

Use in Hepatic Impairment

Studies in patients with hepatic impairment have not been conducted. Haloperidol concentrations may increase in hepatically impaired patients, because it is primarily metabolized by the liver and protein binding may decrease.

ADVERSE REACTIONS

The following adverse reactions are discussed in more detail in other sections of the labeling:
•WARNINGS, Increased mortality in Elderly Patients with Dementia-Related Psychosis

- WARNINGS, Cardiovascular Effects
- WARNINGS, Tardive Dyskinesia
- WARNINGS, Neuroleptic Malignant Syndrome
- WARNINGS, Hypersensitivity Reactions
- WARNINGS, Falls
- WARNINGS, Combined Use of Haloperidol and Lithium
- WARNINGS, General
- PRECAUTIONS, Leukopenia, Neutropenia, and Agranulocytosis
- PRECAUTIONS, Other
- PRECAUTIONS, Usage in Pregnancy

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug, and may not reflect the rates observed in practice. The data described below reflect exposure to haloperidol in 410 patients who participated in 13 clinical trials with haloperidol decanoate (15 to 500 mg/month) in the treatment of schizophrenia or schizoaffective disorder. These clinical trials comprised:

- 1 double-blind, active comparator-controlled trial with fluphenazine decanoate.
- 2 trials comparing the decanoate formulation to oral haloperidol.
- 9 open-label trials.
- 1 dose-response trial.

The most common adverse reactions in haloperidol decanoate-treated patients in the double-blind, active comparator-controlled clinical trial with fluphenazine decanoate (≥5%) were: Parkinsonism, and oculogyric crisis.

Adverse Reactions Reported at ≥1% Incidence in a Double-Blind Active Comparator-Controlled Clinical Trial

Adverse reactions occurring in ≥1% of haloperidol decanoate-treated patients in a double-blind, clinical trial with the active comparator fluphenazine decanoate are shown in Table 1.

Table 1. Adverse Reactions Reported by ≥1% of Haloperidol Decanoate-treated Patients in a Double- Blind Active Comparator-Controlled Clinical Trial with Fluphenazine Decanoate

System/Organ Class Adverse Reaction	Haloperidol decanoate (n=36) %	Fluphenazine decanoate (n=36) %
Gastrointestinal Disorders		
Abdominal pain	2.8	0
Nervous System Disorders		
Extrapyramidal disorder ^a :		
Parkinsonism	30.6	44.4
Oculogyric crisis	5.6	0
Akinesia	2.8	22.2
Akathisia	2.8	13.9
Tremor	2.8	0
Headache	2.8	0

^a Precise incidence for extrapyramidal disorder cannot be determined; reporting rates of some individual symptoms of extrapyramidal disorder are lower for haloperidol decanoate than for the active comparator, but the terms are included here because the events are considered associated with the drug

Additional Adverse Reactions Reported in Double-Blind, Comparator, Open-Label and Dose-Response Clinical Trials

Additional adverse reactions that are listed below were reported by haloperidol decanoate-treated patients in comparator, open-label, and dose-response clinical trials, or at <1% incidence in a double-blind, active comparator-controlled clinical trial with fluphenazine decanoate.

Cardiac Disorders: Tachycardia
Endocrine Disorders: Hyperprolactinemia
Eye Disorders: Vision blurred
Gastrointestinal Disorders: Constipation, Dry mouth, Salivary hypersecretion
General Disorders and Administration Site Conditions: Injection site reaction
Investigations: Weight increased
Musculoskeletal and Connective Tissue Disorders: Muscle rigidity
Nervous System Disorders: Dyskinesia, Dystonia, Cogwheel rigidity, Hypertonia, Masked Facies, Sedation, Somnolence
Reproductive System and Breast Disorders: Erectile dysfunction

Adverse Reactions Identified in Clinical Trials with Haloperidol (Non-Decanoate Formulations)

The adverse reactions listed below were identified with non-decanoate formulations, and reflect exposure to the active moiety haloperidol in the following:

- 284 patients who participated in 3 double-blind, placebo-controlled clinical trials with haloperidol (injection or oral formulation, 2 to 20 mg/day); two trials were in the treatment of schizophrenia and one in the treatment of bipolar disorder.
- 1295 patients who participated in 16 double-blind, active comparator-controlled clinical trials with haloperidol (injection or oral formulation, 1 to 45 mg/day) in the treatment of schizophrenia.

