HALDOL®

haloperidol decanoate

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

HALDOL® haloperidol decanoate 50 mg/mL Injection

HALDOL® CONCENTRATE haloperidol decanoate 100 mg/mL Injection

2. QUANTITATIVE AND QUALITATIVE COMPOSITION

HALDOL® 50 mg/ml

Haloperidol decanoate 70.52 mg, equivalent to 50 mg haloperidol base, per millilitre.

HALDOL® CONCENTRATE 100 mg/ml

Haloperidol decanoate 141.04 mg, equivalent to 100 mg haloperidol base, per millilitre.

For a full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

Injection (depot)

HALDOL Injection (long acting) is a slightly amber, slightly viscous solution, free from visible foreign matter, filled in 1 mL amber glass ampoules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HALDOL is indicated for the maintenance therapy of psychoses, particularly for patients requiring prolonged parenteral neuroleptic therapy.

4.2 Dose and method of administration

HALDOL should be administered by deep intramuscular injection into the gluteal region. A 2 inch long, 21 gauge needle is recommended. The maximum volume per injection site should not exceed 3 mL. The recommended interval between doses is 4 weeks.

DO NOT ADMINISTER INTRAVENOUSLY.

HALDOL is intended for use in chronic psychotic patients who require prolonged parenteral antipsychotic therapy. These patients should be previously stabilised on antipsychotic medication before considering a conversion to HALDOL. Furthermore, it is recommended that patients being considered for HALDOL therapy be initially converted to oral haloperidol to exclude the possibility of an unexpected adverse sensitivity to haloperidol.

The starting dose of HALDOL should be based on the patient's clinical history, physical condition and response to previous antipsychotic therapy. It is recommended that the initial dose of HALDOL be 10-15 times the previous daily dose in oral haloperidol equivalents, but no more than a maximum initial dose of 100 mg (2 mL). The preferred approach to determining the minimum effective dose is to begin with lower initial doses and to adjust the dose upward as needed. Close clinical supervision

is required during the initial period of dose adjustment in order to minimise the risk of over-dosage or reappearance of psychotic symptoms before the next injection. The most appropriate monthly dose of HALDOL is often about 20 times the daily dose of oral haloperidol. During dose adjustment or episodes of exacerbation of psychotic symptoms, HALDOL therapy can be supplemented with short-acting forms of haloperidol.

Haloperidol decanoate has been effectively administered at monthly intervals - however variation in patient response may dictate a need for adjustment of the dosing interval as well as the dose.

Lower initial doses and more gradual adjustments are recommended for elderly or debilitated patients.

Clinical experience with HALDOL at doses greater than 300 mg (6 mL) per month has been limited.

Special Populations

Use in elderly and in debilitated patients

It is recommended to start with low doses, for example 12.5 mg to 25 mg every 4 weeks, only increasing the dose according to the patient's response.

4.3 Contraindications

HALDOL is contraindicated in comatose states from any cause and in the presence of CNS depression due to alcohol or other depressant drugs. It is also contraindicated in patients with significant depressive states, previous spastic diseases, lesions of the basal ganglia and in Parkinson's syndrome, except in the case of dyskinesias due to levodopa treatment. It should not be used in senile patients with pre-existing Parkinson-like symptoms.

HALDOL is also contraindicated in individuals who are hypersensitive to the drug or its excipients.

4.4 Special warnings and precautions for use

Mortality

Rare cases of sudden death have been reported in psychiatric patients receiving antipsychotic agents, 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.

The risk-benefit of haloperidol treatment should be fully assessed before treatment is commenced and patients with risk factors for ventricular arrhythmias such as cardiac disease, family history of sudden death and/or QT prolongation, uncorrected electrolyte disturbances, subarachnoid haemorrhage, starvation or alcohol abuse, should be monitored carefully (ECGs and potassium levels), particularly during the initial phase of treatment, to obtain steady plasma levels.

The risk of QT prolongation and/or ventricular arrhythmias may be increased with higher doses (see **sections 4.5, 4.8** and **4.9**) or with parenteral use, particularly intravenous administration.

HALDOL should be used with caution in patients known to be slow metabolisers of CYP2D6, and during use of cytochrome P450 inhibitors. Concomitant use of antipsychotics should be avoided.

