164 x 190 mm

82 mm

190 mm

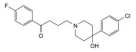
POM

HALOPERIDOL
INJECTION BP 5mg/ml

For I.M. / I.V. Use Only

COMPOSITION:
Each ml contains:
Haloperidol BP ..... 5 mg
Water for injection BP ..... q.s.

DESCRIPTION
Haloperidol Injection BP is available as a sterile parenteral form for intramuscular injection. Haloperidol is the first of the butyrophenone series of major antipsychotics. The chemical designation is 4-(4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl)-1-(4-fluorophenyl)butan-1-one and it has the following structural formula:



The molecular formula of Haloperidol is C21H23ClFNO2 with a molecular weight of 375.9.

CLINICALPHARMACOLOGY
Haloperidol is an antipsychotic belonging to the butyrophenones group. It is a potent central dopamine type 2 receptor antagonist, and at recommended doses, has low alpha-1 antiadrenergic activity and no antihistaminergic or anticholinergic activity.
Haloperidol suppresses delusions and hallucinations as a direct consequence of blocking dopaminergic signalling in the mesolimbic pathway. The central dopamine blocking effect has activity on the basal ganglia (nigrostriatal bundles). Haloperidol causes efficient psychomotor sedation, which explains the favourable effect on mania and other agitation syndromes.
The activity on the basal ganglia probably underlies the undesirable extrapyramidal motor effects (dystonia, akathisia and parkinsonism).
The antidopaminergic effects of haloperidol on lactotropes in the anterior pituitary explain hyperprolactinaemia due to inhibition of dopamine-mediated tonic inhibition of prolactin secretion. Additionally, the antidopaminergic effect on the chemoreceptor-trigger zone of the area postrema explains the activity against nausea and vomiting.

INDICATIONS AND USAGE
Haloperidol Injection BP is indicated for use in the treatment of schizophrenia.
Haloperidol Injection BP is indicated for the control of tics and vocal utterances of Tourette's Disorder.

DOSAGE AND ADMINISTRATION
There is considerable variation from patient to patient in the amount of medication required for treatment. As with all drugs used to treat schizophrenia, dosage should be individualized according to the needs and response of each patient. Dosage adjustments, either upward or downward, should be carried out as rapidly as practicable to achieve optimum therapeutic control.
To determine the initial dosage, consideration should be given to the patient's age, severity of illness, previous response to other antipsychotic drugs, and any concomitant medication or disease state. Debilitated or geriatric patients, as well as those with a history of adverse reactions to antipsychotic drugs, may require less haloperidol. The optimal response in such patients is usually obtained with more gradual dosage adjustments and at lower dosage levels.

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Parenteral medication, administered intramuscularly in doses of 2 to 5 mg, is utilized for prompt control of the acutely agitated schizophrenic patient with moderately severe to very severe symptoms. Depending on the response of the patient, subsequent doses may be given, administered as often as every hour, although 4 to 8 hour intervals may be satisfactory. The maximum dose is 20 mg/day.

Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Switchover Procedure
An oral form should supplant the injectable as soon as practicable. In the absence of bioavailability studies establishing bioequivalence between these two dosage forms the following guidelines for dosage are suggested. For an initial approximation of the total daily dose required, the parenteral dose administered in the preceding 24 hours may be used. Since this dose is only an initial estimate, it is recommended that careful monitoring of clinical signs and symptoms, including clinical efficacy, sedation, and adverse effects, be carried out periodically for the first several days following the initiation of switchover. In this way, dosage adjustments, either upward or downward, can be quickly accomplished. Depending on the patient's clinical status, the first oral dose should be given within 12 to 24 hours following the last parenteral dose.

CONTRAINDICATIONS
Haloperidol Injection is contraindicated in patients with:
•Severe toxic central nervous system depression or comatose states from any cause.
•Hypersensitivity to this drug – hypersensitivity reactions have included anaphylactic reaction and angioedema.
•Parkinson's disease.
•Dementia with Lewy bodies.

WARNINGS
Increased Mortality in Elderly Patients with Dementia-Related **Psychosis:**
Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebocontrolled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group.
Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. Haloperidol injection is not approved for the treatment of patients with dementia-related psychosis.

Pregnancy
A moderate amount of data on pregnant women indicate no malformative or foeto/ neonatal toxicity of haloperidol. However, there have been isolated case reports of birth defects following foetal exposure to haloperidol, mostly in combination with other medicinal products. Animal studies have shown reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of haloperidol during pregnancy.

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Newborn infants exposed to antipsychotics (including haloperidol) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, it is recommended that newborn infants be monitored carefully.

