Annex III

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Note:

This product information is the outcome of the referral procedure to which this Commission decision relates.

The product information may be subsequently updated by the Member State competent authorities, in liaison with the reference Member State, as appropriate, in accordance with the procedures laid down in Chapter 4 of Title III of Directive 2001/83/EC.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

HALDOL Decanoate and associated names (see Annex I) 50 mg/ml solution for injection
HALDOL Decanoate and associated names (see Annex I) 100 mg/ml solution for injection

[See Annex I – To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[To be completed nationally]

3. PHARMACEUTICAL FORM

Solution for injection.

[To be completed nationally]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HALDOL Decanoate is indicated for the maintenance treatment of schizophrenia and schizoaffective disorder in adult patients currently stabilised with oral haloperidol (see section 5.1).

4.2 Posology and method of administration

Treatment initiation and dose titration must be carried out under close clinical supervision.

Posology

The individual dose will depend on both the severity of the symptoms and the current oral haloperidol dose. Patients must always be maintained on the lowest effective dose.

As the initial dose of haloperidol decanoate is based on a multiple of the daily oral haloperidol dose, specific guidance on switching from other antipsychotics cannot be provided (see section 5.1).

Adults aged 18 years and above

Table 1: Haloperidol decanoate dose recommendations for adults aged 18 years and above

Transition from oral haloperidol • A haloperidol decanoate dose of 10 to 15 times the previous daily dose of oral haloperidol is recommended. • Based on this conversion, the haloperidol decanoate dose will be 25 to150 mg for most patients.
Continuation of treatment • It is recommended to adjust the haloperidol decanoate dose by up to 50 mg every 4 weeks (based on individual patient response) until an optimal therapeutic effect is obtained. • The most effective dose is expected to range between 50 and 200 mg. • It is recommended to assess the individual benefit-risk when considering doses above 200 mg every 4 weeks. • A maximum dose of 300 mg every 4 weeks must not be exceeded because the safety concerns outweigh the clinical benefits of treatment.
Dosing interval • Usually 4 weeks between injections. • Adjustment of the dosing interval may be required (based on individual patient response).
Supplementation with non-decanoate haloperidol • Supplementation with with non-decanoate haloperidol may be considered during transition to HALDOL Decanoate, dose adjustment or episodes of exacerbation of psychotic symptoms (based on individual patient response). • The combined total dose of haloperidol from both formulations must not exceed the corresponding maximum oral haloperidol dose of 20 mg/day.

Special populations

Elderly

Table 2: Haloperidol decanoate dose recommendations for elderly patients

Transition from oral haloperidol • A low haloperidol decanoate dose of 12.5 to 25 mg is recommended.
Continuation of treatment • It is recommended only to adjust the haloperidol decanoate dose if required (based on individual patient response) until an optimal therapeutic effect is obtained. • The most effective dose is expected to range between 25 and 75 mg. • Doses above 75 mg every 4 weeks should only be considered in patients who have tolerated higher doses and after reassessment of the patient's individual benefit-risk profile.
Dosing interval • Usually 4 weeks between injections. • Adjustment of the dosing interval may be required (based on individual patient response).

Supplementation with non-decanoate haloperidol

- Supplementation with non-decanoate haloperidol may be considered during transition to HALDOL Decanoate, dose adjustment or episodes of exacerbation of psychotic symptoms (based on individual patient response).
- The combined total dose of haloperidol from both formulations must not exceed the corresponding maximum oral haloperidol dose of 5 mg/day or the previously administered oral haloperidol dose in patients who have received long-term treatment with oral haloperidol.

Renal impairment

The influence of renal impairment on the pharmacokinetics of haloperidol has not been evaluated. No dose adjustment is recommended, but caution is advised when treating patients with renal impairment. However, patients with severe renal impairment may require a lower initial dose, with subsequent adjustments at smaller increments and at longer intervals than in patients without renal impairment (see section 5.2).

Hepatic impairment

The influence of hepatic impairment on the pharmacokinetics of haloperidol has not been evaluated. Since haloperidol is extensively metabolised in the liver, it is recommended to halve the initial dose, and adjust the dose with smaller increments and at longer intervals than in patients without hepatic impairment (see sections 4.4 and 5.2).

Paediatric population

The safety and efficacy of HALDOL Decanoate in children and adolescents below 18 years of age have not been established. No data are available.

Method of administration

HALDOL Decanoate is for intramuscular use only and must not be administered intravenously. It is administered as a deep intramuscular injection in the gluteal region. It is recommended to alternate between the two gluteal muscles. As the administration of volumes greater than 3 ml is uncomfortable for the patient, such large volumes are not recommended. For instructions on handling HALDOL Decanoate, see section 6.6.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Comatose state.
- Central nervous system (CNS) depression.
- Parkinson’s disease.
- Dementia with Lewy bodies.
- Progressive supranuclear palsy.
- Known QTc interval prolongation or congenital long QT syndrome.
- Recent acute myocardial infarction.
- Uncompensated heart failure.
- History of ventricular arrhythmia or torsades de pointes.
- Uncorrected hypokalaemia.
- Concomitant treatment with medicinal products that prolong the QT interval (see section 4.5).

4.4 Special warnings and precautions for use

Increased mortality in elderly people with dementia

Rare cases of sudden death have been reported in psychiatric patients receiving antipsychotics, including haloperidol (see section 4.8).

Elderly patients with dementia-related psychosis treated with antipsychotics are at an increased risk of death. Analyses of seventeen placebo-controlled studies (modal duration of 10 weeks), largely in patients taking atypical antipsychotics, revealed a risk of death in 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 study, the rate of death in patients treated with antipsychotics 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 treatment of elderly patients with haloperidol is also associated with increased mortality. This association may be stronger for haloperidol than for atypical antipsychotic medicinal products, is most pronounced in the first 30 days after the start of treatment, and persists for at least 6 months. The extent to which this association is attributable to the medicinal product, as opposed to being confounded by patient characteristics, has not yet been elucidated.

HALDOL Decanoate is not indicated for the treatment of dementia-related behavioural disturbances.