Musculoskeletal and Connective Tissue Disorders: Torticollis, Trismus, Muscle twitching
Nervous System Disorders: Neuroleptic malignant syndrome, Tardive dyskinesia, Hyperkinesia, Hypokinesia, Dizziness, Nystagmus
Psychiatric Disorders: Loss of libido, Restlessness
Reproductive System and Breast Disorders: Amenorrhea, Galactorrhea, Dysmenorrhea, Menorrhagia, Breast discomfort
Skin and Subcutaneous Tissue Disorders: Acneiform skin reactions
Vascular Disorders: Hypotension, Orthostatic hypotension

Postmarketing Experience

The following adverse reactions relating to the active moiety haloperidol have been identified during postapproval use of haloperidol or haloperidol decanoate. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Blood and Lymphatic System Disorders: Pancytopenia, Agranulocytosis, Thrombocytopenia, Leukopenia, Neutropenia

Cardiac Disorders: Ventricular fibrillation, Torsade de pointes, Ventricular tachycardia, Extrasystoles
Endocrine Disorders: Inappropriate antidiuretic hormone secretion
Gastrointestinal Disorders: Vomiting, Nausea
General Disorders and Administration Site Conditions: Sudden death, Face edema, Edema, Hyperthermia, Hypothermia, Injection site abscess
Hepatobiliary Disorders: Acute hepatic failure, Hepatitis, Cholestasis, Jaundice, Liver function test abnormal
Immune System Disorders: Anaphylactic reaction, Hypersensitivity
Investigations: Electrocardiogram QT prolonged, Weight decreased
Metabolic and Nutritional Disorders: Hypoglycemia
Musculoskeletal and Connective Tissue Disorders: Rhabdomyolysis
Nervous System Disorders: Convulsion, Opisthotonus, Tardive dystonia
Pregnancy, Puerperium and Perinatal Conditions: Drug withdrawal syndrome neonatal
Psychiatric Disorders: Agitation, Confusional state, Depression, Insomnia
Renal and Urinary Disorders: Urinary retention
Reproductive System and Breast Disorders: Priapism, Gynecomastia
Respiratory, Thoracic and Mediastinal Disorders: Laryngeal edema, Bronchospasm, Laryngospasm, Dyspnea
Skin and Subcutaneous Tissue Disorders: Dermatitis exfoliative, Hypersensitivity vasculitis, Photosensitivity reaction, Urticaria, Pruritis, Rash, Hyperhidrosis

OVERDOSAGE

While overdosage is less likely to occur with a parenteral than with an oral medication, information pertaining to haloperidol is presented, modified only to reflect the extended duration of action of haloperidol decanoate.

Manifestations

In general, the symptoms of overdosage would be an exaggeration of known pharmacologic effects and adverse reactions, the most prominent of which would be: 1) severe extrapyramidal reactions, 2) hypotension, or 3) sedation. The patient would appear comatose with respiratory depression and hypotension which could be severe enough to produce a shock-like state. The extrapyramidal reactions would be manifested by muscular weakness or rigidity and a generalized or localized tremor, as demonstrated by the akinetic or agitans types, respectively. With accidental overdosage, hypertension rather than hypotension occurred in a two-year old child. The risk of ECG changes associated with torsade de pointes should be considered. (For further information regarding torsade de pointes, please refer to ADVERSE REACTIONS.)

