## NAME OF THE MEDICINAL PRODUCT

**Tradename**

HALDOL®

**International Non-Proprietary Name (INN)**

haloperidol

## QUALITATIVE AND QUANTITATIVE COMPOSITION

The tablets contain either 1 mg, 2 mg, 5 mg, 10 mg or 20 mg haloperidol.
The oral solution contains 2 mg and 10 mg haloperidol per ml.
The injectable solution contains 5 mg haloperidol per ml.
For excipients, see List of Excipients.

## PHARMACEUTICAL FORM

Tablets.
Oral drops, solution.
Solution for injection.
Appearance***:**

*1 mg tablets*

White, circular, biconvex, cross-scored tablet with the inscription "JANSSEN" on one side.

*2 mg tablets.*

Yellow, circular, biconvex, cross-scored table with the inscription "JANSSEN" on one side.

*5 mg tablets*

Blue, circular, biconvex, cross-scored tablet with the inscription "JANSSEN" on one side**.**

*10 mg tablets*

Yellow, circular, biconvex, half-scored tablet with the inscription "JANSSEN" on one side and "H/10" on the other side.

*20 mg tablets*

White, circular, flat, half-scored tablet with the inscription "JANSSEN" on one side and "H/20" on the other side.

*Due to regulatory and marketing requirements, the tablet may have a specific imprinting.

*2 mg/ml and 10 mg/ml oral solution*

Clear, colourless solution.

*5 mg/ml injectable solution*

Clear, colourless solution, free from visible foreign material.

## CLINICAL PARTICULARS

### Therapeutic Indications

*As a neuroleptic agent in:*

-Delusions and hallucinations in:

- acute and chronic schizophrenia;
- paranoia;
- acute confusion, alcoholism (Korsakoff's syndrome).

-Hypochondriac delusions.

-Personality disorders: paranoid, schizoid, schizotype, antisocial, some “borderline” and other personalities.

*As a psychomotor anti-agitation agent in:*

-Mania, dementia, mental retardation, alcoholism.

-Personality disorders: compulsive, paranoid, histrionic and other personalities.

-Agitation, aggressiveness, and wandering impulsion in the elderly.

-Disorders of behaviour and character in children.

-Choreatic movements.

-Singultus (hiccup).

-Tics, stuttering.

*As an adjuvant in the treatment of severe chronic pain:*

On the basis of its limbic activity, HALDOL often allows the dosage of the analgesic (usually a morphinomimetic) to be reduced.

*As an anti-emetic in:*

Nausea and vomiting of varying origin. HALDOL is the drug of preference if the classical medicines for nausea and vomiting are insufficiently active.

**Posology and Method of Administration**

HALDOL Injection is recommended for IM administration only.

The dosages as suggested below are only averages; one should always try to tailor the dose to the patient’s response. This often implies an upward titration in the acute phase, and a gradual reduction in the maintenance phase, in order to determine the minimal effective dose. Higher doses should only be given to patients responding poorly to lower dosages.

*Adults*

*-As a neuroleptic agent*

- *Acute phase:* acute episodes of schizophrenia, delirium tremens, paranoia, acute confusion, Korsakoff’s syndrome, acute paranoia.
  5 mg IM, may be repeated hourly until sufficient symptom control is achieved or up to a maximum of 20 mg/day. When given orally, doses between 2 and 20 mg/day should be administered either as a single dose or in divided doses.
- *Chronic phase:* chronic schizophrenia, chronic alcoholism, chronic personality disorders.
  1-3 mg orally three times a day, may be increased up to 20 mg per day in divided doses, depending on the response.

*-As a psychomotor anti-agitation agent*

- *Acute phase: mania*, dementia, alcoholism, personality disorders, behaviour and character disorders, singultus, choreatic movements, tics, stuttering.
  5 mg IM may be repeated hourly until sufficient symptom control is achieved or up to a maximum of 20 mg/day.
- *Chronic phase:*
  0.5-1 mg three times a day orally, may be increased to 2-3 mg three times a day, if required, to obtain a response.