Cardiovascular effects

QTc prolongation and/or ventricular arrhythmias, in addition to sudden death, have been reported with haloperidol (see sections 4.3 and 4.8). The risk of these events appears to increase with high doses, high plasma concentrations, in predisposed patients or with parenteral use, particularly intravenous administration.

HALDOL Decanoate must not be administered intravenously.

Caution is advised in patients with bradycardia, cardiac disease, family history of QTc prolongation or history of heavy alcohol exposure. Caution is also required in patients with potentially high plasma concentrations (see section 4.4, Poor metabolisers of CYP2D6).

A baseline ECG is recommended before treatment. During therapy, the need for ECG monitoring for QTc interval prolongation and for ventricular arrhythmias must be assessed in all patients. Whilst on therapy, it is recommended to reduce the dose if QTc is prolonged, but haloperidol must be discontinued if the QTc exceeds 500 ms.

Electrolyte disturbances such as hypokalaemia and hypomagnesaemia increase the risk for ventricular arrhythmias and must be corrected before treatment with haloperidol is started. Therefore, baseline and periodic electrolyte monitoring is recommended.

Tachycardia and hypotension (including orthostatic hypotension) have also been reported (see section 4.8). Caution is recommended when haloperidol is administered to patients manifesting hypotension or orthostatic hypotension.

Cerebrovascular events

In randomised, placebo-controlled clinical studies 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 found an 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 Decanoate must be used with caution in patients with risk factors for stroke.

Neuroleptic malignant syndrome

Haloperidol has been associated with neuroleptic malignant syndrome: a rare idiosyncratic response characterized by hyperthermia, generalised muscle rigidity, autonomic instability, altered consciousness and increased serum creatine phosphokinase levels. Hyperthermia is often an early sign of this syndrome. Antipsychotic treatment must be withdrawn immediately and appropriate supportive therapy and careful monitoring instituted.

Tardive dyskinesia

Tardive dyskinesia may appear in some patients on long-term therapy or after discontinuation of the medicinal product. 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 dose is increased or when a switch is made to a different antipsychotic. If signs and symptoms of tardive dyskinesia appear, the discontinuation of all antipsychotics, including HALDOL Decanoate, must be considered.

Extrapyramidal symptoms

Extrapyramidal symptoms may occur (e.g. tremor, rigidity, hypersalivation, bradykinesia, akathisia, acute dystonia). The use of haloperidol has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness and need to move, often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Acute dystonia may occur during the first few days of treatment with haloperidol, but later onset as well as onset after dose increases has been reported. Dystonic symptoms can include, but are not limited to, torticollis, facial grimacing, trismus, tongue protrusion, and abnormal eye movements, including oculogyric crisis. Males and younger age groups are at higher risk of experiencing such reactions. Acute dystonia may necessitate stopping the medicinal product.

Antiparkinson medicinal products of the anticholinergic type may be prescribed as required to manage extrapyramidal symptoms, but it is recommended that they are not prescribed routinely as a preventive measure. If concomitant treatment with an antiparkinson medicinal product is required, it may have to be continued after stopping HALDOL Decanoate if its excretion is faster than that of haloperidol in order to avoid the development or aggravation of extrapyramidal symptoms. The possible increase in intraocular pressure must be considered when anticholinergic medicinal products, including antiparkinson medicinal products, are administered concomitantly with HALDOL Decanoate.

Seizures/convulsions

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

Hepatobiliary concerns

As haloperidol is metabolised by the liver, dose adjustment and caution is advised in patients with hepatic impairment (see sections 4.2 and 5.2). Isolated cases of liver function abnormalities or hepatitis, most often cholestatic, have been reported (see section 4.8).

Endocrine system concerns

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

Hormonal effects of antipsychotics include hyperprolactinaemia, which may cause galactorrhoea, gynaecomastia and oligomenorrhea or amenorrhoea (see section 4.8). Tissue culture studies suggest that cell growth in human breast tumours may be stimulated by prolactin. Although no clear association with the administration of antipsychotics and human breast tumours has been demonstrated in clinical and epidemiological studies, caution is recommended in patients with relevant medical history. HALDOL Decanoate must be used with caution in patients with pre-existing hyperprolactinaemia and in patients with possible prolactin-dependent tumours (see section 5.3).

Hypoglycaemia and syndrome of inappropriate antidiuretic hormone secretion have been reported with haloperidol (see section 4.8).

Venous thromboembolism

Cases of venous thromboembolism (VTE) have been reported with antipsychotics. 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 Decanoate and preventive measures undertaken.

Treatment initiation

Patients being considered for HALDOL Decanoate therapy must be initially treated with oral haloperidol to reduce the possibility of an unexpected adverse sensitivity to haloperidol.

Patients with depression

It is recommended that HALDOL Decanoate is not used alone in patients in whom depression is predominant. It may be combined with antidepressants to treat those conditions in which depression and psychosis coexist (see section 4.5).

Poor metabolisers of CYP2D6

HALDOL Decanoate should be used with caution in patients who are known poor metabolisers of cytochrome P450 (CYP) 2D6 and who are coadministered a CYP3A4 inhibitor.

Excipients of HALDOL Decanoate

[To be completed nationally]

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

Cardiovascular effects

HALDOL Decanoate is contraindicated in combination with medicinal products known to prolong the QTc interval (see section 4.3). Examples include:

- Class IA antiarrhythmics (e.g. disopyramide, quinidine).
- Class III antiarrhythmics (e.g. amiodarone, dofetilide, dronedarone, ibutilide, sotalol).

- Certain antidepressants (e.g. citalopram, escitalopram).
- Certain antibiotics (e.g. azithromycin, clarithromycin, erythromycin, levofloxacin, moxifloxacin, telithromycin).
- Other antipsychotics (e.g. phenothiazine derivatives, sertindole, pimozide, ziprasidone)
- Certain antifungals (e.g. pentamidine).
- Certain antimalarials (e.g. halofantrine).
- Certain gastrointestinal medicinal products (e.g. dolasetron).
- Certain medicinal products used in cancer (e.g. toremifene, vandetanib).
- Certain other medicinal products (e.g. bepridil, methadone).

This list is not exhaustive.

Caution is advised when HALDOL Decanoate is used in combination with medicinal products known to cause electrolyte imbalance (see section 4.4).