Baseline ECG is recommended prior to treatment in all patients, especially in the elderly and patients with a positive personal or family history of cardiac disease or abnormal findings on cardiac clinical examination. During therapy, the need for ECG monitoring (e.g. at dose escalation) should be assessed on an individual basis. Whilst on therapy, the dose should be reduced if QT is prolonged, and haloperidol should be discontinued if the QTc exceeds 500 ms.

Periodic electrolyte monitoring is recommended, especially for patients taking diuretics, or during intercurrent illness.

HALDOL (haloperidol decanoate) MUST NOT BE ADMINISTERED INTRAVENOUSLY.

Tachycardia and hypotension have also been reported in occasional patients.

Cerebrovascular Events

In randomized, placebo-controlled clinical trials in the dementia population, there was an approximately 3-fold increased risk of cerebrovascular adverse events with some atypical antipsychotics. Observational studies comparing the stroke rate in elderly patients exposed to any antipsychotic to the stroke rate in those not exposed to such medicinal products reported an approximately 1.6- to 1.8-fold increased stroke rate among exposed patients. This increase may be higher with all butyrophenones, including haloperidol. The mechanism for this increased risk is not known. An increased risk cannot be excluded for other patient populations. HALDOL must be used with caution in patients with risk factors for stroke.

Tardive Dyskinesia

Tardive dyskinesia, a syndrome consisting of potentially irreversible involuntary, dyskinetic movements, is known to occur in patients treated with neuroleptics with antipsychotic properties and other drugs with substantial neuroleptic activity. The syndrome is characterised by rhythmical involuntary movements of the tongue, face, mouth or jaw. Although the dyskinetic syndrome may remit partially or completely if the medication is withdrawn, it is irreversible in some patients. The prevalence of the syndrome appears to be highest among the elderly, especially elderly women. At the present time there is uncertainty as to whether neuroleptic drugs differ in their potential to cause tardive dyskinesia.

Since there is a significant prevalence of this syndrome associated with the use of neuroleptic drugs, and since there is no known effective treatment, chronic use of these drugs should generally be restricted to patients for whom there is no alternative therapy available with better risk acceptability. If manifestations of tardive dyskinesia are detected during the use of a neuroleptic, the drug should be discontinued.

The risk of a patient developing tardive dyskinesia and of the syndrome becoming irreversible appear to increase with the duration of treatment and the total amount of drugs administered, although, in some instances, tardive dyskinesia may develop after relatively short periods of treatment at low doses. The risk of developing tardive dyskinesia may, therefore, be minimised by reducing the dose of the neuroleptic drug used and its duration of administration, consistent with the effective management of the patient's condition. Continued use of neuroleptics should be periodically reassessed.

Neuroleptic Malignant Syndrome

As with other neuroleptic drugs, a symptom complex sometimes referred to as neuroleptic malignant syndrome (NMS) has been reported. Cardinal features of NMS are hyperthermia, hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs), and evidence of autonomic instability (irregular pulse or blood pressure). Additional signs may include elevated CPK, myoglobinuria (rhabdomyolysis), and acute renal failure. Hyperthermia is often an early sign of this

syndrome. NMS is potentially fatal, requires intensive symptomatic treatment and immediate discontinuation of neuroleptic treatment. Dantrolene and bromocriptine have been used for the treatment of NMS.

Extrapyramidal Symptoms

In common with all antipsychotics, 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

Seizures can be triggered by haloperidol. If indicated, adequate anticonvulsant therapy should be concomitantly maintained. Caution is advised in patients suffering from epilepsy and in conditions predisposing to convulsions (e.g. alcohol withdrawal and brain damage).

Hepatobiliary concerns

Since HALDOL is metabolised in 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.

Suicide

The possibility of a suicide attempt is inherent in schizophrenia and bipolar disorder, and close supervision of high-risk patients should accompany therapy.

Treatment initiation

When HALDOL is used to control mania in bipolar disorders, there may be a rapid mood swing to depression.

Antiemetic action may obscure the diagnosis of an underlying condition characterised by nausea and vomiting.

It is advisable to carefully observe the patients who receive haloperidol decanoate for a long period in order to identify any changes in the skin or eyes. Oculocutaneous changes have been observed following use of butyrophenones structurally related to haloperidol.

Patients with depression

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 (see **section 4.5**).

It is recommended that patients being considered for HALDOL therapy be initially put on oral haloperidol to exclude the possibility of an unexpected adverse sensitivity to haloperidol.