*-As an adjuvant in chronic pain therapy*

0.5-1 mg three times a day orally, may be adjusted if needed.

*-As an anti-emetic*

- Centrally induced vomiting: 5 mg IM.
- Prophylaxis of postoperative vomiting: 2.5-5 mg IM at the end of surgery.

*In elderly patients*

Treatment should start with half the dosage stated for adults and adjusted according to the results if necessary.

*In children*

0.1 mg/3 kg body weight three times a day orally; may be adjusted if needed.

**Contraindications**

Comatose state; CNS depression due to alcohol or other depressant drug; Parkinson's disease; known hypersensitivity to HALDOL; lesion of the basal ganglia.

**Special Warnings and Special Precautions for Use**

Rare cases of sudden death have been reported in psychiatric patients receiving antipsychotic drugs, including HALDOL.

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled 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.

*Cardiovascular effects*

Very rare reports of QT prolongation and/or ventricular arrhythmias, in addition to rare reports of sudden death, have been reported with haloperidol. They may occur more frequently with high doses and in predisposed patients.

As QT-prolongation has been observed during HALDOL treatment, caution is advised in patients with QT-prolonging conditions (long QT-syndrome, hypokalaemia, electrolyte imbalance, drugs known to prolong QT, cardiovascular diseases, family history of QT prolongation), especially if HALDOL is given parenterally (see Interactions with Other Medicinal Products and Other Forms of Interaction). The risk of QT prolongation and/or ventricular arrhythmias may be increased with higher doses (see Undesirable Effects and Overdose) or with parenteral use, particularly intravenous administration. Continuous ECG monitoring should be performed for QT interval prolongation and for serious cardiac dysrhythmias if HALDOL is administered intravenously.

HALDOL Injection is recommended for IM administration only.

Tachycardia and hypotension have also been reported in occasional patients.

*Neuroleptic malignant syndrome*

In common with other antipsychotic drugs, HALDOL has been associated with neuroleptic malignant syndrome: a rare idiosyncratic response characterized by hyperthermia, generalised muscle rigidity, autonomic instability, altered consciousness. Hyperthermia is often an early sign of this syndrome. Antipsychotic treatment should be withdrawn immediately and appropriate supportive therapy and careful monitoring instituted.

*Tardive dyskinesia*

As with all antipsychotic agents, tardive dyskinesia may appear in some patients on long-term therapy or after drug discontinuation. The syndrome is mainly characterized by rhythmic involuntary movements of the tongue, face, mouth or jaw. The manifestations may be permanent in some patients. The syndrome may be masked when treatment is reinstituted, when the dosage is increased or when a switch is made to a different antipsychotic drug. Treatment should be discontinued as soon as possible.

*Extrapyramidal symptoms*

In common with all neuroleptics, extrapyramidal symptoms may occur, e.g. tremor, rigidity, hypersalivation, bradykinesia, akathisia, acute dystonia.

Antiparkinson drugs of the anticholinergic type may be prescribed as required, but should not be prescribed routinely as a preventive measure. If concomitant antiparkinson medication is required, it may have to be continued after stopping HALDOL if its excretion is faster than that of HALDOL in order to avoid the development or aggravation of extrapyramidal symptoms. The physician should keep in mind the possible increase in intraocular pressure when anticholinergic drugs, including antiparkinson agents, are administered concomitantly with HALDOL.

*Seizures/Convulsions*

It has been reported that seizures can be triggered by HALDOL. Caution is advised in patients suffering from epilepsy and in conditions predisposing to convulsions (e.g., alcohol withdrawal and brain damage).

*Hepatobiliary concerns*

As HALDOL is metabolized by the liver, caution is advised in patients with liver disease. Isolated cases of liver function abnormalities or hepatitis, most often cholestatic, have been reported.

*Endocrine system concerns*

Thyroxin may facilitate HALDOL toxicity. Antipsychotic therapy in patients with hyperthyroidism should be used only with great caution and must always be accompanied by therapy to achieve a euthyroid state.

