Haloperidol Decanoate Injection

Haloperidol Decanoate Injection is available only by an order that includes the創作下文提到的關於藥物治療的相關信息。Drug treatment should be considered for patients who do not respond to the initial treatment. However, some patients may require treatment despite the presence of the syndrome. For further information about the duration of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS.

Neuroleptic Malignant Syndrome (NMS)
A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, mental status changes (e.g., confusion, encephalopathy), muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and hypotension) and may incline toward a neuroleptic malignant syndrome resembling a neuroleptic malignant syndrome. The clinical presentation includes both central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

Tardive Dyskinesia

A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their propensity to cause tardive dyskinesia is unknown.

Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is thereby masked, which may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is thereby masked.

The patient should be carefully monitored, since recurrences of NMS have been reported. Hyperpyrexia and heat stroke, not associated with the above symptom complex, have also been reported with haloperidol.

PRECAUTIONS
Haloperidol Decanoate should be administered cautiously to patients:

- with severe cardiovascular disorders, because of the possibility of transient hypotension and/or precipitation of organic heart disease. Should hypotension occur and a vasopressor be required, metaraminol, a sympathomimetic, should be used rather than phenylephrine, since haloperidol may block its vasopressor activity, and paradoxical further lowering of the blood pressure may occur. Instead, metaraminol, phenylephrine, or norepinephrine should be used.

- receiving antipsychotic medications, with a history of seizures, or with severe cardiovascular disorders, because of the possibility of transient hypotension and/or precipitation of organic heart disease. Should hypotension occur and a vasopressor be required, metaraminol, a sympathomimetic, should be used rather than phenylephrine, since haloperidol may block its vasopressor activity, and paradoxical further lowering of the blood pressure may occur. Instead, metaraminol, phenylephrine, or norepinephrine should be used.

- with known allergies, or with a history of allergic reactions to drugs.

- receiving anticonvulsant medications, with a history of seizures, or with severe cardiovascular disorders, because of the possibility of transient hypotension and/or precipitation of organic heart disease. Should hypotension occur and a vasopressor be required, metaraminol, a sympathomimetic, should be used rather than phenylephrine, since haloperidol may block its vasopressor activity, and paradoxical further lowering of the blood pressure may occur. Instead, metaraminol, phenylephrine, or norepinephrine should be used.

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**PACKAGE INSERT**

with haloperidol, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate.

**CNS Effects**

Extrapyramidal Symptoms (EPS)

EPS during the administration of haloperidol have been reported frequently, often during the first few days of treatment. EPS can be categorized generally as Parkinson-like symptoms, akathisia, or dystonia (including ophthalmoptosis and oculocutaneous crisis). While all can occur at relatively low doses, they occur more frequently and with greater severity at higher doses. The symptoms may be controlled with dose reductions or administration of antiparkinson drugs such as benztropine mesylate USP or trihexyphenidyl hydrochloride USP. It should be noted that persistent EPS have been reported; the drug may have to be discontinued in such cases.

Withdrawal Emergent Neurological Signs

Generally, patients receiving short-term therapy experience no problems with abrupt discontinuation of antipsychotic drugs. However, some patients on maintenance treatment experience transient dystonic signs after abrupt withdrawal. In certain of these cases the dystonic movements are indistinguishable from the syndrome described below under "Tardive Dyskinesia" of long duration. Although the long acting properties of haloperidol decanoate provide gradual withdrawal, it is not known whether gradual withdrawal of antipsychotic drugs will reduce the rate of occurrence of withdrawal emergent neurological signs.

Tardive Dyskinesia

As with all antipsychotic agents haloperidol has been associated with persistent dystokinesia. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dystonic movements, may appear in some patients on long-term therapy with haloperidol decanoate or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients with a higher daily dose of haloperidol decanoate, especially females. The symptoms are persistent and in some patients appear irreversible. The syndrome is characterized by rhythmic involuntary movements of tongue, face, arm, leg, (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk.

There is no known effective treatment for tardive dyskinesia. Antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked.

It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop.