Medicinal products that may increase haloperidol plasma concentrations

Haloperidol is metabolised by several routes (see section 5.2). The major pathways are glucuronidation and ketone reduction. The cytochrome P450 enzyme system is also involved, particularly CYP3A4 and, to a lesser extent, CYP2D6. Inhibition of these routes of metabolism by another medicinal product or a decrease in CYP2D6 enzyme activity may result in increased haloperidol concentrations. The effect of CYP3A4 inhibition and of decreased CYP2D6 enzyme activity may be additive (see section 5.2). Based on limited and sometimes conflicting information, the potential increase in haloperidol plasma concentrations when a CYP3A4 and/or CYP2D6 inhibitor is coadministered may range between 20 to 40%, although in some cases, increases of up to 100% have been reported. Examples of medicinal products that may increase haloperidol plasma concentrations (based on clinical experience or drug interaction mechanism) include:

- CYP3A4 inhibitors – alprazolam, fluvoxamine, indinavir, itraconazole, ketoconazole, nefazodone, posaconazole, saquinavir, verapamil, voriconazole.
- CYP2D6 inhibitors – bupropion, chlorpromazine, duloxetine, paroxetine, promethazine, sertraline, venlafaxine.
- Combined CYP3A4 and CYP2D6 inhibitors: fluoxetine, ritonavir.
- Uncertain mechanism – buspirone.

This list is not exhaustive.

Increased haloperidol plasma concentrations may result in an increased risk of adverse events, including QTc-prolongation (see section 4.4). 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 is recommended that patients who take haloperidol concomitantly with such medicinal products be monitored for signs or symptoms of increased or prolonged pharmacologic effects of haloperidol, and the HALDOL Decanoate dose be decreased as deemed necessary.

Medicinal products that may decrease haloperidol plasma concentrations

Coadministration of haloperidol with potent enzyme inducers of CYP3A4 may gradually decrease the plasma concentrations of haloperidol to such an extent that efficacy may be reduced. Examples include:

- Carbamazepine, phenobarbital, phenytoin, rifampicin, St John's Wort (*Hypericum, perforatum*).

This list is not exhaustive.

Enzyme induction may be observed after a few days of treatment. Maximal enzyme induction is generally seen in about 2 weeks and may then be sustained for the same period of time after the cessation of therapy with the medicinal product. During combination treatment with inducers of CYP3A4, it is recommended that patients be monitored and the HALDOL Decanoate dose increased as deemed necessary. After withdrawal of the CYP3A4 inducer, the concentration of haloperidol may gradually increase and therefore it may be necessary to reduce the HALDOL Decanoate dose.

Sodium valproate is known to inhibit glucuronidation, but does not affect haloperidol plasma concentrations.

Effect of haloperidol on other medicinal products

Haloperidol can increase the CNS depression produced by alcohol or CNS-depressant medicinal products, including hypnotics, sedatives or strong analgesics. An enhanced CNS effect, when combined with methyldopa, has also been reported.

Haloperidol may antagonise the action of adrenaline and other sympathomimetic medicinal products (e.g. stimulants like amphetamines) and reverse the blood pressure-lowering effects of adrenergic-blocking medicinal products such as guanethidine.

Haloperidol may antagonise the effect of levodopa and other dopamine agonists.

Haloperidol is an inhibitor of CYP2D6. Haloperidol inhibits the metabolism of tricyclic antidepressants (e.g. imipramine, desipramine), thereby increasing plasma concentrations of these medicinal products.

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, 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 Decanoate, therapy must be stopped immediately if such symptoms occur.

Antagonism of the effect of the anticoagulant phenindione has been reported.

4.6 Fertility, pregnancy and lactation

Pregnancy

A moderate amount of data on pregnant women (more than 400 pregnancy outcomes) indicate no malformative or foeto/ neonatal toxicity of haloperidol. However, there have been isolated case reports of birth defects following foetal exposure to haloperidol in combination with other medicinal products. Animal studies have shown reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of HALDOL Decanoate during pregnancy.

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.

Breastfeeding

Haloperidol is excreted in human milk. Small amounts of haloperidol have been detected in plasma and urine of breast-fed newborns of mothers treated with haloperidol. There is insufficient information on the effects of haloperidol in breast-fed infants. A decision must be made whether to discontinue breastfeeding or to discontinue HALDOL Decanoate therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Fertility

Haloperidol elevates prolactin level. Hyperprolactinaemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotropin secretion. This may inhibit reproductive function by impairing gonadal steroidogenesis in both female and male patients (see section 4.4).

4.7 Effects on ability to drive and use machines

HALDOL Decanoate has a moderate influence on the 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. It is recommended that patients be advised not to drive or operate machines during treatment, until their susceptibility is known.

4.8 Undesirable effects

The safety of haloperidol decanoate was evaluated in 410 patients who participated in 3 comparator studies (1 comparing haloperidol decanoate versus fluphenazine and 2 comparing the decanoate formulation to oral haloperidol), 9 open label studies and 1 dose response study.

Based on pooled safety data from these clinical studies, the most commonly reported adverse reactions were: extrapyramidal disorder (14%), tremor (8%), parkinsonism (7%), muscle rigidity (6%) and somnolence (5%).

In addition, the safety of haloperidol was evaluated in 284 haloperidol-treated patients who participated in 3 placebo-controlled clinical studies and in 1295 haloperidol-treated patients who participated in 16 double-blind active comparator-controlled clinical studies.

Table 3 lists adverse reactions as follows:

- Reported in clinical studies with haloperidol decanoate.
- Reported in clinical studies with haloperidol (non-decanoate formulations) and relate to the active moiety.
- From postmarketing experience with haloperidol decanoate and haloperidol.

Adverse reaction frequencies are based on (or estimated from) clinical trials or epidemiology studies with haloperidol decanoate, and classified using 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
Not known:	cannot be estimated from the available data.

The adverse reactions are presented by System Organ Class and in order of decreasing seriousness within each frequency category.