Hormonal effects of antipsychotic neuroleptic drugs include hyperprolactinaemia, which may cause galactorrhoea, gynaecomastia and oligo- or amenorrhoea. Very rare cases of hypoglycaemia and of Syndrome of Inappropriate ADH Secretion have been reported.

*Venous thromboembolism*

Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with HALDOL and preventive measures undertaken.

*Additional considerations*

In schizophrenia, the response to antipsychotic drug treatment may be delayed. Also, if drugs are withdrawn, recurrence of symptoms may not become apparent for several weeks or months. Acute withdrawal symptoms including nausea, vomiting and insomnia have very rarely been described after abrupt cessation of high doses of antipsychotic drugs. Relapse may also occur and gradual withdrawal is advisable.

As with all antipsychotic agents, HALDOL should not be used alone where depression is predominant. It may be combined with antidepressants to treat those conditions in which depression and psychosis coexist.

**Interactions with Other Medicinal Products and Other Forms of Interaction**

As with other antipsychotics, caution is advised when prescribing haloperidol with medications known to prolong the QT interval.
Haloperidol is metabolized by several routes, including glucuronidation and the cytochrome P450 enzyme system (particularly CYP 3A4 or CYP 2D6). Inhibition of these routes of metabolism by another drug or a decrease in CYP 2D6 enzyme activity may result in increased haloperidol concentrations and an increased risk of adverse events, including QT-prolongation. 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 CYP 3A4 or CYP 2D6 isozymes, such as, itraconazole, nefazodone, buspirone, venlafaxine, alprazolam, fluvoxamine, quinidine, fluoxetine, sertraline, chlorpromazine, and promethazine. A decrease in CYP2D6 enzyme activity may result in increased haloperidol concentrations. Increases in QTc have been observed when haloperidol was given with a combination of the metabolic inhibitors ketoconazole (400 mg/day) and paroxetine (20 mg/day). It may be necessary to reduce the haloperidol dosage.
Caution is advised when used in combination with drugs known to cause electrolyte imbalance.
*Effect of Other Drugs on Haloperidol*
When prolonged treatment with enzyme-inducing drugs such as carbamazepine, phenobarbital, rifampicine is added to HALDOL therapy, this results in a significant reduction of haloperidol plasma levels. Therefore, during combination treatment, the HALDOL dose should be adjusted, when necessary. After stopping such drugs, it may be necessary to reduce the dosage of HALDOL.
Sodium valproate, a drug known to inhibit glucuronidation, does not affect haloperidol plasma concentrations.
*Effect of Haloperidol on Other Drugs*
In common with all neuroleptics, HALDOL can increase the central nervous system depression produced by other CNS-depressant drugs, including alcohol, hypnotics, sedatives or strong analgesics. An enhanced CNS effect, when combined with methyldopa, has also been reported.
HALDOL may antagonise the action of adrenaline and other sympathomimetic agents and reverse the blood-pressure-lowering effects of adrenergic-blocking agents such as guanethidine.
HALDOL may impair the antiparkinson effects of levodopa.
Haloperidol is an inhibitor of CYP 2D6. HALDOL inhibits the metabolization of tricyclic antidepressants, thereby increasing plasma levels of these drugs.
*Other Forms of Interaction*
In rare cases the following symptoms were reported during the concomitant use of lithium and haloperidol: encephalopathy, extrapyramidal symptoms, tardive dyskinesia, neuroleptic malignant syndrome, brain stem disorder, acute brain syndrome and coma. Most of these symptoms were reversible. It remains unclear whether this represents a distinct clinical entity.
Nonetheless, it is advised that in patients, who are treated concomitantly with lithium and HALDOL, therapy should be stopped immediately if such symptoms occur.
Antagonism of the effect of the anticoagulant phenindione has been reported.
**Pregnancy and Lactation**

Animal studies have demonstrated a teratogenic effect of haloperidol (see Preclinical Safety Data).

Neonates exposed to antipsychotic drugs (including haloperidol) during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms that may vary in severity following delivery. These symptoms in the neonates may include agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder.

