Etomidate induction is associated with a transient 20 to 30% decrease in cerebral blood flow. This reduction in blood flow appears to be uniform in the absence of intracranial space occupying lesions. As with other intravenous induction agents, reduction in cerebral oxygen utilization is roughly proportional to the reduction in cerebral blood flow. In patients with and without intracranial space occupying lesions, etomidate induction is usually followed by a moderate lowering of intracranial pressure, lasting several minutes. All of these studies provided unambiguous evidence of significant reduction in regional cerebral perfusion in patients with intracranial space occupying lesions is too limited to permit definitive conclusions.

Etomidate injection, USP is indicated by intravenous injection for the induction and maintenance of anesthesia. When considering use of etomidate, the usefulness of its hemodynamic properties (see CLINICAL PHARMACOLOGY) should be weighed against the high frequency of transient skeletal muscle movements (see ADVERSE REACTIONS).

Etomidate is chemically identified as (R)-(+)-ethyl-1-(1-phenylethyl)-1H-indole-3-carboxylic acid and has the following structural formula:

\[
\text{C}_9\text{H}_7\text{N}_2\text{O}_2
\]


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\]

Limited pharmacokinetic data in patients with cirrhosis and esophageal varices have shown that the amount following administration of thiopental under conditions where there was little or no change in heart rate following administration of etomidate. However, clinical data indicates that etomidate administration is a sterile, nonpyrogenic solution. Each milliliter contains 2 mg/mL etomidate. These persist for approximately 6 to 8 hours and appear to be unresponsive to ACTH administration.

Because elderly patients are more likely to have decreased renal function, care should be taken when etomidate is used in patients with recent severe trauma or hypovolemia to predict cardiovascular response under such circumstances.

The most characteristic effect of intravenous etomidate on the respiratory system is a slight depression in arterial carbon dioxide tension (PCO₂). See also ADVERSE REACTIONS.

Clinical experience and special studies to date suggest that standard dose of intravenous etomidate ordinarily neither elevates plasma histamine nor causes signs of histamine release.

Limited clinical studies, as well as animal studies, suggest that inadvertent intra-arterial injection of etomidate, unlike thiobarbiturates, will not usually be followed by tissue damage to the site of injection. Intravenous injection of etomidate is, however, not recommended.

Indications and Usage.  Etomidate is intended for the induction of general anesthesia by intravenous injection. It is intended for the induction of general anesthesia by intravenous injection. It is not intended for administration by prolonged infusion.

Etomidate has been shown to have an enterochromaffin effect in rats when given in doses of 0.1, 0.3, 1.0, and 3.0 mg/kg to rats, the human dose is extrapolated to multiples of these doses. Preliminary data suggests that the volume of distribution and elimination half-life of etomidate are approximately double that seen in healthy subjects. (References: H. V. Bame, et al., Anesthesiology 38 (Supp 38):61-62, July 1973.)

In clinical studies, elderly patients demonstrated decreased initial distribution volumes and total clearance of etomidate. Protein binding of etomidate to serum albumin was also significantly decreased in these individuals. Reduced plasma elimination rates have been noted following induction doses of etomidate. These results persist for approximately 8 to 10 hours and appear to be unresponsive to ACTH administration. This probably represents tissular inhibition of beta hydroxylation within the arterial cortex. (References: J.F. Fairgrieve, et al., Anesthesiology 62:652-656, 1980. B.L. Wagner & P.F. White, Anesthesiology 51:447-451, 1979. T.D. Duckett, et al., Clin. Endocrinol. and Metabolism 35:1143-1147, 1986, and three additional studies of Multiple Antigens, 448:123-128, April 30, 1985.)

Etomidate should be immediately followed by a moderate lowering of intraocular pressure.

Because of the hazards of prolonged suppression of endogenous cortisol and adrenocortical production, this formulation is not intended for administration by prolonged infusion.