Table 3: Adverse reactions

System Organ Class	Adverse Reaction				
	Frequency				
	Very Common	Common	Uncommon	Rare	Not known
Blood and lymphatic system disorders					Pancytopenia Agranulocytosis Thrombocytopenia Leukopenia Neutropenia
Immune system disorders					Anaphylactic reaction Hypersensitivity
Endocrine disorders					Inappropriate antidiuretic hormone secretion Hyperprolactinaemia
Metabolic and nutritional disorders					Hypoglycaemia
Psychiatric disorders		Depression Insomnia			Psychotic disorder Agitation Confusional state Loss of libido Libido decreased Restlessness
Nervous system disorders	Extrapyramidal disorder	Akathisia Parkinsonism Masked facies Tremor Somnolence Sedation	Akinesia Dyskinesia Dystonia Cogwheel rigidity Hypertonia Headache		Neuroleptic malignant syndrome Tardive dyskinesia Convulsion Bradykinesia Hyperkinesia Hypokinesia Dizziness Muscle contractions involuntary Motor dysfunction Nystagmus
Eye disorders			Oculogyric crisis Vision blurred Visual disturbance		
Cardiac disorders			Tachycardia		Ventricular fibrillation Torsade de pointes Ventricular tachycardia Extrasystoles
Vascular disorders					Hypotension Orthostatic hypotension
Respiratory, thoracic and mediastinal disorders					Laryngeal oedema Bronchospasm Laryngospasm Dyspnoea
Gastrointestinal disorders		Constipation Dry mouth Salivary hypersecretion			Vomiting Nausea

System Organ Class	Adverse Reaction				
	Frequency				
	Very Common	Common	Uncommon	Rare	Not known
Hepatobiliary disorders					Acute hepatic failure Hepatitis Cholestasis Jaundice Liver function test abnormal
Skin and subcutaneous tissue disorders					Angioedema Dermatitis exfoliative Leukocytoclastic vasculitis Photosensitivity reaction Urticaria Pruritus Rash Hyperhidrosis
Musculoskeletal and connective tissue disorders		Muscle rigidity			Rhabdomyolysis Torticollis Trismus Muscle spasms Muscle twitching Musculoskeletal stiffness
Renal and urinary disorders					Urinary retention
Pregnancy, puerperium and perinatal conditions					Drug withdrawal syndrome neonatal (see section 4.6)
Reproductive system and breast disorders		Sexual dysfunction			Priapism Amenorrhoea Galactorrhoea Dysmenorrhoea Menorrhagia Erectile dysfunction Gynaecomastia Menstrual disorder Breast pain Breast discomfort
General disorders and administration site conditions		Injection site reaction			Sudden death Face oedema Oedema Hyperthermia Hypothermia Gait disturbance Injection site abscess
Investigations		Weight increased			Electrocardiogram QT prolonged Weight decreased

Electrocardiogram QT prolonged, ventricular arrhythmias (ventricular fibrillation, ventricular tachycardia), torsade de pointes and sudden death have been reported with haloperidol.

Class effects of antipsychotics

Cardiac arrest has been reported with antipsychotics.

Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis, have been reported with antipsychotics. The frequency is unknown.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

While overdose is less likely to occur with parenteral than with oral medication, the following details are based on oral haloperidol, also taking into account the extended duration of action of HALDOL Decanoate.

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 QTc prolongation, must be considered.

Treatment

There is no specific antidote. Treatment is supportive. Dialysis is not recommended in the treatment of overdose because it removes only very small amounts of haloperidol (see section 5.2).

For comatose patients, a patent airway must be established by use of an oropharyngeal airway or endotracheal tube. Respiratory depression may necessitate artificial respiration.

It is recommended that ECG and vital signs be monitored, and that monitoring continues until the ECG is normal. Treatment of severe arrhythmias with appropriate anti-arrhythmic measures is recommended.

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 must not be used because it might cause profound hypotension in the presence of haloperidol.

In cases of severe extrapyramidal reactions, it is recommended that an antiparkinson medicinal product be administered, and continued for several weeks. Antiparkinson medicinal products must be withdrawn very cautiously as extrapyramidal symptoms may emerge.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: psycholeptics; antipsychotics; butyrophenone derivatives, ATC code: N05AD01.

Mechanism of action

Haloperidol decanoate is an ester of haloperidol and decanoic acid, and as such, a depot antipsychotic 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 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.

Pharmacodynamic effects

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.

Clinical studies

In clinical studies, patients were mostly reported to have received prior treatment with orally administered haloperidol before converting to haloperidol decanoate. Occasionally, patients had previously been treated orally with another antipsychotic medicinal product.

5.2 Pharmacokinetic properties

Absorption

Administration of haloperidol decanoate as a depot intramuscular injection results in a slow and sustained release of free haloperidol. The plasma concentrations rise gradually, usually peaking within 3 to 9 days after injection.

Steady state plasma levels are reached within 2 to 4 months in patients receiving monthly injections.

Distribution

Mean haloperidol plasma protein binding in adults is approximately 88 to 92%. There is a high inter-subject variability for plasma protein binding. Haloperidol is rapidly distributed to various tissues and organs, as indicated by the large volume of distribution (mean values 8 to 21 l/kg after intravenous dosing). Haloperidol crosses the blood-brain barrier easily. It also crosses the placenta and is excreted in breast milk.

Biotransformation

Haloperidol is extensively metabolised in the liver. The main metabolic pathways of haloperidol in humans include glucuronidation, ketone reduction, oxidative N-dealkylation and formation of pyridinium metabolites. The metabolites of haloperidol are not considered to make a significant contribution to its activity; however, the reduction pathway accounts approximately for 23% of the biotransformation, and back-conversion of the reduced metabolite of haloperidol to haloperidol cannot be fully ruled out. The cytochrome P450 enzymes CYP3A4 and CYP2D6 are involved in haloperidol metabolism. Inhibition or induction of CYP3A4, or inhibition of CYP2D6, may affect haloperidol metabolism. A decrease in CYP2D6 enzyme activity may result in increased haloperidol concentrations.

Elimination

The terminal elimination half-life of haloperidol after intramuscular injection with haloperidol decanoate is on average 3 weeks. This is longer than for the non-decanoate formulations, where the haloperidol terminal elimination half-life is on average 24 hours after oral administration and 21 hours after intramuscular administration.