HALDOL has shown no significant increase in fetal anomalies in large population studies. There have been isolated case reports of birth defects following fetal exposure to HALDOL, mostly in combination with other drugs. HALDOL should be used during pregnancy only if the anticipated benefit justifies the potential risk to the fetus.

HALDOL is excreted in breast milk. If the use of HALDOL is considered essential, the benefits of breast-feeding should be balanced against its potential risks. Extrapyramidal symptoms have been observed in breast-fed infants of HALDOL treated women.

**Effects on Ability to Drive and Use Machines**

Some degree of sedation or impairment of alertness may occur, particularly with higher doses and at the start of treatment and may be potentiated by alcohol. Patients should be advised not to drive or operate machinery during treatment, until their susceptibility is known.

**Undesirable Effects**

***Clinical Trial Data***

*Placebo-Controlled Double-Blind Data – Adverse Drug Reactions Reported at ≥1% Incidence*

The safety of HALDOL (2-20 mg/day) was evaluated in 566 subjects (of which 284 were treated with HALDOL, 282 were given placebo) who participated in 3 placebo-controlled, double-blind clinical trials, two in the treatment of schizophrenia and the third in the treatment of bipolar disorder.

Adverse Drug Reactions (ADRs) reported by ≥1% of HALDOL-treated subjects in these trials are shown in Table 1.

**Table 1. Adverse Drug Reactions Reported by ≥1% of HALDOL-treated Subjects in 3 Double-Blind Parallel Placebo-Controlled Clinical Trials of HALDOL**

| **System/Organ Class**<br>Adverse Reaction | **Haloperidol (n=284) %** | **Placebo (n=282) %** |
|---|---|---|
| **Nervous System Disorders** | | |
| Extrapyramidal disorder | 34.2 | 8.5 |
| Hyperkinesia | 10.2 | 2.5 |
| Tremor | 8.1 | 3.6 |
| Hypertonia | 7.4 | 0.7 |
| Dystonia | 6.3 | 0.4 |
| Somnolence | 5.3 | 1.1 |
| Bradykinesia | 4.2 | 0.4 |
| **Eye Disorders** | | |
| Visual disturbance | 1.8 | 0.4 |

**Table 1. Adverse Drug Reactions Reported by ≥1% of HALDOL-treated Subjects in 3 Double-Blind Parallel Placebo-Controlled Clinical Trials of HALDOL**

| System/Organ Class<br>Adverse Reaction | Haloperidol (n=284)<br>% | Placebo (n=282)<br>% |
|---|---|---|
| **Gastrointestinal Disorders** | | |
| Constipation | 4.2 | 1.8 |
| Dry mouth | 1.8 | 0.4 |
| Salivary hypersecretion | 1.2 | 0.7 |

*Active Comparator-Controlled Data – Adverse Drug Reactions Reported at ≥1% Incidence*

Sixteen double-blind active comparator-controlled trials were selected to determine the incidence of ADRs. In these 16 studies, 1295 subjects were treated with 1-45 mg/day HALDOL, in the treatment of schizophrenia.

ADRs reported by ≥1% of HALDOL-treated subjects noted in the active-comparator controlled clinical trials are shown in Table 2.

**Table 2. Adverse Drug Reactions Reported by ≥1% of HALDOL-treated Subjects in 16 Double-Blind Active Comparator Clinical Trials of HALDOL**

| System/Organ Class<br>Adverse Reaction | Haloperidol (n=1295)<br>% |
|---|---|
| **Nervous System Disorder** | |
| Dizziness | 4.8 |
| Akathisia | 2.9 |
| Dyskinesia | 2.5 |
| Hypokinesia | 2.2 |
| Tardive dyskinesia | 1.62 |
| **Eye Disorders** | |
| Oculogyric crisis | 1.24 |
| **Vascular Disorders** | |
| Orthostatic hypotension | 6.6 |
| Hypotension | 1.47 |
| **Reproductive System and Breast Disorders** | |
| Erectile dysfunction | 1.0 |
| **Investigations** | |
| Weight increased | 7.8 |

*Placebo- and Active Comparator-Controlled Data – Adverse Drug Reactions Reported at <1% Incidence*

Additional ADRs that occurred in <1% of HALDOL-treated subjects either of the above 2 clinical datasets are listed below in Table 3.