Etomidate is contraindicated in patients who have shown hypersensitivity to it.

Etomidate should be administered only by personnel trained in the administration of general anaesthetics and in the management of complications encountered during the conduct of general anaesthesia.

G) should be weighed against the high frequency of transient skeletal muscle movements (see ADVERSE REACTIONS).

Clinical experience and special studies to date suggest that standard dose of intravenous etomidate ordinarily neither elevates plasma histamine nor causes signs of histamine release.

Etomidate injection, USP is a sterile, nonpyrogenic solution. Each milliliter contains 2 mg/mL etomidate. These persist for approximately 6 to 8 hours and appear to be unresponsive to ACTH administration.

Etomidate is rapidly metabolized in the liver. Minimal hypnotic plasma levels of etomidate are equal to or higher than 0.23 mcg/mL; they decrease rapidly over the first 15 minutes. In the presence of cirrhosis and esophageal varices, hydrolisis of etomidate, and accounts for about 80% of the urinary excretion.

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Induction doses of etomidate have been associated with reduction in plasma cortisol and aldosterone concentrations (see CLINICAL PHARMACOLOGY). These have not been associated with changes in vital signs or evidence of increased mortality; however, where concern exists for patients undergoing severe stress, exogenous replacement should be considered.

ADVERSE REACTIONS

The most frequent adverse reactions associated with use of intravenous etomidate are transient venous pain on injection and transient skeletal muscle movements, including myoclonus.

1. Transient venous pain was observed immediately following intravenous injection of etomidate in about 20% of the patients, with considerable difference in the reported incidence (1.2% to 42%). This pain is usually described as mild to moderate in severity but it is occasionally judged disabling. The duration of venous pain is not associated with a rise in usual incidence of thrombophlebitis at the injection site. Pain may also appear to be less frequently noted when larger, more proximal arm veins are employed and it appears to be more frequently noted when smaller more distal, hand or wrist veins are employed.

2. Transient skeletal muscle movements were noted following use of intravenous etomidate in about 32% of the patients, with considerable difference in the reported incidence (2% to 63%). Most of these observations were judged mild to moderate in severity but some were judged disabling. The incidence of disabling movements was less when 0.1 mg fentanyl was given immediately before injection. These movements have been classified as myoclonic in the majority of cases (74%), but protruding movements (7%), tonic movements (10%), and eye movements (9%) have also been reported. No exact classification is available, but these movements may also be placed into three groups by location:

   a. Major movements are bilateral. The arms, legs, shoulders, neck, chest wall, trunk and all four extremities have been described in some cases, with one or more of these muscle groups predominating in each individual case. Results of electromyographic studies suggest that these muscle movements are a manifestation of disorganization of cortical activity, cortical electroencephalograms, taken during periods when these muscle movements were observed, have failed to reveal seizure activity.

   b. Other movements are described as either unilateral or having a predominance of activity on one side of the body. These movements sometimes resemble a localized response to some stimuli, such as venous pain on injection, in the lightly anesthetized patient (averting movements). Any muscle group or groups may be involved, but a predominance of movement of the arm in which the intravenous solution was injected is frequently noted.

   c. Still other movements probably represent a mixture of the first two types. Skeletal muscle movements appear to be more frequent in patients who also manifest venous pain on injection.

OTHER ADVERSE OBSERVATIONS

Respiratory System: Hyperventilation, hyperventilation, apnea of short duration (5 to 60 seconds with spontaneous recovery), laryngospasm, hiccup and sneezing suggestive of partial upper airway obstruction have been observed in some patients. These conditions were managed by conventional countermeasures.

Circulatory System: Hypotension, hypertension, tachycardia, bradycardia and other arrhythmias have occasionally been observed during induction and maintenance of anesthesia. One case of severe hypertension and tachycardia, judged to be anaphylactoid in character, have been reported. (Reference: M. Sold and A. Rothhammer, Anaesthesist 34:208-210, 1985. Submitted to ASA 15-229 on 16 May 1985.)