Haloperidol apparent clearance after extravascular administration ranges from 0.9 to 1.5 l/h/kg and is reduced in poor metabolisers of CYP2D6. Reduced CYP2D6 enzyme activity may result in increased concentrations of haloperidol. The inter-subject variability (coefficient of variation, %) in haloperidol clearance was estimated to be 44% in a population pharmacokinetic analysis in patients with schizophrenia. After intravenous haloperidol administration, 21% of the dose was eliminated in the faeces and 33% in the urine. Less than 3% of the dose is excreted unchanged in the urine.

Linearity/non-linearity

The pharmacokinetics of haloperidol following intramuscular injections of haloperidol decanoate are dose-related. The relationship between dose and plasma haloperidol level is approximately linear for doses below 450 mg.

Special populations

Elderly

Haloperidol plasma concentrations in elderly patients were higher than in younger adults administered the same dose. Results from small clinical studies suggest a lower clearance and a longer elimination half-life of haloperidol in elderly patients. The results are within the observed variability in haloperidol pharmacokinetics. Dose adjustment is recommended in elderly patients (see section 4.2).

Renal impairment

The influence of renal impairment on the pharmacokinetics of haloperidol has not been evaluated. About one-third of a haloperidol dose is excreted in urine, mostly as metabolites. Less than 3% of administered haloperidol is eliminated unchanged in the urine. Haloperidol metabolites are not considered to make a significant contribution to its activity, although for the reduced metabolite of haloperidol, back-conversion to haloperidol cannot be fully ruled out. Even though impairment of renal function is not expected to affect haloperidol elimination to a clinically relevant extent, caution is advised in patients with renal impairment, and especially those with severe impairment, due to the long half-life of haloperidol and its reduced metabolite, and the possibility of accumulation (see section 4.2).

Because of the high haloperidol distribution volume and its high protein binding, only very small amounts are removed by dialysis.

Hepatic impairment

The influence of hepatic impairment on the pharmacokinetics of haloperidol has not been evaluated. However, hepatic impairment may have significant effects on the pharmacokinetics of haloperidol because it is extensively metabolised in the liver. Therefore, dose adjustment and caution is advised in patients with hepatic impairment (see sections 4.2 and 4.4).

Pharmacokinetic/pharmacodynamics relationships

Therapeutic concentrations

Based on published data from multiple clinical studies, therapeutic response is obtained in most patients with acute or chronic schizophrenia at plasma concentrations of 1 to 10 ng/ml. A subset of patients may require higher concentrations as a consequence of a high inter-subject variability in haloperidol pharmacokinetics.

In patients with first-episode schizophrenia treated with short-acting haloperidol formulations, therapeutic response may be obtained at concentrations as low as 0.6 to 3.2 ng/ml, as estimated based on measurements of D2 receptor occupancy and assuming that a D2 receptor occupancy level of 60 to 80% is most appropriate for obtaining therapeutic response and limiting extrapyramidal symptoms. On average, concentrations in this range would be obtained with doses of 1 to 4 mg daily.

Due to the high inter-subject variability in haloperidol pharmacokinetics and the concentration-effect relationship, it is recommended to adjust the individual haloperidol decanoate dose based on the patient's response. This must take into account the time after a change in dose to achieve a new steady state plasma concentration and the additional time to elicit a therapeutic response. Measurement of haloperidol blood concentrations may be considered in individual cases.

Cardiovascular effects

The risk of QTc prolongation increases with haloperidol dose and with haloperidol plasma concentrations.

Extrapyramidal symptoms

Extrapyramidal symptoms can occur within the therapeutic range, although the frequency is usually higher with doses producing higher than therapeutic concentrations.

5.3 Preclinical safety data

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

In a carcinogenicity study of haloperidol, dose-dependent increases in pituitary gland adenomas and mammary gland carcinomas were seen in female mice. These tumours may be caused by prolonged dopamine D2 antagonism and hyperprolactinaemia. The relevance of these tumour findings in rodents in terms of human risk is unknown.

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, producing C_{max} plasma levels at least 7 to 14 times higher than the therapeutic plasma concentrations of 1 to 10 ng/ml that were effective in the

majority of patients in clinical studies. These intravenous doses, which prolonged QTc, did not cause arrhythmias. In some animal studies, higher intravenous haloperidol doses of 1 mg/kg or greater caused QTc prolongation and/or ventricular arrhythmias at C_{max} plasma levels at least 38 to 137 times higher than the therapeutic plasma concentrations that were effective in the majority of patients in clinical studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[To be completed nationally]

6.2 Incompatibilities

[To be completed nationally]

6.3 Shelf life

[To be completed nationally]

6.4 Special precautions for storage

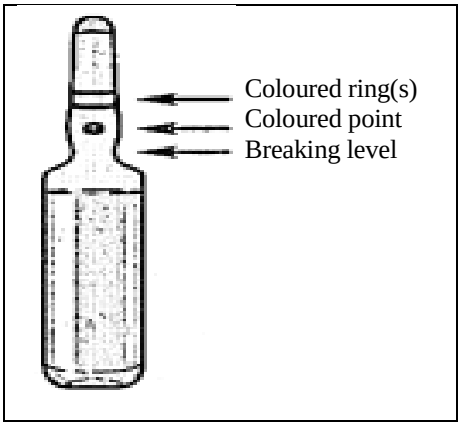
[To be completed nationally]

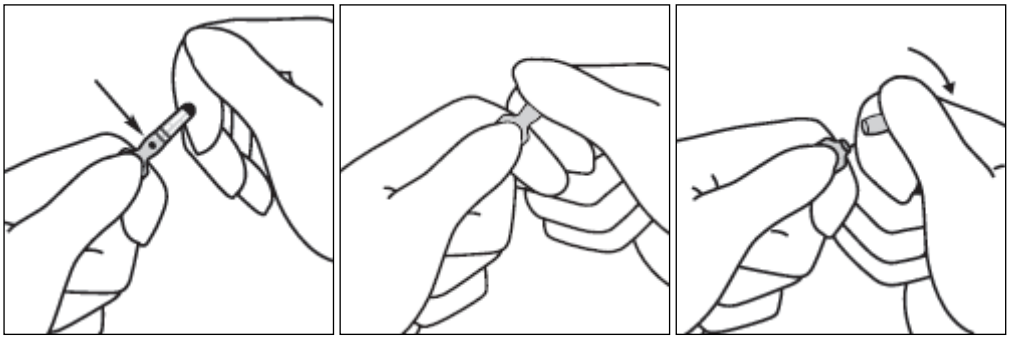
6.5 Nature and contents of container

[To be completed nationally]

6.6 Special precautions for disposal and other handling

- Before using the ampoule, roll it briefly between both hand palms to warm up the product.
- Hold the ampoule between the thumb and index finger, leaving the tip of the ampoule free.
- 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 parallel to the identification coloured rings.
- Keeping the thumb on the point, sharply break the tip of ampoule while holding firmly the other part of the ampoule in the hand.





Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[See Annex I – To be completed nationally]

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}
Date of latest renewal: {DD month YYYY}

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

[To be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

HALDOL Decanoate and associated names (see Annex I) 50 mg/ml solution for injection

[See Annex I – To be completed nationally]

haloperidol

2. STATEMENT OF ACTIVE SUBSTANCE(S)

[To be completed nationally]

3. LIST OF EXCIPIENTS

[To be completed nationally]

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

[To be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use only
Usually 4 weeks between injections
Read the package leaflet before use

[To be completed nationally]

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I – To be completed nationally]

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

[To be completed nationally]

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

AMPOULE

1. NAME OF THE MEDICINAL PRODUCT

HALDOL Decanoate and associated names (see Annex I) 50 mg/ml solution for injection

[See Annex I – To be completed nationally]

haloperidol

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I – To be completed nationally]

{Name}

3. EXPIRY DATE

EXP

4. BATCH NUMBER

[To be completed nationally]

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

HALDOL Decanoate and associated names (see Annex I) 100 mg/ml solution for injection

[See Annex I – To be completed nationally]

haloperidol

2. STATEMENT OF ACTIVE SUBSTANCE(S)

[To be completed nationally]

3. LIST OF EXCIPIENTS

[To be completed nationally]

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

[To be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use only
Usually 4 weeks between injections
Read the package leaflet before use
[To be completed nationally]

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I – To be completed nationally]

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

[To be completed nationally]

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

AMPOULE

1. NAME OF THE MEDICINAL PRODUCT

HALDOL Decanoate and associated names (see Annex I) 100 mg/ml solution for injection

[See Annex I – To be completed nationally]

haloperidol

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I – To be completed nationally]

{Name}

3. EXPIRY DATE

EXP

4. BATCH NUMBER

[To be completed nationally]

5. OTHER

PACKAGE LEAFLET

Package leaflet: Information for the patient

HALDOL Decanoate and associated names (see Annex I) 50 mg/ml solution for injection
HALDOL Decanoate and associated names (see Annex I) 100 mg/ml solution for injection

[See Annex I – To be completed nationally]

haloperidol

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Haldol Decanoate is and what it is used for

The name of your medicine is Haldol Decanoate.

Haldol Decanoate contains the active substance haloperidol (as haloperidol decanoate). This belongs to a group of medicines called ‘antipsychotics’.

Haldol Decanoate is used in adults whose condition has previously been treated with haloperidol taken by mouth. It is used for illnesses affecting the way you think, feel or behave. These include mental health problems (such as schizophrenia). These illnesses may make you:
- Feel confused (delirium)
- See, hear, feel or smell things that are not there (hallucinations)
- Believe things that are not true (delusions)
- Feel unusually suspicious (paranoia)
- Feel very excited, agitated, enthusiastic, impulsive or hyperactive
- Feel very aggressive, hostile or violent.

2. What you need to know before you are given Haldol Decanoate

Do not use Haldol Decanoate if:
- You are allergic to haloperidol or any of the other ingredients of this medicine (listed in section 6) [To be completed nationally]
- You are less aware of things around you or your reactions become unusually slow
- You have Parkinson’s disease
- You have a type of dementia called ‘Lewy body dementia’
- You have progressive supranuclear palsy (PSP)

- You have a heart condition called ‘prolonged QT interval’, or any other problem with your heart rhythm that shows as an abnormal tracing on an ECG (electrocardiogram)
- You have heart failure or recently had a heart attack
- You have a low level of potassium in your blood, which has not been treated
- You take any of the medicines listed under ‘Other medicines and Haldol Decanoate – Do not use Haldol Decanoate if you are taking certain medicines for’.

This medicine must not be used if any of the above applies to you. If you are not sure, talk to your doctor, pharmacist or nurse before being given Haldol Decanoate.

Warnings and precautions

Serious side effects
Haldol Decanoate can cause problems with the heart, problems controlling body or limb movements and a serious side effect called ‘neuroleptic malignant syndrome’. It can also cause severe allergic reactions and blood clots. You must be aware of serious side effects while you are using Haldol Decanoate because you may need urgent medical treatment. See ‘Look out for serious side effects’ in section 4.

Elderly people and people with dementia
A small increase in deaths and strokes has been reported for elderly people with dementia who are taking antipsychotic medicines. Talk to your doctor before being given Haldol Decanoate if you are elderly, particularly if you have dementia.

Talk to your doctor if you have:
- A slow heart beat, heart disease or anyone in your close family has died suddenly of heart problems
- Low blood pressure, or feel dizzy upon sitting up or standing up
- A low level of potassium or magnesium (or other ‘electrolyte’) in your blood. Your doctor will decide how to treat this
- Ever had bleeding in the brain, or your doctor has told you that you are more likely than other people to have a stroke
- Epilepsy or have ever had fits (convulsions)
- Problems with your kidneys, liver or thyroid gland
- A high level of the hormone 'prolactin' in your blood, or cancer that may be caused by high prolactin levels (such as breast cancer)
- A history of blood clots, or someone else in your family has a history of blood clots
- Depression.

You may need to be more closely monitored, and the amount of Haldol Decanoate you are given may have to be altered.

If you are not sure if any of the above applies to you, talk to your doctor or nurse before you are given Haldol Decanoate.