**Table 3. Adverse Drug Reactions Reported by <1% of HALDOL-treated Subjects in Either the Placebo- or Comparator-controlled Clinical Trials.**

| |
|---|
| **Endocrine Disorders** |
| Hyperprolactinaemia |
| **Psychiatric Disorders** |
| Libido decreased |
| Loss of libido |
| Restlessness |

**Nervous System Disorders**
Motor dysfunction
Muscle contractions involuntary
Neuroleptic malignant syndrome
Nystagmus
Parkinsonism
Sedation

**Eye Disorders**
Vision blurred

**Cardiac Disorders**
Tachycardia

**Musculoskeletal and Connective Tissue Disorders**
Trismus
Torticollis
Muscle rigidity
Muscle Spasms
Musculoskeletal stiffness
Muscle Twitching

**Reproductive System and Breast Disorders**
Amenorrhoea
Breast discomfort
Breast pain
Galactorrhoea
Dysmenorrhoea
Sexual dysfunction
Menstrual disorder
Menorrhagia

**General Disorders and Administration Site Conditions**
Gait disturbance

***Postmarketing Data***

Adverse events first identified as ADRs during postmarketing experience with haloperidol are included in Table 4. The postmarketing review was based on review of all cases where there was a use of the active moiety haloperidol (both haloperidol and haloperidol decanoate). In the table, the frequencies are provided according to the following convention:

| | |
|---|---|
| Very common | ≥1/10 |
| Common | ≥1/100 to <1/10 |
| Uncommon | ≥1/1000 to <1/100 |
| Rare | ≥1/10000 to <1/1000 |
| Very rare | <1/10000, including isolated reports |

In Table 4, ADRs are presented by frequency category based on spontaneous reporting rates.

**Table 4: Adverse Drug Reactions Identified During Postmarketing Experience with Haloperidol (oral, solution, or decanoate) by Frequency Category Estimated From Spontaneous Reporting Rates**

| | |
|---|---|
| **Blood and Lymphatic System Disorders** | |
| *Very rare* | Agranulocytosis, Pancytopenia, Thrombocytopenia, Leukopenia, Neutropenia |
| **Immune System Disorders** | |
| *Very rare* | Anaphylactic reaction, Hypersensitivity |
| **Endocrine Disorders** | |
| *Very rare* | Inappropriate antidiuretic hormone secretion |

**Table 4: Adverse Drug Reactions Identified During Postmarketing Experience with Haloperidol (oral, solution, or decanoate) by Frequency Category Estimated From Spontaneous Reporting Rates**

| | |
|---|---|
| **Metabolic and Nutritional Disorders** | |
| *Very rare* | Hypoglycaemia |
| **Psychiatric Disorders** | |
| *Very rare* | Psychotic disorder, Agitation, Confusional state, Depression, Insomnia |
| **Nervous System Disorders** | |
| *Very rare* | Convulsion, Headache |
| **Cardiac Disorders** | |
| *Very rare* | Torsade de pointes, Ventricular fibrillation, Ventricular tachycardia, Extrasystoles |
| **Respiratory, thoracic and mediastinal disorders** | |
| *Very rare* | Bronchospasm, Laryngospasm, Laryngeal oedema, Dyspnoea |
| **Gastrointestinal Disorders** | |
| *Very rare* | Vomiting, Nausea |
| **Hepatobiliary Disorders** | |
| *Very rare* | Acute Hepatic Failure, Hepatitis, Cholestasis, Jaundice, Liver function test abnormal |
| **Skin and subcutaneous tissue disorders** | |
| *Very rare* | Leukocytoclastic vasculitis, Dermatitis exfoliative, Urticaria, Photosensitivity reaction, Rash, Pruritis, Hyperhidrosis |
| **Renal and Urinary Disorders** | |
| *Very rare* | Urinary retention |
| **Pregnancy, Puerperium and Perinatal Conditions** | |
| *Very rare* | Drug withdrawal syndrome neonatal |
| **Reproductive System and Breast Disorders** | |
| *Very rare* | Priapism, Gynaecomastia |
| **General Disorders and Administration Site Conditions** | |
| *Very rare* | Sudden Death, Face oedema, Oedema, Hypothermia, Hyperthermia |
| **Investigations** | |
| *Very rare* | Electrocardiogram QT prolonged, Weight decreased |