Breast-feeding
Since haloperidol is excreted in human breast milk, infants should not be nursed during drug treatment with haloperidol.
Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

DRUG INTERACTIONS
Drug-drug interactions can be pharmacodynamic (combined pharmacologic effects) or pharmacokinetic (alteration of plasma levels). The risks of using haloperidol in combination with other drugs have been evaluated as described below.
Pharmacodynamic Interactions
Since QT-prolongation has been observed during haloperidol treatment, caution is advised when prescribing to a patient with QT-prolongation conditions (long QT-syndrome, hypokalemia, electrolyte imbalance) or to patients receiving medications known to prolong the QT-interval or known to cause electrolyte imbalance.
If concomitant antiparkinson medication is required, it may have to be continued after haloperidol is discontinued because of the difference in excretion rates. If both are discontinued simultaneously, extrapyramidal symptoms may occur. The physician should keep in mind the possible increase in intraocular pressure when anticholinergic drugs, including antiparkinson agents, are administered concomitantly with haloperidol.
As with other antipsychotic agents, it should be noted that haloperidol may be capable of potentiating CNS depressants such as anesthetics, opiates and alcohol.
Ketoconazole is a potent inhibitor of CYP3A4. Increases in QTc have been observed when haloperidol was given in combination with the metabolic inhibitors ketoconazole (400 mg/day) and paroxetine (20 mg/day). It may be necessary to reduce the haloperidol dosage.
Pharmacokinetic Interactions
The Effect of Other Drugs on Haloperidol
Haloperidol is metabolized by several routes, including the glucuronidation and the cytochrome P450 enzyme system. Inhibition of these routes of metabolism by another drug may result in increased haloperidol concentrations and potentially increase the risk of certain adverse events, including QT-prolongation.
Drugs Characterized as Substrates, Inhibitors or Inducers of CYP3A4, CYP2D6 or Glucuronidation
In pharmacokinetic studies, mild to moderately increased haloperidol concentrations have been reported when haloperidol was given concomitantly with drugs characterized as substrates or inhibitors of CYP3A4 or CYP2D6 isoenzymes, such as itraconazole, nefazodone, buspirone, venlafaxine, alprazolam, fluvoxamine, quinidine, fluoxetine, sertraline, chlorpromazine, and promethazine.
When prolonged treatment (1 to 2 weeks) with enzyme-inducing drugs such as rifampin or carbamazepine is added to haloperidol therapy, this results in a significant reduction of haloperidol plasma levels.

Rifampin
In a study of 12 schizophrenic patients co-administered oral haloperidol and rifampin, plasma haloperidol levels were decreased by a mean of 70% and mean scores on the Brief Psychiatric Rating Scale were increased from baseline. In 5 other schizophrenic patients treated with haloperidol and rifampin, discontinuation of rifampin produced a mean 3.3-fold increase in haloperidol concentrations.

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Carbamazepine
In a study in 11 schizophrenic patients co-administered haloperidol and increasing doses of carbamazepine, haloperidol plasma concentrations decreased linearly with increasing carbamazepine concentrations.
Thus, careful monitoring of clinical status is warranted when enzyme inducing drugs such as rifampin or carbamazepine are administered or discontinued in haloperidol-treated patients. During combination treatment, the haloperidol dose should be adjusted, when necessary. After discontinuation of such drugs, it may be necessary to reduce the dosage of haloperidol.

Valproate
Sodium valproate, a drug known to inhibit glucuronidation, does not affect haloperidol plasma concentrations.

ADVERSE REACTIONS
Based on the pooled safety data, the most common adverse reactions in haloperidoltreated
patients from these double-blind placebo-controlled clinical trials (≥5%) were:
extrapyramidal disorder, hyperkinesia, tremor, hypertonia, dystonia, and somnolence.
Gastrointestinal Disorders: Constipation, Dry mouth, Salivary hyper secretion
Nervous System Disorders: Extrapyramidal disorder, Hyperkinesia, Tremor, Hypertonia, Dystonia, Bradykinesia, Somnolence
Cardiac Disorders: Tachycardia
Endocrine Disorders: Hyperprolactinemia
Eye Disorders: Vision blurred
Investigations: Weight increased
Musculoskeletal and Connective Tissue Disorders: Torticollis, Trismus, Muscle rigidity, Muscle twitching
Nervous System Disorders: Akathisia, Dizziness, Dyskinesia, Hypokinesia, Neuroleptic malignant syndrome, Nystagmus, Oculogyric crisis, Parkinsonism, Sedation, Tardive dyskinesia
Psychiatric Disorders: Loss of libido, Restlessness
Reproductive System and Breast Disorders: Amenorrhea, Galactorrhea, Dysmenorrhea,
Erectile dysfunction, Menorrhagia, Breast discomfort
Skin and Subcutaneous Tissue Disorders: Acneiform skin reactions
Vascular Disorders: Hypotension, Orthostatic hypotension

STORAGE
Store below 30°C.
Protect from light.
Keep out of reach of children.

PACKING
HALOPERIDOL INJECTION BP 5mg/ml is available in pack of 100 x 1ml and 10 x 1ml Ampoule.

Manufactured in India by
ANGEL BIOGENICS PVT. LIMITED
Shapar-Veraval, Dist. Rajkot - 360 024
At : 46/4-7, Vill. Zak, Tal.Dehgam,
Gandhinagar - 382 305 (India.)

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Front | Back | Back | Front

164.00 mm