Medical check ups
Your doctor may want to take an electrocardiogram (ECG) before or during your treatment with Haldol Decanoate. The ECG measures the electrical activity of your heart.

Blood tests
Your doctor may want to check the levels of potassium or magnesium (or other ‘electrolyte’) in your blood before or during your treatment with Haldol Decanoate.

Children and adolescents
Haldol Decanoate should not be used in children and adolescents below 18 years. This is because it has not been studied in these age groups.

Other medicines and Haldol Decanoate
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.

Do not use Haldol Decanoate if you are taking certain medicines for:
- Problems with your heart beat (such as amiodarone, dofetilide, disopyramide, dronedarone, ibutilide, quinidine and sotalol)
- Depression (such as citalopram and escitalopram)
- Psychoses (such as fluphenazine, levomepromazine, perphenazine, pimozide, prochlorperazine, promazine, sertindole, thiorizadine, trifluoperazine, triflupromazine and ziprasidone)
- Bacterial infections (such as azithromycin, clarithromycin, erythromycin, levofloxacin, moxifloxacin and telithromycin)
- Fungal infections (such as pentamidine)
- Malaria (such as halofantrine)
- Nausea and vomiting (such as dolasetron)
- Cancer (such as toremifene and vandetanib).

Also tell your doctor if you are taking bepridil (for chest pain or to lower blood pressure) or methadone (a pain killer or to treat drug addiction).
These medicines may make heart problems more likely, so talk to your doctor if you are taking any of these and do not use Haldol Decanoate (see 'Do not use Haldol Decanoate if').

Special monitoring may be needed if you are using lithium and Haldol Decanoate at the same time. Tell your doctor straight away and stop taking both medicines if you get:
- Fever you can't explain or movements you can't control
- Confused, disoriented, a headache, balance problems and feel sleepy.

These are signs of a serious condition.

Certain medicines may affect the way that Haldol Decanoate works or may make heart problems more likely
Tell your doctor if you are taking:
- Alprazolam or buspirone (for anxiety)
- Duloxetine, fluoxetine, fluvoxamine, nefazodone, paroxetine, sertraline, St John's Wort (*Hypericum, perforatum*) or venlafaxine (for depression)
- Bupropion (for depression or to help you stop smoking)
- Carbamazepine, phenobarbital or phenytoin (for epilepsy)
- Rifampicin (for bacterial infections)
- Itraconazole, posaconazole or voriconazole (for fungal infections)
- Ketoconazole tablets (to treat Cushing's syndrome)
- Indinavir, ritonavir or saquinavir (for human immunodeficiency virus or HIV)
- Chlorpromazine or promethazine (for nausea and vomiting)
- Verapamil (for blood pressure or heart problems).

Also tell your doctor if you are taking any other medicines to lower blood pressure, such as water tablets (diuretics).

Your doctor may have to change your dose of Haldol Decanoate if you are taking any of these medicines.

Haldol Decanoate can affect the way the following types of medicine work
Tell your doctor if you are taking medicines for:
- Calming you down or helping you to sleep (tranquillisers)
- Pain (strong pain killers)
- Depression ('tricyclic antidepressants')

- Lowering blood pressure (such as guanethidine and methyldopa)
- Severe allergic reactions (adrenaline)
- Attention deficit hyperactivity disorder (ADHD) or narcolepsy (known as ‘stimulants’)
- Parkinson’s disease (such as levodopa)
- Thinning the blood (phenindione).

Talk to your doctor or nurse before being given Haldol Decanoate if you are taking any of these medicines.

Haldol Decanoate and alcohol
Drinking alcohol while you are using Haldol Decanoate might make you feel sleepy and less alert. This means you should be careful how much alcohol you drink. Talk to your doctor about drinking alcohol while using Haldol Decanoate, and let your doctor know how much you drink.

Pregnancy, breast-feeding and fertility
Pregnancy – if you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice. Your doctor may advise you not to use Haldol Decanoate while you are pregnant.

The following problems may occur in newborn babies of mothers that use Haldol Decanoate in the last 3 months of their pregnancy (the last trimester):
- Muscle tremors, stiff or weak muscles
- Being sleepy or agitated
- Problems breathing or feeding.

The exact frequency of these problems is unknown. If you used Haldol Decanoate while pregnant and your baby develops any of these side effects, contact your doctor.

Breast-feeding – talk to your doctor if you are breast-feeding or planning to breast-feed. This is because small amounts of the medicine may pass into the mother’s milk and on to the baby. Your doctor will discuss the risks and benefits of breast-feeding while you are using Haldol Decanoate.

Fertility – Haldol Decanoate may increase your levels of a hormone called ‘prolactin’, which may affect fertility in men and women. Talk to your doctor if you have any questions about this.

Driving and using machines
Haldol Decanoate can affect your ability to drive and use tools or machines. Side effects, such as feeling sleepy, may affect your alertness, particularly when you first start using it or after a high dose. Do not drive or use any tools or machines without discussing this with your doctor first.

Haldol Decanoate contains
[To be completed nationally]

3. How to use Haldol Decanoate

How much medicine will you be given
Your doctor will decide how much Haldol Decanoate you need and for how long. Your doctor will adjust the dose to suit you, and may also give you a type of haloperidol that you take by mouth. Your dose of haloperidol decanoate will depend on:
- Your age
- Whether you have problems with your kidneys or liver
- How you have reacted to haloperidol in the past
- Other medicines you are taking.

Adults
- Your starting dose will normally be between 25 mg and 150 mg.

- Your doctor may adjust the dose by up to 50 mg every 4 weeks to find the dose that suits you best (normally between 50 mg and 200 mg every 4 weeks).
- You will not be given more than 300 mg every 4 weeks.

Elderly people
- Elderly people will normally start on a lower dose, usually 12.5 mg to 25 mg every 4 weeks.
- The dose may be adjusted until the doctor finds the dose that suits you best (normally between 25 mg and 75 mg every 4 weeks).
- You will only be given a higher dose than 75 mg every 4 weeks if your doctor decides it is safe to do so.

How Haldol Decanoate is given
Haldol Decanoate will be given by a doctor or nurse. It is for intramuscular use, and is given as an injection deep into a muscle. A single dose of Haldol Decanoate will normally last for 4 weeks. Haldol Decanoate must not be injected into a vein.