HALDOL should be administered with caution to:

Patients with severe cardiovascular disorders, because of the possibility of transient hypotension and/or precipitation of anginal pain. When antihypertensives and haloperidol are used concomitantly the use of vasopressors such as noradrenaline may be indicated if the resulting hypotension is prolonged and severe. Adrenaline should not be used since haloperidol may reverse its action and cause profound hypotension.

Patients receiving anticonvulsant medications with a history of seizures, or with EEG abnormalities, because haloperidol may lower the convulsive threshold.

Patients who are elderly or debilitated. These patients should be observed for evidence of over-sedation, which, unless alleviated, could result in complications such as terminal stasis pneumonia.

Patients with thyrotoxicosis. Antipsychotic medication, including HALDOL may result in severe neurotoxicity (rigidity, inability to walk or talk). Antipsychotic treatment in these patients should always be accompanied by appropriate monitoring and therapy.

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

Patients receiving anticoagulants (see **section 4.5**).

Use in Children

Safety and efficacy in children have not been established; therefore, HALDOL is not recommended for use in the paediatric age group.

Information for Patients

HALDOL may impair the mental and/or physical abilities required for the performance of hazardous tasks such as operating machinery or driving a motor vehicle. The ambulatory patient should be warned accordingly.

The use of alcohol with this drug should be avoided due to possible additive effects and hypotension.

4.5 Interactions with other medicines and other forms of interaction

Haloperidol is metabolised 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 characterised 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 (400mg/day) and paroxetine (20mg/day). It may be necessary to reduce the haloperidol dosage.

Caution is advised when used in combination with drugs known to cause electrolyte imbalance.

Concomitant QT Prolonging Drugs

Concomitant use of haloperidol with drugs known to prolong the QT interval may increase the risk of ventricular arrhythmias, including torsade de pointes. Therefore, concomitant use of these products is not recommended.

Examples include certain antiarrhythmics, such as those of Class 1A (such as quinidine, disopyramide and procainamide) and class III (such as amiodarone, sotalol and dofetilide), certain antimicrobials (sparfloxacin, moxifloxacin, erythromycin IV), tricyclic antidepressants (such as amitriptyline), certain tetracyclic antidepressants (such as maprotiline), other neuroleptics (e.g. phenothiazines, pimozide and sertindole), certain antihistamines (such as terfenadine), cisapride, bretylium and certain antimalarials such as quinine and mefloquine. This list is not comprehensive.

Effect of Other Drugs on HALDOL

When prolonged treatment with enzyme inducing drugs such as carbamazepine, phenobarbital, rifampicin is added to HALDOL therapy, a significant fall in haloperidol plasma levels occurs. Therefore, during combination treatment, the Haldol Decanoate dose or the dosage interval should be adjusted, when necessary. After stopping such drugs, it may be necessary to reduce the dosage of Haldol Decanoate.

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

Effect of HALDOL on Other Drugs

Although HALDOL does not provoke a respiratory depression, it can have a potentiating effect on CNS depressants such as anaesthetics, opiates, hypnotics (barbiturates) and alcohol.

An enhanced CNS effect (disorientation, memory loss, mental retardation, aggression, irritability) when combined with methyldopa has 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 antiparkinsonian effects of levodopa.

HALDOL is an inhibitor of CYP 2D6. HALDOL inhibits the metabolism of tricyclic antidepressants, increasing blood levels of these drugs. This may result in increased tricyclic antidepressant toxicity.

Other Forms of Interaction

An encephalopathic syndrome with reported symptoms including weakness, lethargy, fever, tremulousness and confusion, extrapyramidal symptoms, tardive dyskinesia, neuroleptic malignant syndrome, leukocytosis, elevated serum enzymes and BUN and coma, followed by irreversible brain damage has occurred in a few patients treated with lithium plus haloperidol; a causal relationship has not been established. However, patients receiving such combined therapy should be monitored closely for early evidence of neurological toxicity and treatment discontinued should such signs appear.

Haloperidol has been reported to interfere with the activity of phenindione and coumarin anticoagulants.

4.6 Fertility, pregnancy and lactation

Pregnancy (Category C)

Non-teratogenic class effect: Neonates exposed to antipsychotic drugs (including HALDOL) during the third trimester of pregnancy are at risk of experiencing extrapyramidal neurological disturbances and/or withdrawal symptoms following delivery. There have been post-market reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, and feeling disorder in these

neonates. These complications have varied in severity; while in some cases symptoms have been self-limited; in other cases neonates have required additional medical treatment or monitoring.

