Exposure to excessive amounts of benzyl alcohol has been associated with toxicity (hypotension, prolonged respiratory effects of VERSED. The severe fluid or electrolyte disturbances.

Injectable VERSED should not be administered by rapid injection in the neonatal population.

When used for sedation/anxiolysis/amnesia, VERSED should always be titrated slowly in adult or pediatric patients. Adverse hemodynamic events have been reported in pediatric patients with cardiovascular instability, rapid intravenous administration should also be avoided.

There have been limited reports of intra-arterial injection of VERSED. Adverse events have included local necrosis, acute alcohol intoxication with depression of vital signs. Particular care should be exercised in the use of VERSED in patients with COPD. These reactions are due to inadequate or excessive dosing or improper administration of VERSED; however, consideration should be given to the possibility of cerebral hypoxia or true paradoxical reactions. Should such reactions occur, the response to each dose of VERSED and all other drugs, including local anesthetics, should be evaluated before proceeding. Reversal of such responses with flumazenil has been reported in pediatric patients. Continuous use of barbiturates, alcohol or other central nervous system depressants may increase the risk of hypotension, airway obstruction, desaturation, or apnea and may contribute to prolonged and/or profound drug effect. Narcotic premedication also depresses the respiratory response to carbon dioxide stimulation.

High risk adult and pediatric surgical patients, elderly patients and debilitated adult and pediatric patients require lower doses, whether or not concomitant sedating medications are used.VERSED should not be administered intrathecal or intraventricularly. The decision as to when patients who have received injectable VERSED, particularly on an outpatient basis, may again engage in activities requiring complete mental alertness, operate hazardous machinery or drive a motor vehicle from the effects of VERSED. VERSED is not intended for intrathecal or epidural administration due to the presence of the preservative benzyl alcohol in the dosage form.

CONTRAINDICATIONS: Injectable VERSED is contraindicated in patients with a known hypersensitivity to the drug. Benzodiazepines are contraindicated in patients with acute narrow-angle glaucoma. VERSED is not intended for intrathecal or epidural administration due to the presence of the preservative benzyl alcohol in the dosage form. VERSED should not be administered by rapid injection in the neonatal population. VERSED administered rapidly as an intravenous injection (less than 2 minutes) has been associated with severe hypotension in neonates following rapid intravenous administration. Seizures have been reported in pediatric patients with cardiovascular instability, rapid intravenous administration should also be avoided.

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VERSED® (midazolam HCl)

requires more than the recommended dosages or other medications containing this preservative.

The following additional adverse reactions were reported subsequent to intravenous administration as a single sedative/anxiolytic/amnesic agent in adult patients: hiccough (3.3%), nausea (2.8%), vomiting (2.5%), coughing (1.3%), “overdose” (1.8%), headache (2.5%), tachycardia (1.2%), local at MI injection site: tenderness (5.6%), pain during injection (0.3%), redness (2.6%), induration (1.7%).

VE22A

EDUCATION & DEPENDENCE: Midazolam is subject to Schedule IV control under the Controlled Substances Act of 1970. Midazolam was actively self-administered in prime animals used to assess the positive reinforcing effects of psychoactive drugs. Midazolam produced physical dependence of a mild to moderate intensity in cynomolgus monkeys after 5 to 10 weeks of administration. Available data concerning the drug abuse and dependence potential of midazolam suggest that its abuse potential is at least equivalent to that of diazepam. Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol (convulsions, hallucinations, tremor, altered mental state and withdrawal) have been observed in patients. Although a relatively small number of patients have been reported to have exhibited symptoms of withdrawal following abrupt discontinuation.

The sedative effect of intravenous VERSED is accentuated by any concomitantly administered medication, which depresses the central nervous system, particularly narcotics (eg, morphine, meperidine and fentanyl) and anxiolytics (eg, benzodiazepines). Use with other CNS depressants: The combination of sedation with other CNS depressants (eg, morphine, meperidine, fentanyl, propofol, opioids, tricyclic antidepressants) can have additive effects.

