

# INAPSINE<sup>®</sup>

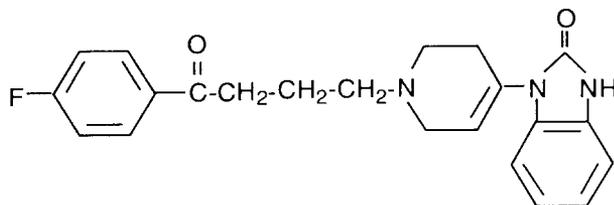
## (DROPERIDOL) INJECTION

FOR INTRAVENOUS OR INTRAMUSCULAR USE ONLY

**R<sub>x</sub> only**

### DESCRIPTION

INAPSINE contains droperidol, a neuroleptic (tranquilizer) agent. Inapsine (droperidol) Injection is available in ampoules and vials. Each milliliter contains 2.5 mg of droperidol in an aqueous solution adjusted to pH  $3.4 \pm 0.4$  with lactic acid. Droperidol is chemically identified as 1-(1-[3-(p-fluorobenzoyl) propyl]-1,2,3,6-tetrahydro-4-pyridyl)-2-benzimidazolinone with a molecular weight of 379.43. The structural formula of droperidol is:



Molecular formula: C<sub>22</sub>H<sub>22</sub>FN<sub>3</sub>O<sub>2</sub>, partition coefficient in n-octanol: water: 3.46, pKa: 7.46

INAPSINE is a sterile, non-pyrogenic, aqueous solution for intravenous or intramuscular injection.

### CLINICAL PHARMACOLOGY

INAPSINE (droperidol) produces marked tranquilization and sedation. It allays apprehension and provides a state of mental detachment and indifference while maintaining a state of reflex alertness.

INAPSINE produces an antiemetic effect as evidenced by the antagonism of apomorphine in dogs. It lowers the incidence of nausea and vomiting during surgical procedures and provides antiemetic protection in the postoperative period.

INAPSINE potentiates other CNS depressants. It produces mild alpha-adrenergic blockade, peripheral vascular dilatation and reduction of the pressor effect of epinephrine. It can produce hypotension and decreased peripheral vascular resistance and may decrease pulmonary arterial pressure (particularly if it is abnormally high). It may reduce the incidence of epinephrine-induced arrhythmias, but it does not prevent other cardiac arrhythmias.

The onset of action of single intramuscular and intravenous doses is from three to ten minutes following administration, although the peak effect may not be apparent for up to thirty minutes. The duration of the tranquilizing and sedative effects generally is two to four hours, although alteration of alertness may persist for as long as twelve hours.

### INDICATIONS AND USAGE

INAPSINE (droperidol) is indicated:

- to produce tranquilization and to reduce the incidence of nausea and vomiting in surgical and diagnostic procedures.
- for premedication, induction, and as an adjunct in the maintenance of general and regional anesthesia.
- in neuroleptanalgesia in which INAPSINE is given concurrently with an opioid analgesic, such as SUBLIMAZE<sup>®</sup> (fentanyl citrate) Injection, to aid in producing tranquility and decreasing anxiety and pain.

### CONTRAINDICATIONS

INAPSINE (droperidol) is contraindicated in patients with known hypersensitivity to the drug.

### WARNINGS

FLUIDS AND OTHER COUNTERMEASURES TO MANAGE HYPOTENSION SHOULD BE READILY AVAILABLE.

As with other CNS depressant drugs, patients who have received INAPSINE (droperidol) should

have appropriate surveillance.

It is recommended that opioids, when required, initially be used in reduced doses.

As with other neuroleptic agents, very rare reports of neuroleptic malignant syndrome (altered consciousness, muscle rigidity and autonomic instability) have occurred in patients who have received INAPSINE (droperidol).

Since it may be difficult to distinguish neuroleptic malignant syndrome from malignant hyperpyrexia in the perioperative period, prompt treatment with dantrolene should be considered if increases in temperature, heart rate or carbon dioxide production occur.

Cases of sudden death have been reported following use of droperidol at high doses (generally 25 mg or greater) in patients at risk for cardiac dysrhythmia due to anoxia, hypercarbia, severe electrolyte disturbances, or alcohol withdrawal. While these reports do not establish the cause of such death, QT prolongation after INAPSINE administration has been reported and there is at least one case of nonfatal torsade de pointes confirmed by rechallenge.