If you have too much Haldol Decanoate
A doctor or nurse will give this medicine to you, so it is unlikely that you will be given too much. If you are worried, tell the doctor or nurse.

If you miss a dose or stop using Haldol Decanoate
You should not stop this medicine unless told to do so by your doctor as your symptoms may return. If you miss an appointment, contact your doctor right away to make a new appointment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Look out for serious side effects
Tell your doctor or nurse straight away if you notice or suspect any of the following. You may need urgent medical treatment.

Problems with the heart:
- Abnormal heart rhythm – this stops the heart working normally and may cause loss of consciousness
- Abnormally fast heart beat
- Extra heart beats.

Heart problems are uncommon in people using Haldol Decanoate (may affect up to 1 in 100 people). Sudden deaths have occurred in patients using this medicine, but the exact frequency of these deaths is unknown. Cardiac arrest (the heart stops beating) has also occurred in people taking antipsychotic medicines.

A serious problem called 'neuroleptic malignant syndrome'. This causes a high fever, severe muscle stiffness, confusion and loss of consciousness. The exact frequency of this side effect in people using Haldol Decanoate is unknown.

Problems controlling movements of the body or limbs (extrapyramidal disorder), such as:
- Movements of the mouth, tongue, jaw and sometimes limbs (tardive dyskinesia)
- Feeling restless or difficulty sitting still, increased body movements
- Slow or reduced body movements, jerking or twisting movements
- Muscle tremors or stiffness, a shuffling walk

- Being unable to move
- Lack of normal facial expression that sometimes looks like a mask.

These are very common in people using Haldol Decanoate (may affect more than 1 in 10 people). If you get any of these effects, you may be given an additional medicine.

Severe allergic reaction that may include:
- A swollen face, lips, mouth, tongue or throat
- Difficulty swallowing or breathing
- Itchy rash (hives).

The exact frequency of an allergic reaction in people using Haldol Decanoate is unknown.

Blood clots in the veins, usually in the legs (deep vein thrombosis or DVT). These have been reported in people taking antipsychotic medicines. The signs of a DVT in the leg include swelling, pain and redness in the leg, but the clot may move to the lungs causing chest pain and difficulty in breathing. Blood clots can be very serious, so tell your doctor straight away if you notice any of these problems.

Tell your doctor straight away if you notice any of the serious side effects above.

Other side effects

Tell your doctor if you notice or suspect any of the following side effects.

Common (may affect up to 1 in 10 people):
- Depression
- Difficulty sleeping or feeling sleepy
- Constipation
- Dry mouth or increased saliva
- Problems having sex
- Irritation, pain or collection of pus (abscess) where the injection is given
- Weight gain.

Uncommon (may affect up to 1 in 100 people):
- Abnormal muscle tension
- Headache
- Upward movement of the eyes or fast eye movements that you cannot control
- Problems with vision, such as blurred vision.

The following side effects have also been reported, but their exact frequency is unknown:
- Serious mental health problem, such as believing things that are not true (delusions) or seeing, feeling, hearing or smelling things that are not there (hallucinations)
- Feeling agitated or confused
- Fits (seizures)
- Feeling dizzy, including upon sitting up or standing up
- Low blood pressure
- Problems that could cause difficulty breathing, such as:
  - Swelling around the voice box, or brief spasm of the vocal cords that affects speaking
  - Narrowed airways in the lungs
  - Being short of breath
- Nausea, vomiting
- Changes in the blood, such as:
  - Effects on blood cells – low number of all types of blood cells, including severe decreases in white blood cells and low number of ‘platelets’ (cells that help blood to clot)

    - High level of certain hormones in the blood – 'prolactin' and 'antidiuretic hormone' (syndrome of inappropriate antidiuretic hormone secretion)
    - Low level of sugar in the blood
- Changes that show up in blood tests of the liver and other liver problems, such as:
    - Yellowing of the skin or whites of the eyes (jaundice)
    - Inflamed liver
    - Sudden liver failure
- Decreased bile flow in the bile duct
- Skin problems, such as:
    - Rash or itching
    - Increased sensitivity to sunlight
    - Flaking or peeling skin
    - Inflamed small blood vessels, leading to a skin rash with small red or purple bumps
- Excessive sweating
- Breakdown of muscle tissue (rhabdomyolysis)
- Muscle spasms, twitching or contractions that you cannot control, including a spasm in the neck causing the head to twist to one side
- Difficulty or being unable to open the mouth
- Stiff muscles and joints
- Being unable to pass urine or empty the bladder completely
- Persistent and painful erection of the penis
- Difficulty getting and keeping an erection (impotence)
- Loss of sex drive or decreased sex drive
- Changes in menstrual cycle (periods), such as no periods, or long, heavy, painful periods
- Breast problems, such as:
    - Pain or discomfort
    - Unexpected production of breast milk
    - Enlarged breasts in men
- Swelling caused by fluid build up in the body
- High or low body temperature
- Problems walking
- Weight loss.

Reporting of side effects

- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Haldol Decanoate

Keep this medicine out of the sight and reach of children.

Haldol Decanoate should not be used after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

[To be completed nationally]

6. Contents of the pack and other information

What Haldol Decanoate contains

The active substance is haloperidol.

[To be completed nationally]

What Haldol Decanoate looks like and contents of the pack
[To be completed nationally]

Marketing Authorisation Holder and Manufacturer
[See Annex I – To be completed nationally]

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria:	Haldol Decanoat
Belgium, France, Italy, Luxembourg, Netherlands:	Haldol Decanoas
Cyprus, Ireland, Malta, United Kingdom:	Haldol Decanoate
Denmark:	Serenase Dekanoat
Finland:	Seranase Depot
Germany:	Haldol-Janssen Decanoat Depot
Greece:	Aloperidin Decanoas
Iceland, Norway, Sweden:	Haldol Depot
Portugal:	Haldol Decanoato

This leaflet was last revised in {month YYYY}.
[To be completed nationally]

<Other sources of information>
<Detailed information on this medicine is available on the website of {MS/Agency}>

[To be completed nationally]