## Overdose

*Symptoms*

The manifestations are an exaggeration of the known pharmacological effects and adverse reactions. The most prominent symptoms are: severe extrapyramidal reactions, hypotension, sedation. An extrapyramidal reaction is manifest by muscular rigidity and a generalised or localised tremor. Hypertension rather than hypotension is also possible.

In extreme cases, the patient would appear comatose with respiratory depression and hypotension that could be severe enough to produce a shock-like state. The risk of ventricular arrhythmias, possibly associated with QT-prolongation, should be considered.

*Treatment*

There is no specific antidote. Treatment is largely supportive. Activated charcoal may be administered.
For comatose patients, a patent airway should be established by use of an oropharyngeal airway or endotracheal tube. Respiratory depression may necessitate artificial respiration.
ECG and vital signs should be monitored and monitoring should continue until the ECG is normal. Severe arrhythmias should be treated with appropriate anti-arrhythmic measures.
Hypotension and circulatory collapse may be counteracted by use of intravenous fluids, plasma, or concentrated albumin and vasopressor agents such as dopamine or noradrenaline. Adrenaline should not be used, since it might cause profound hypotension in the presence of HALDOL.
In cases of severe extrapyramidal reactions, antiparkinson medication (e.g. benztropine mesylate 1 to 2 mg IM or IV) should be administered parenterally.

## PHARMACOLOGICAL PROPERTIES

### Pharmacodynamic Properties

ATC Code N05AD01
Haloperidol is a neuroleptic, belonging to the group of the butyrophenones. Haloperidol is a potent central dopamine receptor antagonist and, therefore, is classified among the very incisive neuroleptics. Haloperidol has no antihistaminergic or anticholinergic activity.
As a direct consequence of the central dopamine blocking effect, haloperidol has an incisive activity on delusions and hallucinations (probably due to an interaction in the mesocortical and limbic tissues) and an activity on the basal ganglia (nigrostriatal bundles). Haloperidol causes efficient psychomotor sedation, which explains the favourable effect on mania and other agitation syndromes (see Indications).
On the basis of its limbic activity, haloperidol exerts a neuroleptic sedative activity and has been shown to be useful as an adjuvant in the treatment of chronic pain.
The activity on the basal ganglia probably underlies the extrapyramidal motor side-effects (dystonia, akathisia and parkinsonism).
The more peripheral antidopaminergic effects explain the activity against nausea and vomiting (via the chemoreceptor-trigger zone), the relaxation of the gastro-intestinal sphincters and the increased prolactin release (through an inhibition of the activity of the prolactin inhibiting factor, PIF, at the level of the adenohypophysis).

### Pharmacokinetic Properties

*Absorption*
Following oral administration, the bioavailability of the drug is 60 to 70%. Peak plasma levels of haloperidol occur within two to six hours of oral dosing and about twenty minutes after intramuscular administration.
*Distribution*
Plasma protein binding is 92%. The volume of distribution at steady state (VDss) is large (7.9 ± 2.5 L/kg). Haloperidol crosses the blood-brain barrier easily.
*Metabolism*
Haloperidol is metabolized by several routes including the cytochrome P450 enzyme system (particularly CYP 3A4 or CYP 2D6) and glucuronidation.
*Elimination*

The mean plasma half-life (terminal elimination) is 24 hours (range 12 to 38 hours) after oral administration and 21 hours (range 13 to 36 hours) after intramuscular administration. Excretion occurs with the faeces (60%) and the urine (40%). About 1% of the ingested haloperidol is excreted unchanged with the urine.