Gastrointestinal System: Transient nausea and vomiting following use of intravenous etomidate have failed to reveal seizure activity. The most frequent adverse reactions associated with use of intravenous etomidate include:

   a. Most movements are bilateral. The arms, legs, shoulders, neck, chest wall, trunk and all four extremities have been described in some cases, with one or more of these muscle groups predominating in each individual case. Results of electromyographic studies suggest that these muscle movements are a manifestation of disorganization of cortical activity, cortical electroencephalograms, taken during periods when these muscle movements were observed, have failed to reveal seizure activity.

   b. Other movements are described as either unilateral or having a predominance of activity on one side of the body. These movements sometimes resemble a localized response to some stimuli, such as venous pain on injection, in the lightly anesthetized patient (averting movements). Any muscle group or groups may be involved, but a predominance of movement of the arm in which the intravenous solution was injected is frequently noted.

   c. Still other movements probably represent a mixture of the first two types. Skeletal muscle movements appear to be more frequent in patients who also manifest venous pain on injection.

OVERTOXICITY

Overtreatment may occur from too rapid or repeated injections. Too rapid injection may be followed by a fall in blood pressure. No adverse cardiovascular or respiratory effects attributable to etomidate toxicity have been reported. In the event of suspected or apparent overtreatment, the drug should be discontinued, a patent airway established (intubate, if necessary) and oxygen administration with assisted ventilation, if necessary. The LD₅₀ of etomidate administered intravenously to rats is 20.4 mg/kg.

DOSEAGE AND ADMINISTRATION

Etomidate injection is intended for administration only by the intravenous route (see CLINICAL PHARMACOLOGY). The dose for induction of anesthesia in adult patients and in children above the age of ten (10) years will vary between 0.2 and 0.6 mg/kg of body weight and it must be individualized in each case. The usual dose for induction in these patients is 0.3 mg/kg, injected over a period of 30 to 60 seconds. There are inadequate data to make dosage recommendations for induction of anesthesia in patients below the age of ten (10) years; therefore, such use is not recommended. Geriatric patients may require reduced doses of etomidate.

Smaller increments of intravenous etomidate may be administered to adult patients during short operative procedures to supplement somnopentyl anesthesia, agents such as nitrous oxide. The dosage employed under these circumstances, although smaller than that for the original induction dose, must be individualized. There are insufficient data to support this use of etomidate for longer adult procedures or for any procedures in pediatric patients; therefore, such use is not recommended. The use of intravenous fentanyl and other neuroactive drugs employed during the conduct of anesthesia may alter the etomidate dosage requirements. Consult the prescribing information for all other such drugs before using.

Premedication: Etomidate injection is compatible with commonly administered preanesthetic medications, which may be employed as indicated. See also CLINICAL PHARMACOLOGY, ADVERSE REACTIONS, and dosage recommendations for maintenance of anesthesia.

Etomidate hypnosis does not significantly alter the usual dosage requirements of nonrespiratory blocking agents employed for endotracheal intubation or other purposes shortly after induction of anesthesia.

Parenteral drug products should be inspected visually for particulate matter and discontinue prior to administration, whenever solution and container permit. To prevent needle-stick injuries, needles should not be recap'ed, purposely bent, or broken by hand.

HOW SUPPLIED

Etomidate Injection, USP 30 mg/10 mL is supplied as follows:

NDC Number Packaging

0069-0006-01 vial of 10 mL Single-dose vials

Etomidate Injection, USP 40 mg/20 mL is supplied as follows:

NDC Number Packaging

0069-0006-02 vial of 10 mL Single-dose vials

Store at 20° to 25° C (68° to 77° F). [see USP Controlled Room Temperature].

Discard unused portion.

Rx Only

Infectables

Manufactured by Pfizer Labs

Pfizer Inc
New York, NY 10017

Revised July 2012
1019130