Treatment

Since there is no specific antidote, treatment is primarily supportive. A patent airway must be established by use of an oropharyngeal airway or endotracheal tube or, in prolonged cases of coma, by tracheostomy. Respiratory depression may be counteracted by artificial respiration and mechanical respirators. Hypotension and circulatory collapse may be counteracted by use of intravenous fluids, plasma, or concentrated albumin, and vasopressor agents such as metaraminol, phenylephrine and norepinephrine. Epinephrine should not be used. In case of severe extrapyramidal reactions, antiparkinson medication should be administered, and should be continued for several weeks, and then withdrawn gradually as extrapyramidal symptoms may emerge. ECG and vital signs should be monitored especially for signs of Q-T prolongation or dysrhythmias and monitoring should continue until the ECG is normal. Severe arrhythmias should be treated with appropriate anti-arrhythmic measures.

DOSE AND ADMINISTRATION

Haloperidol decanoate injection, 50 mg (base)/mL and haloperidol decanoate injection, 100 mg (base)/mL should be administered by deep intramuscular injection. A 21 gauge needle is recommended. The maximum volume per injection site should not exceed 3 mL. DO NOT ADMINISTER INTRAVENOUSLY.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Haloperidol decanoate injection, 50 mg (base)/mL and haloperidol decanoate injection, 100 mg (base)/mL are intended for use in schizophrenic patients who require prolonged parenteral antipsychotic therapy. These patients should be previously stabilized on antipsychotic medication before considering a conversion to haloperidol decanoate, USP. Furthermore, it is recommended that patients being considered for haloperidol decanoate, USP therapy have been treated with, and tolerate well, short-acting haloperidol, USP in order to reduce the possibility of an unexpected adverse sensitivity to haloperidol, USP. Close clinical supervision is required during the initial period of dose adjustment in order to minimize the risk of overdosage or reappearance of psychotic symptoms before the next injection. During dose adjustment or episodes of exacerbation of symptoms of schizophrenia, haloperidol decanoate, USP therapy can be supplemented with short-acting forms of haloperidol, USP.

The dose of haloperidol decanoate injection, 50 mg (base)/mL or haloperidol decanoate injection, 100 mg (base)/mL should be expressed in terms of its haloperidol, USP content. The starting dose of haloperidol decanoate, USP should be based on the patient's age, clinical history, physical condition, and response to previous antipsychotic therapy. The preferred approach to determining the minimum effective dose is to begin with lower initial doses and to adjust the dose upward as needed. For patients previously maintained on low doses of antipsychotics (e.g. up to the equivalent of 10 mg/day oral haloperidol), it is recommended that the initial dose of haloperidol decanoate, USP be 10-15 times the previous daily dose in oral haloperidol equivalents; limited clinical experience suggests that lower initial doses may be adequate.

Initial Therapy

Conversion from oral haloperidol to haloperidol decanoate, USP can be achieved by using an initial dose of haloperidol decanoate, USP that is 10 to 20 times the previous daily dose in oral haloperidol equivalents.

In patients who are elderly, debilitated, or stable on low doses of oral haloperidol (e.g. up to the equivalent of 10 mg/day oral haloperidol), a range of 10 to 15 times the previous daily dose in oral haloperidol equivalents is appropriate for initial conversion.

In patients previously maintained on higher doses of antipsychotics for whom a low dose approach risks recurrence of psychiatric decompensation and in patients whose long-term use of haloperidol, USP has resulted in a tolerance to the drug, 20 times the previous daily dose in oral haloperidol equivalents should be considered for initial conversion, with downward titration on succeeding injections.

The initial dose of haloperidol decanoate, USP should not exceed 100 mg regardless of previous antipsychotic dose requirements. If, therefore, conversion requires more than 100 mg of haloperidol decanoate, USP as an initial dose, that dose should be administered in two injections, i.e. a maximum of 100 mg initially followed by the balance in 3 to 7 days.

Maintenance Therapy

The maintenance dosage of haloperidol decanoate, USP must be individualized with titration upward or downward based on therapeutic response. The usual maintenance range is 10 to 15 times the previous daily dose in oral haloperidol equivalents dependent on the clinical response of the patient.