*Therapeutic Concentrations*

It has been suggested that a plasma haloperidol concentration range from 4 µg/L to an upper limit of 20 to 25 µg/L is required for a therapeutic response.

**Preclinical Safety Data**

Nonclinical data reveal no special hazards for humans based on conventional studies of repeat dose toxicity, genotoxicity and carcinogenicity. In rodents, haloperidol administration showed a decrease in fertility, limited teratogenicity as well as embryo-toxic effects.

Haloperidol has been shown to block the cardiac hERG channel in several published studies *in vitro*. In a number of *in vivo* studies intravenous administration of haloperidol in some animal models has caused significant QTc prolongation, at doses around 0.3 mg/kg i.v., giving $C_{max}$ plasma levels 3 to 7 times higher than the effective human plasma concentrations of 4 to 20ng/ml. These intravenous doses which prolonged QTc did not cause arrhythmias. In some studies higher intravenous doses of 1 to 5 mg/kg haloperidol i.v. caused QTc prolongation and/or ventricular arrhythmias at $C_{max}$ plasma levels 19 to 68 times higher than the effective human plasma concentrations.

## PHARMACEUTICAL PARTICULARS

**List of Excipients**

*1 mg tablets:* Lactose monohydrate, maize starch, sucrose, talc, cottonseed oil hydrogenated, purified water.

*2 mg tablets:* Lactose monohydrate, maize starch, sucrose, talc, cottonseed oil hydrogenated, quinoline yellow, purified water.

*5 mg tablets:* Lactose monohydrate, maize starch, talc, cottonseed oil hydrogenated, indigotindisulphonate sodium, purified water.

*10 mg tablets:* Calcium hydrogen phosphate dihydrate, maize starch, calcium stearate, quinoline yellow, purified water.

*20 mg tablets:* Calcium hydrogen phosphate dihydrate, maize starch, pregelatinized potato starch, calcium stearate, purified water.

*2 mg/ml oral solution (1 ml = 20 drops):* Lactic acid, methyl parahydroxybenzoate, purified water.

*10 mg/ml oral solution (1 ml = 20 drops).*

methyl parahydroxybenzoate, propyl parahydroxybenzoate, lactic acid, purified water.

*5 mg/ml injectable solution:* Lactic acid, water for injection.

**Incompatibilities**

None known.

**Shelf Life**

Observe expiry date on the outer pack.

**Special Precautions for Storage**

*Tablets*

Store between 15° and 30° C.

*Oral solution*

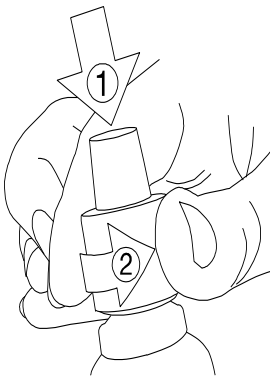
Store between 15° and 30°C. Do not freeze.
*Injectable solution*
Store between 15° and 30°C. Protect from light.
Keep out of reach of children.

**Nature and Contents of Container**

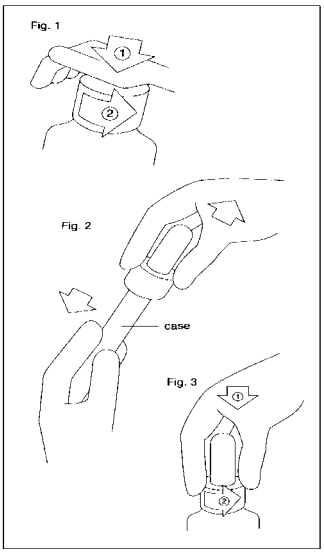
Tablets are supplied in PVC/Aluminum foil blister packs or polypropylene bottles with LDPE cap with either 1 mg, 2 mg, 5 mg, 10 mg or 20 mg tablets.
The 2 mg/ml oral solution is either supplied in a 15 ml dropper bottle (0.1 mg per drop) or in a 100 ml glass bottle with a pipette. The 10 mg/ml oral solution is supplied in a 100 ml amber glass bottle with a pipette.
Injectable solution is supplied in 1 ml amber colored glass ampoules Type I.