Because of these reports, INAPSINE is not recommended in the treatment of alcohol withdrawal or in other clinical situations where high doses are likely to be needed in patients at risk for dysrhythmia.

### **PRECAUTIONS**

**General:** The initial dose of INAPSINE (droperidol) should be appropriately reduced in elderly, debilitated and other poor-risk patients. The effect of the initial dose should be considered in determining incremental doses.

Certain forms of conduction anesthesia, such as spinal anesthesia and some peridural anesthetics, can alter respiration by blocking intercostal nerves and can cause peripheral vasodilatation and hypotension because of sympathetic blockade. Through other mechanisms (see CLINICAL PHARMACOLOGY), INAPSINE can also alter circulation. Therefore, when INAPSINE is used to supplement these forms of anesthesia, the anesthetist should be familiar with the physiological alterations involved, and be prepared to manage them in the patients elected for these forms of anesthesia.

If hypotension occurs, the possibility of hypovolemia should be considered and managed with appropriate parenteral fluid therapy. Repositioning the patient to improve venous return to the heart should be considered when operative conditions permit. It should be noted that in spinal and peridural anesthesia, tilting the patient into a head-down position may result in a higher level of anesthesia than is desirable, as well as impair venous return to the heart. Care should be exercised in moving and positioning of patients because of a possibility of orthostatic hypotension. If volume expansion with fluids plus these other countermeasures do not correct the hypotension, then the administration of pressor agents other than epinephrine should be considered. Epinephrine may paradoxically decrease the blood pressure in patients treated with INAPSINE due to the alpha-adrenergic blocking action of INAPSINE.

Since INAPSINE may decrease pulmonary arterial pressure, this fact should be considered by those who conduct diagnostic or surgical procedures where interpretation of pulmonary arterial pressure measurements might determine final management of the patient.

Vital signs should be monitored routinely.

When the EEG is used for postoperative monitoring, it may be found that the EEG pattern returns to normal slowly.

**Impaired Hepatic or Renal Function:** INAPSINE should be administered with caution to patients with liver and kidney dysfunction because of the importance of these organs in the metabolism and excretion of drugs.

**Pheochromocytoma:** In patients with diagnosed/suspected pheochromocytoma, severe hypertension and tachycardia have been observed after the administration of INAPSINE (droperidol).

**Drug Interactions:** Other CNS depressant drugs (e.g. barbiturates, tranquilizers, opioids and general anesthetics) have additive or potentiating effects with INAPSINE. When patients have received such drugs, the dose of INAPSINE required will be less than usual. Following the administration of INAPSINE, the dose of other CNS depressant drugs should be reduced.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** No carcinogenicity studies have been carried out with INAPSINE. The micronucleus test in female rats revealed no mutagenic effects in single oral doses as high as 160 mg/kg. An oral study in rats (Segment I) revealed no impairment of fertility in either male or females at 0.63, 2.5 and 10 mg/kg doses (approximately 2, 9 and 36 times maximum recommended human iv/im dosage).

**Pregnancy - Category C:** INAPSINE administered intravenously has been shown to cause a slight increase in mortality of the newborn rat at 4.4 times the upper human dose. At 44 times the upper human dose, mortality rate was comparable to that for control animals. Following intramuscular administration, increased mortality of the offspring at 1.8 times the upper human dose is attributed to CNS depression in the dams who neglected to

remove placentae from their offspring. INAPSINE has not been shown to be teratogenic in animals. There are no adequate and well-controlled studies in pregnant women. INAPSINE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Labor and Delivery:** There are insufficient data to support the use of INAPSINE in labor and delivery. Therefore, such use is not recommended.

**Nursing Mothers:** It is not known whether INAPSINE is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when INAPSINE is administered to a nursing mother.

**Pediatric Use:** The safety of INAPSINE in children younger than two years of age has not been established.

### **ADVERSE REACTIONS**

The most common somatic adverse reactions reported to occur with INAPSINE (droperidol) are mild to moderate hypotension and tachycardia, but these effects usually subside without treatment. If hypotension occurs and is severe or persists, the possibility of hypovolemia should be considered and managed with appropriate parenteral fluid therapy.

The most common behavioral adverse effects of INAPSINE (droperidol) include dysphoria, postoperative drowsiness, restlessness, hyperactivity and anxiety, which can either be the result of an inadequate dosage (lack of adequate treatment effect) or of an adverse drug reaction (part of the symptom complex of akathisia).