HALOPERIDOL DECANOATE, USP DOSING RECOMMENDATIONS

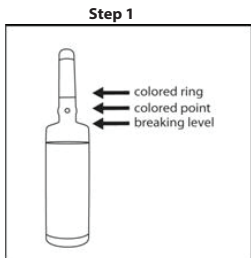
Patients	Monthly 1 st Month	Maintenance
Stabilized on low daily oral doses (up to 10 mg/day) Elderly or Debilitated	10-15 x Daily Oral Dose	10-15 x Previous Daily Oral Dose
High dose Risk of relapse Tolerant to oral haloperidol	20 x Daily Oral Dose	10-15 x Previous Daily Oral Dose

Close clinical supervision is required during initiation and stabilization of haloperidol decanoate, USP therapy. Haloperidol decanoate, USP is usually administered monthly or every 4 weeks. However, variation in patient response may dictate a need for adjustment of the dosing interval as well as the dose (see CLINICAL PHARMACOLOGY).

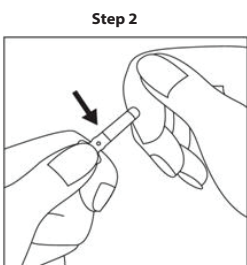
Clinical experience with haloperidol decanoate, USP at doses greater than 450 mg per month has been limited.

INSTRUCTIONS FOR OPENING AMPULE

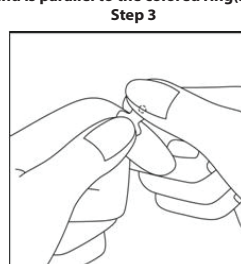
1. Medication often rests in the top part of the ampule. Before breaking the ampule, lightly tap the top of the ampule with your finger until all fluid moves to the bottom portion of the ampule. The ampule has a colored ring(s) and colored point which aids in the placement of fingers while breaking the ampule.



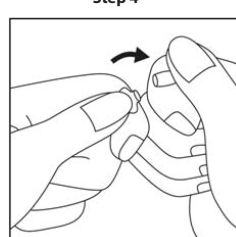
2. Hold the ampule between thumb and index finger with the colored point facing you.



3. Position the index finger of the other hand to support the neck of the ampule. Position the thumb so that it covers the colored point and is parallel to the colored ring(s).



4. Keeping the thumb on the colored point and with the index fingers close together, apply firm pressure on the colored point in the direction of the arrow to snap the ampule open.



HOWSUPPLIED

Haloperidol Decanoate Injection is clear, pale yellow color solution supplied as follows:

NDC No.	Strength	Size
70069-030-03	50 mg (base)/mL	1 mL fill in 1 mL Ampule, in packages of 3
70069-030-05		1 mL fill in 1 mL Ampule, in packages of 5
70069-031-05	100 mg (base)/mL	1 mL fill in 1 mL Ampule, in packages of 5
70069-381-01	50 mg (base)/mL	1 mL fill in 2 mL Single- Dose Vial, in packages of 1
70069-381-10		1 mL fill in 2 mL Single- Dose Vial, in packages of 10
70069-382-05		5 mL fill in 5 mL Multiple- Dose Vial, in packages of 5
70069-382-01		5 mL fill in 5 mL Multiple- Dose Vial, in package of 1
70069-383-01	100 mg (base)/mL	1 mL fill in 2 mL Single- Dose Vial, in packages of 1
70069-383-05		1 mL fill in 2 mL Single- Dose Vial, in packages of 5
70069-383-10		1 mL fill in 2 mL Single- Dose Vial, in packages of 10
70069-384-05		5 mL fill in 5 mL Multiple- Dose Vial, in packages of 5
70069-384-01		5 mL fill in 5 mL Multiple- Dose Vial, in package of 1

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature]. Do not refrigerate or freeze. Protect from Light.

Keep out of reach of children.

For Product Inquiry call 1-800-417-9175.

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