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Drug/Laboratory Test Interactions: Midazolam has not been shown to interfere with results obtained in the following laboratory tests: prothrombin time, partial thromboplastin time, bleeding time, platelet count, electrolyte determinations, blood urea nitrogen, creatinine, bilirubin, SGOT, SGPT, alkaline phosphatase, lipid determinations, prostatic acid phosphatase, uric acid, magnesium, calcium, copper, zinc, sodium, potassium, chloride, phosphorus, blood glucose, thyroid function, 24 hour urine steroid screen, gonadotropin, cortisol, and corticosteroid assays.

Cardiovascular: Tachycardia, Bradycardia, Hypertension, Hypotension, Palpitations.

Cardiac: Arrhythmias, Cardiac arrest, Myocardial ischemia, Myocardial infarction, Atrioventricular block.

Diabetes: Hypoglycemia, Hyperglycemia.

Endocrine: Changes in carbohydrate metabolism, sodium balance, and electrolyte balance. The use of VERSED in patients with metabolic and endocrine diseases may be associated with changes in carbohydrate metabolism, sodium balance, and electrolyte balance.

Eye: Photophobia, Pupillary constriction, Pupillary dilation, Retinitis, Retinal hemorrhage.

GI: Anemia, Gastric stenosis, Gastritis, Oesophageal stricture, Peptic ulcer, Ulcerative colitis, Hemorrhage from peptic ulcer, Hemorrhage from ulcerative colitis.

Hematologic: Anemia, Leukopenia, Lymphocytosis, Leukocytosis, Thrombocytopenia.

Hepatic: Hepatomegaly, Jaundice, Hepatitis, Cholestatic jaundice, Acute hepatic necrosis.

Infectious: Bacterial infections, Pulmonary infection, Septicemia, Herpes simplex.

Lacrimal: Lacrimation.

Musculo-Skeletal: Arthritis, Arthralgia, Muscle stiffness (0.3%).

Musculoskeletal: Arthritis.

Nervous System: Convulsions, Dizziness, Drowsiness, Nystagmus, Paresthesia, Tinnitus, Vertigo.

Respiratory: Apnea, Bronchitis, Coughing, Dyspnea, Hyperventilation, Hypoventilation, Oxygen desaturation, Oxygenation, Pulmonary edema, Pulmonary fibrosis, Pulmonary hypertension, Sinusitis, Tachypnea, Tachyapnea, Unilateral and bilateral deafness, Voice change, Voice disturbance.

Renal: Acute renal failure, Arterial hemorrhage, Hematuria, Nephritis, Renal failure.


Other Reactions: Local effects at injection site, Injection site reactions (1.3%), Local effects at IM injection site: pain, (3.7%), heat (3.1%), induration (0.9%), redness (3.5%), swelling (0.3%). Administration of IM VERSED to elderly and/or higher risk surgical patients is transferred transplacentally and because other benzodiazepines given in the last weeks of pregnancy have been observed in infants of mothers who received VERSED during the last trimester.
VERSED®
midazolam HCl (IV)
INJECTION
VERSED is available in 1 mg/mL and 5 mg/mL strengths.

IMPORTANT SAFETY AND DOSING CONSIDERATIONS
Because serious and life-threatening cardiorespiratory adverse events have been reported with VERSED (midazolam HCl), standard precautions for IV administration should include continuous monitoring (ie, pulse oximetry), detection and correction of these reactions, and immediate availability of oxygen and age- and size-appropriate resuscitative equipment. Ensure the availability of personnel skilled in early detection of hypoventilation, maintenance of a patent airway and ventilatory support. For deeply sedated pediatric patients, a dedicated individual, other than the practitioner performing the procedure, should monitor the patient throughout the procedure.

VERSED should be titrated slowly, never given as a bolus. Respiratory depression and/or arrest may result from excess doses or rapid or single bolus. VERSED is 3 to 4 times as potent per mg as diazepam.

When VERSED is given in conjunction with opioids or other sedatives, the potential for respiratory depression/airway obstruction is increased, and the minimum effective VERSED dose is generally reduced.

Please see adjacent page for boxed warning and summary of product information.

Please visit us at the AANA Annual Meeting in Nashville, August 1-3, Booth #s 400/402