Care should be taken to search for extrapyramidal signs and symptoms (dystonia, akathisia, oculogyric crisis) to differentiate these different clinical conditions. When extrapyramidal symptoms are the cause, they can usually be controlled with anticholinergic agents.

Postoperative hallucinatory episodes (sometimes associated with transient periods of mental depression) have also been reported.

Other less common reported adverse reactions include anaphylaxis, dizziness, chills and/or shivering, laryngospasm, and bronchospasm.

Elevated blood pressure, with or without pre-existing hypertension, has been reported following administration of INAPSINE combined with SUBLIMAZE (fentanyl citrate) or other parenteral analgesics. This might be due to unexplained alterations in sympathetic activity following large doses; however, it is also frequently attributed to anesthetic or surgical stimulation during light anesthesia.

### **OVERDOSAGE**

**Manifestations:** The manifestations of INAPSINE (droperidol) overdose are an extension of its pharmacologic actions.

**Treatment:** In the presence of hypoventilation or apnea, oxygen should be administered and respiration should be assisted or controlled as indicated. A patent airway must be maintained; an oropharyngeal airway or endotracheal tube might be indicated. The patient should be carefully observed for 24 hours; body warmth and adequate fluid intake should be maintained. If hypotension occurs and is severe or persists, the possibility of hypovolemia should be considered and managed with appropriate parenteral fluid therapy (see PRECAUTIONS).

If significant extrapyramidal reactions occur in the context of an overdose, an anticholinergic should be administered.

The intravenous LD<sub>50</sub> of INAPSINE is 20-43 mg/kg in mice; 30 mg/kg in rats; 25 mg/kg in dogs and 11-13 mg/kg in rabbits. The intramuscular LD<sub>50</sub> of INAPSINE is 195 mg/kg in mice; 104-110 mg/kg in rats; 97 mg/kg in rabbits and 200 mg/kg in guinea pigs.

### **DOSAGE AND ADMINISTRATION**

**Dosage should be individualized.** Some of the factors to be considered in determining the dose are age, body weight, physical status, underlying pathological condition, use of other drugs, type of anesthesia to be used and the surgical procedure involved.

Vital signs should be monitored routinely.

#### **Usual Adult Dosage**

- I. **Premedication** - (to be appropriately modified in the elderly, debilitated and those who have received other depressant drugs) 2.5 to 10 mg (1 to 4 mL) may be administered intramuscularly 30 to 60 minutes preoperatively.
- II. **Adjunct to General Anesthesia** -  
*Induction* - 2.5 mg (1 mL) per 20 to 25 pounds may be administered (usually intravenously) along with an analgesic and/or general anesthetic. Smaller doses may be adequate. The total amount of INAPSINE

(droperidol) administered should be titrated to obtain the desired effect based on the individual patient's response.

*Maintenance* - 1.25 to 2.5 mg (0.5 to 1 mL) usually intravenously.

III. *Use without a general anesthetic in diagnostic procedures* - Administer the usual I.M. premedication 2.5 to 10 mg (1 to 4 mL) 30 to 60 minutes before the procedure. Additional 1.25 to 2.5 mg (0.5 to 1 mL) amounts of INAPSINE may be administered, usually intravenously.

NOTE: When INAPSINE is used in certain procedures, such as bronchoscopy, appropriate topical anesthesia is still necessary.

IV. *Adjunct to regional anesthesia* - 2.5 to 5 mg (1 to 2 mL) may be administered intramuscularly or slowly intravenously when additional sedation is required.

#### **Usual Children's Dosage**

For children two to 12 years of age, a reduced dose as low as 1.0 to 1.5 mg (0.4 to 0.6 mL) per 20 to 25 pounds is recommended for premedication or for induction of anesthesia.

See WARNINGS and PRECAUTIONS for use of INAPSINE with other CNS depressants and in patients with altered response.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If such abnormalities are observed, the drug should not be administered.

#### **HOW SUPPLIED**

INAPSINE (droperidol) Injection is available as:

NDC 11098-010-01. 2.5 mg/mL, 1 mL ampoules in packages of 10

NDC 11098-010-02. 2.5 mg/mL, 2 mL ampoules in packages of 10

NDC 11098-531-01. 2.5 mg/mL, 1 mL vials in packages of 25

NDC 11098-531-02. 2.5 mg/mL, 2 mL vials in packages of 25

PROTECT FROM LIGHT. STORE AT ROOM TEMPERATURE 15°C-25°C (59°F-77°F).



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