should receive a dose of 0.5 mcg/kg/minute for conscious sedation during mechanical ventilation.
 - Children should receive a loading dose of 0.05-2 mcg/kg/minute followed by continuous infusion 1-2 mcg/kg/minute for conscious sedation during mechanical ventilation.
 - Children should receive 0.05 mg/kg 3 minutes before procedure for conscious sedation prior to procedures.
 - Elderly patients should receive 0.5 mg slow I.V. followed by up to 1.5 mg two minutes later, if necessary. Additional doses in increments of 1 mg may be administered in 2-minute intervals thereafter.
3. Preoperative sedation.
 - IM: 0.07-0.08 mg/kg, 30-60 minutes prior to surgery.
 - IV: 0.035 mg/kg/dose, repeat over several minutes as required up to a total dose of 0.1-0.2 mg/kg.

Among patients administered Versed® for any medical reason, the route of administration used most frequently is by continuous intravenous infusion. Accordingly, the introduction of an ADD-Vantage® continuous intravenous delivery system for Midazolam 5 mg/mL, 10 mL vials represents an improvement in the generic drug marketplace over conventional vials by enhancing healthcare workers safety, efficiency, and convenience of drug delivery.

Background

Midazolam hydrochloride is a short-acting benzodiazepine whose clinical applications include preoperative sedation and conscious sedation prior to diagnostic or radiographic procedures via the intramuscular, direct intravenous or continuous intravenous routes. This product is most commonly used in the intensive care setting for sedation of intubated and mechanically ventilated patients as a component of anesthesia. It is safe and effective for use in both pediatric and adult patient populations. Midazolam is the sedative of choice in many intensive care units, and is usually administered as a continuous intravenous infusion with or without a preceding bolus dose. Continuous intravenous infusion is the preferred route because it produces more predictable and reliable anxiolysis than does an intermittent IV bolus dose.

The availability of an ADD-Vantage[®] formulation of Midazolam Hydrochloride Injection 5 mg/mL, 10 mL vials offers several benefits over conventional vials used for continuous intravenous infusion. First, the ADD-Vantage[®] vials are easy and quick to assemble. This reduces the turnaround time between drug admixture and administration and is particularly important for drugs used in the intensive care setting such as Midazolam. Second, since assembled, un-activated ADD-Vantage[®] drugs have a 30-day shelf life, they can be reused in the event that an unused unit is returned to the pharmacy. Third, ADD-Vantage[®] units are assembled without the use of needles, which reduces the risk of accidental needle sticks to healthcare workers. Fourth, the time saved by using an ADD-Vantage[®] unit can be spent on clinical activities and patient care. Finally, each ADD-Vantage[®] unit includes a log sheet affixed to the outside of the IV bag that facilitates record keeping for this schedule IV drug product.

Conclusion

The safety and efficacy of Midazolam Hydrochloride Injection is well established. The majority of patients require an initial bolus dosage of 0.01-0.05 mg/kg followed by continuous intravenous infusion of Midazolam at a rate of 0.02-0.1 mg/kg/hour. Our proposed product is capable of delivering Midazolam Hydrochloride at any of these infusion rates in the same manner as the listed drug, Versed[®]. In summary, an ADD-Vantage[®] system containing Midazolam Hydrochloride 5 mg/mL (Preservative Free) in a 10 mL vial would bring significant benefits to the healthcare providers and, in turn, to the patient. It will provide for improved efficiency in compounding leading to cost savings, while minimizing risks for dosage errors and, reducing the potential of "needle sticks" for the healthcare workers.