Midazolam Injection, USP

Indications and Usage
Midazolam hydrochloride is a water-soluble benzodiazepine available as a sterile, nonpyrogenic parenteral dosage form for intravenous or intra muscular administration. It is indicated as an adjunct to general anesthesia to facilitate endotracheal intubation and to reduce the incidence of peroperative recall. Midazolam has also been used for sedation in critically ill patients requiring close monitoring, for premedication prior to general anesthesia and for sedation before and during procedures such as arteriography, cardiac catheterization, endoscopy, bronchoscopy, and minor surgery. It has been used for the treatment of sleep disorders, the control of minor pain, cough, and anxiety associated with terminal illness, and to produce moderate degrees of sedation in healthy volunteers. It has also been used to control the intrusive behavior of violent, mentally ill patients who are not otherwise manageable with standard treatments. Midazolam hydrochloride is not intended for intrathecal or epidural administration due to the presence of the preservative benzyl alcohol in the formulation.

Contraindications
Midazolam should only be administered intramuscularly or intravenously. Midazolam hydrochloride is contraindicated in patients who are hypersensitive to any benzodiazepine. In addition, midazolam hydrochloride should not be administered to patients who are receiving other medications that may potentiate the response to a benzodiazepine, such as antipsychotic drugs, antidepressants, alcohol, or other sedative, hypnotic, or anxiolytic drugs. Midazolam hydrochloride should not be administered to patients with acute narrow-angle glaucoma. Benzodiazepines may be used in patients with open-angle glaucoma only if they are receiving topical beta blockers. Midazolam hydrochloride should not be administered to patients with acute narrow-angle glaucoma. Benzodiazepines may be used in patients with open-angle glaucoma only if they are receiving topical beta blockers.

Warnings
Serious cardiorespiratory adverse events have occurred after administration of midazolam. These have included respiratory depression, airway obstruction, and apnea and may contribute to profound and/or prolonged drug effect. Narcotic premedication also depresses the ventilatory response to CO2 and may potentiate the respiratory depression associated with the use of midazolam. The intravenous administration of midazolam hydrochloride decreases the minimum alveolar concentration (MAC) of halothane required for general anesthesia. Caution is advised when midazolam is administered to patients receiving erythromycin since this may result in a decrease in the plasma clearance of midazolam.

Precautions
Midazolam hydrochloride is not intended for use in patients with a history of drug abuse or alcoholism. Midazolam hydrochloride should be used with caution in patients with hepatic or renal disease. Midazolam hydrochloride should be used with caution in patients receiving concomitant treatment with other medications that may potentiate the response to a benzodiazepine. Midazolam hydrochloride should be used with caution in patients with a history of respiratory depression, brainstem hypofunction, or sleep apnea.

Adverse Reactions
The following additional adverse reactions have been reported subsequent to intravenous administration as a single sedative/anxiolytic/amnestic agent: abdominal pain, anaphylactic reactions, bronchospasm, bradycardia, coughing, cramps, vomiting, sweating, abdominal distention, and unusual dreams. Abnormal electrocardiograms and an increase in heart rate were observed in some patients. Coughing, cramps, vomiting, and sweating were more common in neonates than in adults. No reports of CNS depression were made in patients older than 1 year. The incidence of abnormal dreams was higher in infants than in adults. Abnormal dreams were more common following midazolam administration than following that of placebo. Abnormal dreams were more common following midazolam administration than following that of placebo.

Pharmacokinetics
The immediate-acting property of midazolam injection allows for rapid onset of its pharmacologic effect. Midazolam hydrochloride is rapidly absorbed following intramuscular or intravenous administration, and pharmacokinetic studies have demonstrated that it is extensively distributed at both sites. Approximately 70% of the unmetabolized drug is excreted in the urine, with less than 1% excreted in the feces. The plasma half-life of midazolam is about 1 hour. The drug is extensively metabolized in the liver. The primary metabolite, 1-hydroxy-midazolam, is at least as potent as the parent drug. The relationship between accumulating metabolite levels and prolonged sedation is unclear.

Midazolam hydrochloride is a semi-synthetic benzodiazepine available as a sterile, nonpyrogenic parenteral dosage form for intravenous or intra muscular administration. It is indicated as an adjunct to general anesthesia to facilitate endotracheal intubation and to reduce the incidence of peroperative recall. Midazolam has also been used for sedation in critically ill patients requiring close monitoring, for premedication prior to general anesthesia and for sedation before and during procedures such as arteriography, cardiac catheterization, endoscopy, bronchoscopy, and minor surgery. It has been used for the treatment of sleep disorders, the control of minor pain, cough, and anxiety associated with terminal illness, and to produce moderate degrees of sedation in healthy volunteers. It has also been used to control the intrusive behavior of violent, mentally ill patients who are not otherwise manageable with standard treatments. Midazolam hydrochloride is not intended for intrathecal or epidural administration due to the presence of the preservative benzyl alcohol in the formulation.

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MIDAZOLAM FOR SEDATION

MIDAZOLAM IS WARNED TO BE USED WITH CAUTION IN PATIENTS WHO HAVE RECEIVED ANESTHETICS OR OTHER CNS DEPRESSANTS IN THE PREVIOUS 4 HOURS AS INCREASED DEPRESSION OF RESPIRATION MAY OCCUR. IN SUCH SITUATIONS, THE DEGREE OF DEPRESSION OF RESPIRATION SHOULD BE DETERMINED BY CLINICAL MONITORING AND THE RATE OF INTRAVENOUS INFUSION SHOULD BE DETERMINED BY THE CLINICAL SITUATION, IF INDICATED, AND OTHER APPROPRIATE INTERVENTIONS. THERE IS NO INFORMATION AS TO WHETHER PERITONEAL DIALYSIS, FORCED DIURESIS OROTHER THERAPIES TO ALTER SYSTEMIC CLEARANCE ARE EFFECTIVE IN INDIVIDUALS WITH BENZODIAZEPINE OVERDOSE. PERITONEAL DIALYSIS OR HEMODIALYSIS IS NOT RECOMMENDED. IN SOME PATIENTS WITH SEVERE SYSTEMIC DISEASE OR DEBILITATION, AS LITTLE AS 0.15 MG/KG MAY SUFFICE.

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