HALDOL should be used during pregnancy only if the anticipated benefit outweighs the risk and the administered dose and duration of treatment should be as low and as short as possible.

Breast-feeding

Since haloperidol is excreted in human breast milk, infants should not be nursed during treatment with HALDOL. Extrapyramidal symptoms have been observed in breast-fed infants of HALDOL treated women.

4.8 Undesirable Effects

Clinical Trial Data

Comparator and Open-Label Trial Data – Adverse Drug Reactions Reported at ≥1% Incidence

The safety of HALDOL (15-500 mg/month) was evaluated in 410 subjects who participated in 13 clinical trials in the treatment of schizophrenia or a schizoaffective disorder.

Adverse reactions reported by ≥1% of HALDOL-treated subjects in these trials are shown in **Table 1**.

Table 1. Adverse Reactions Reported by ≥1% of HALDOL-treated Subjects in Comparator and Open-Label Clinical Trials of HALDOL

System/Organ Class Adverse Reaction	**Haloperidol decanoate (n=410)** **%**
Nervous System Disorders	
Extrapyramidal disorder	13.6
Tremor	8.0
Parkinsonism	7.3
Somnolence	4.9
Masked facies	4.1
Akathisia	3.4
Sedation	2.7
Gastrointestinal Disorders	
Dry mouth	3.4
Constipation	2.0
Salivary hypersecretion	1.2
Musculoskeletal and Connective Tissue Disorders	
Muscle rigidity	6.1
Reproductive System and Breast Disorders	
Sexual dysfunction	1.5
General Disorders and Administration Site Conditions	
Injection site reaction	1.2
Investigations	
Weight increased	2.9

Comparator and Open-Label Trial Data – Adverse Drug Reactions Reported at <1% Incidence

Additional adverse reactions that occurred in <1% of HALDOL DECANOATE-treated subjects either of the above trial data are listed below in **Table 2**.

Table 2. Adverse Drug Reactions Reported by <1 % of HALDOL DECANOATE-treated Subjects in Comparator and Open-Label Clinical Trials of HALDOL DECANOATE

Nervous System Disorders
Akinesia
Dyskinesia
Hypertonia
Dystonia
Cogwheel rigidity
Eye disorders
Vision blurred
Visual disturbance
Oculogyric Crisis
Cardiac Disorders
Tachycardia

Cardiac effects such as QT-interval prolongation, Torsade de pointes, ventricular arrhythmias including ventricular fibrillation and ventricular tachycardia, and cardiac arrest, have been reported rarely. Cases of sudden unexplained death have also been reported.

Adverse reactions identified in clinical trials with haloperidol (non-decanoate formulations)

Adverse reactions relating to the active moiety that were identified in clinical trials with haloperidol (non-decanoate formulations) are listed in **Table 3**.

Table 3. Adverse Reactions Identified in Clinical Trials with Haloperidol (Non-Decanoate Formulations)

Endocrine Disorders
Hyperprolactinemia
Psychiatric Disorders
Libido decreased, Loss of libido, Restlessness
Nervous System Disorders
Neuroleptic malignant syndrome, Tardive dyskinesia, Bradykinesia, Dizziness, Hyperkinesia, Hypokinesia, Motor dysfunction, Muscle contractions involuntary, Nystagmus
Vascular Disorders
Hypotension, Orthostatic hypotension
Musculoskeletal and Connective Tissue Disorders
Trismus, Torticollis, Muscle spasms, Musculoskeletal stiffness, Muscle twitching
Reproductive System and Breast Disorders
Amenorrhea, Galactorrhea, Menstrual disorder, Erectile dysfunction, Breast discomfort, Breast pain, Dysmenorrhea, Menorrhagia
General Disorders and Administration Site Conditions
Gait disturbance

Postmarketing Data

Adverse events first identified as adverse reactions during postmarketing experience with haloperidol, presented by frequency category based on incidence in clinical trials, when known, are included in **Table 4**. The postmarketing review was based on review of all cases including haloperidol and haloperidol decanoate containing products. The frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥1/1,000 to <1/100
Rare	≥1/10,000 to <1/1,000
Very rare	<1/10,000, including isolated reports