Tardive Dystonia

Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of dystonic movements, is often persistent, and has the potential of becoming irreversible.

Other CNS Effects

Insomnia, moodiness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

Body as a Whole

Neuropsychiatric malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with haloperidol. (See WARNINGS for further information concerning NMS.)

Cardiovascular Effects

Tachycardia, hypertension, hypotension, and ECG changes including prolongation of the Q-T interval and ECG pattern changes compatible with the polymorphic configuration of torsades de pointes.

Hematologic Effects

Reports have appeared citing the occurrence of mild and usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphocytosis. Agranulocytosis has rarely been reported to have occurred with the use of haloperidol, and then only in association with other medication.

Liver Effects

Impaired liver function and/or jaundice have been reported.

Dermatologic Reactions

Maculopapular and exfoliant skin reactions and isolated cases of photosensitivity and loss of hair.

Endocrine Disorders

Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyperthermia.

Gastrointestinal Effects

Anorexia, constipation, diarrhea, hyperabsorption, dyspepsia, nausea and vomiting.

Respiratory Effects

Laryngospasm, bronchospasm and increased depth of respiration.

Special Senses

Catarsis, retinopathy and visual disturbances.

Other

Cases of sudden and unexpected death have been reported in association with the administration of haloperidol. The nature of the evidence makes it impossible to determine definitively what role, if any, haloperidol played in the outcome of the reported cases. The possibility that haloperidol caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychiatric patients when they are untreated or when they are treated with other antipsychotic drugs.

Postmarketing Events

Hyperammonemia has been reported in a 5 year old child with cihollineuria, an inherited disorder of ammonia excretion, following treatment with haloperidol.

OVERDOSE

While overdose 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 overdose 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 akinetik or agitans types, respectively. With accidental overdose, hypotension rather than hypotension occurred in a 2-year old child. The risk of ECG changes associated with torsades de pointes should be considered. (For further information regarding torsades de pointes, please refer to ADVERSE REACTIONS.)

Treatment

Since there is no specific antidote, treatment is primarily supportive. A patent airway must be maintained 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 countered 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.

DOSAGE AND ADMINISTRATION

Haloperidol Decanoate Injection should be administered by deep intramuscular injection. A 21 gauge needle is recommended. The maximum volume of 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 is intended for use in chronic psychotic patients who require prolonged parenteral antipsychotic therapy. These patients should be previously stabilized to antipsychotic medication before considering a conversion to haloperidol decanoate. Furthermore, it is recommended that patients who have been considered for haloperidol decanoate therapy have been treated with, and tolerate well, short-acting haloperidol in order to reduce the possibility of an unexpected adverse sensitivity to haloperidol. Close clinical supervision is required during the initial period of dose adjustment in order to minimize the risk of overdose or reappearance of psychotic symptoms before the next injection. During dose adjustment or episodes of exacerbation of symptoms of schizophrenia, haloperidol decanoate therapy can be supplemented with short-acting forms of haloperidol.

The dose of Haloperidol Decanoate Injection should be expressed in terms of its haloperidol content. The starting dose of haloperidol decanoate 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 be 10 to 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 can be achieved by using an initial dose of haloperidol decanoate 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 the maintenance dosage of haloperidol decanoate must be individualized. Maintenance Therapy

Haloperidol decanoate 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 at doses greater than 450 mg per month has been limited.

HOW SUPPLIED

Haloperidol Decanoate Injection, 50 mg/ml, 50 mg haloperidol as 70.5 mg per ml haloperidol decanoate in 5 ml multiple dose vials and 1 ml single dose vials packaged in cartons of 10.

Haloperidol Decanoate Injection, 100 mg/ml, 100 mg haloperidol as 141 mg per ml haloperidol decanoate in 5 ml multiple dose vials and 1 ml single dose vials packaged in cartons of ten.

Store at 20° - 25°C (68° - 77°F) [See USP Controlled Room Temperature]. Do not refreeze or freeze.

Protect from light. Retain vial in carton until contents are used.

Mfg by: Apotex Inc.
Toronto, Ontario
Canada M6L 1T9

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