**Instructions for Use and Handling and Disposal**

*Oral Drops:*
HALDOL is supplied in a 15 ml LDPE dropper bottle with a child-proof cap and is opened as follows: push the plastic screw cap down while turning it counter clockwise.
After removal of the screw cap, the required number of drops can be obtained by means of the drop counter, which is fitted on the bottle.



*Oral solution: (glass pipette)*




The 100 ml amber glass bottle comes with a child-proof cap, that you should replace by the child-proof drop counter. These two accessories work as follows:
Push the plastic screw cap down, while turning it counter clockwise.
*When using the bottle for the first time:*
-*Fig. 1*: Remove the cap from the bottle.
-*Fig. 2*: Pull the drop counter out of its case.
-Now, fit the drop counter on the bottle.
*From then on, whenever you need the medicine, proceed as below:*
-*Fig. 3*: Remove the drop counter from the bottle.
-Take the amount of liquid you need to give. You will find the number of millilitres or milligrams on the drop counter.
-Fit the drop counter back on the bottle after each use.

*Oral solution: (plastic pipette)*

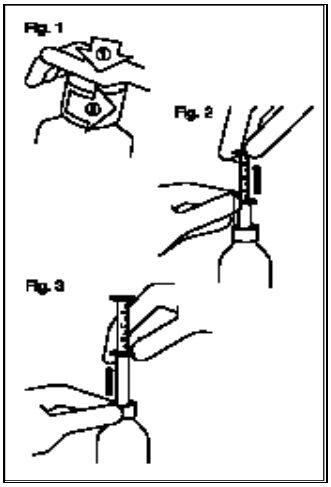
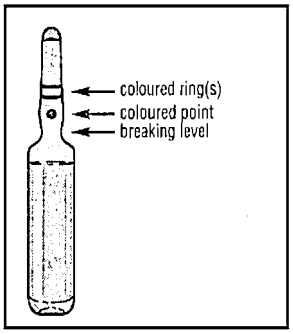



*Fig. 1*: The 100 ml amber glass bottle comes with a child-resistant cap, and should be opened as follows:
-Push the plastic screw cap down while turning it counter clockwise.
-Remove the unscrewed cap.
*Fig. 2*: Insert the pipette into the bottle.
While holding the bottom ring, pull the top ring up to the mark that corresponds to the number of milliliters or milligrams you need to give.
*Fig. 3*: Holding the bottom ring, remove the entire pipette from the bottle.
Empty the pipette into a cup by sliding the upper ring down and drink it immediately.
Close the bottle.
Rinse the pipette with some water for future use.

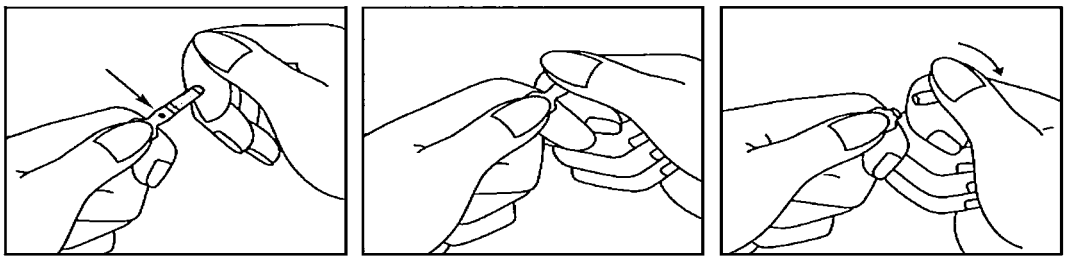
*Ampoules*:




1. Hold the ampoule between the thumb and index finger, leaving the tip of the ampoule free.

2. With the other hand, hold the tip of ampoule putting the index finger against the neck of ampoule, and the thumb on the coloured point in parallel to the identification coloured ring(s).

3. Keeping the thumb on the point, sharply break the tip of ampoule while holding firmly the other part of the ampoule in the hand.



**MANUFACTURED BY**
See outer carton.

**DATE OF REVISION OF THE TEXT**
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