Table 4. Adverse 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 (presenting with hyponatraemia)
Metabolic and Nutritional Disorders	
Very rare	Hypoglycaemia, Hyperglycaemia
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	Angioedema, Leukocytoclastic vasculitis, Dermatitis exfoliative, Urticaria, Photosensitivity reaction, Rash, Pruritis, Hyperhidrosis
Musculoskeletal and Connective Tissue Disorders	
Very rare	Rhabdomyolysis
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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https//nzphvc.otago.ac.nz/reporting/

4.9 Overdose

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

Symptoms and signs

The manifestations of haloperidol overdose are an exaggeration of the known pharmacological effects and adverse reactions. The most prominent symptoms are: severe extrapyramidal reactions, hypotension and 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 primarily supportive. 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.

In case of severe extrapyramidal reactions, antiparkinson medication should be administered and continued for several weeks. Antiparkinson medication must be withdrawn very cautiously as extrapyramidal symptoms may emerge.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Butyrophenone Derivatives, ATC Code: N05AD01

Actions

Haloperidol decanoate is an ester of haloperidol and decanoic acid, and as such, a depot neuroleptic belonging to the butyrophenones group. After intramuscular injection, haloperidol decanoate is gradually released from muscle tissue and hydrolysed slowly into free haloperidol which enters the systemic circulation. Haloperidol decanoate is a potent dopamine antagonist and, therefore, a very incisive neuroleptic.

In the brain, haloperidol has an incisive action on delusions and hallucinations (probably through an interaction with dopamine receptors in the mesocortical and limbic tissues) and an inhibitory effect through its activity on the basal ganglia, i.e. nigrostriatal bundles, which also underlies the extrapyramidal motor side effects (namely dystonia, akathisia and parkinsonism).

Haloperidol presents an effective psychomotor sedative effect, which also explains the favourable effect on mania and other agitation syndromes.

A resocialising effect has been observed in emotionally withdrawn patients. The more peripheral antidopaminergic effects explain the increased prolactin release (through an inhibition of the activity of the prolactin-inhibiting factor, PIF, at the level of the adenohypophysis).

5.2 Pharmacokinetic properties

Absorption

Administration of haloperidol decanoate as a depot intramuscular injection results in a slow and sustained release of haloperidol. The plasma concentrations rise gradually, usually peaking within the first week after injection. The pharmacokinetics of haloperidol decanoate following intramuscular injections are dose-related. The relationship between dose and plasma haloperidol level is roughly linear for doses below 450 mg.

Distribution

Haloperidol crosses the blood-brain barrier easily. Plasma protein binding is 92%.

Metabolism

HALDOL is metabolised by several routes including the cytochrome P450 enzyme system (particularly CYP 3A4 or CYP 2D6) and glucuronidation.Haloperidol is metabolized by several routes including the cytochrome P450 enzyme system (particularly CYP 3A4 or CYP 2D6) and glucuronidation.Haloperidol is metabolized by several routes including the cytochrome P450 enzyme system (particularly CYP 3A4 or CYP 2D6) and glucuronidation. Haloperidol is metabolized by several routes including the cytochrome P450 enzyme system (particularly CYP 3A4 or CYP 2D6) and glucuronidation.

Excretion

After reaching peak plasma concentrations, levels fall with an apparent half-life of about 3 weeks. Haloperidol is excreted in the urine (40%) and faeces (60%). About 1% of the dose 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.

Steady state plasma levels are reached within 3 to 6 months in chronic psychotic patients receiving monthly injections.

5.3 Preclinical safety data

Carcinogenicity, genotoxicity, impairment of fertility, teratogenicity

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sesame oil

Benzyl alcohol

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

50 mg/mL: 1mL amber glass ampoules, in boxes of 5s.
100 mg/mL: 1mL ampoules, in boxes of 5s.

6.6 Special precautions for disposal and other handling

Before use, roll the ampoule between the palms of the hands for a moment to warm up.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Janssen-Cilag (New Zealand) Ltd
Auckland, NEW ZEALAND
Telephone: 0800 800 806
Fax: (09) 588 1398
Email: medinfo@janau.jnj.com

9. DATE OF FIRST APPROVAL

15 December 1988 (HALDOL)
24 September 1991 (HALDOL CONCENTRATE)

10. DATE OF REVISION OF TEXT

23 October 2017

Summary table of changes

Section changes	Summary of new information
4.4	Addition of more detailed information relating to tardive dyskinesia