SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

DROPERIDOL EQUITY, 1,25 mg/mL droperidol, solution for injection (IV)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of the solution contains droperidol 1,25 mg.

Contains sugar (mannitol 47,0 mg per mL).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Clear, sterile solution, free from any visible particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Prevention and treatment of post-operative nausea and vomiting (PONV), in adults and, as second line, in children (from 2 to 11 years) and adolescents (12 - 18 years).
- Prevention of nausea and vomiting induced by morphine and its derivatives, during post-operative patient-controlled analgesia (PCA) in adults.

Some precautions are required during the administration of droperidol (see sections 4.2, 4.3 and 4.4).

4.2 Posology and method of administration

Posology

Hospital use only. This medicine must be administered by specialised healthcare professionals.

The dosage should be adapted to each individual case. The factors to be considered here include age, body

2025.06.17

weight, the· use of other medicines, the type of anaesthesia to be used and the surgical or diagnostic procedure involved.

Vital signs and ECG should be monitored routinely. To minimise the risk of ventricular dysrhythmia an electrocardiograph (ECG) should be performed and examined for evidence of QT prolongation before any operation commences. ECG monitoring should continue during the surgical or diagnostic procedure and subsequently for a period consistent with best medical judgement, but at least 7 hours after the end of the procedure (see section 4.3 and 4.8).

Prevention and treatment of post-operative nausea and vomiting (PONV):

Adults

0,625 mg to 1,25 mg (0,5 mL to 1 mL).

Elderly patients (65 years): 0,625 mg (0,5 mL)

Renal/hepatic impairment: 0,625 mg (0,5 mL)

Paediatric population

Children (2 to 11 years) and adolescents (12 to 18 years): 10 to 50 microgram/kg (up to a maximum of 1,25 mg).

Children (below the age of 2 years): not recommended.

Administration of DROPERIDOL EQUITY is recommended 30 minutes before the anticipated end of surgery. Repeat doses may be given every 6 hours as required.

Prevention of nausea and vomiting induced by morphine derivatives during post-operative patient controlled analgesia (PCA):

Adults:

15 to 50 micrograms droperidol per mg of morphine, up to a maximum daily dose of 5 mg droperidol.

Elderly (over 65 years), renal and hepatic impairment: no data in patient controlled analgesia (PCA) available.

2025.06.17

Paediatric population

Children (2 to 11 years) and adolescents (12 to 18 years): not indicated in patient controlled analgesia (PCA).

Continuous pulse oximetry should be performed in patients with identified or suspected risk of ventricular dysrhythmia and should continue for 30 minutes following single IV administration.

Method of administration

Intravenous route.

For instructions on dilution of the medicine before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to droperidol, butyrophenones or to any of the excipients of DROPERIDOL EQUITY listed in section 6.1
- Known or suspected QT interval prolongation (QTc > 450 ms in females and > 440 ms in males).
  This includes patients with congenital long QT syndrome, patients with a family history of congenital QT prolongation and patients treated concomitantly with medicines known for the risk of inducing torsades de pointes through QT prolongation (see section 4.5): Class IA and III anti-dysrhythmic agents (amiodarone, amisulpride, disopyramide, dronedarone, hydroquinidine, quinidine, sotalol), citalopram, escitalopram, cocaine, domperidone, erythromycin administered by intravenous route, hydroxyzine, mequitazine, moxifloxacin, piperaquine, spiramycin, toremifene, vincamine, vandetanib.
- Hypokalaemia or hypomagnesaemia
- Bradycardia (< 55 heartbeats per minute)
- Known concomitant treatment leading to bradycardia
- Phaeochromocytoma
- Comatose states
- Parkinson's Disease
- Severe depression

2025.06.17

- Combination with dopaminergic agents (amantadine, apomorphine, bromocriptine, cabergoline, entacapone, lisuride, piribedil, pramipexole, quinagolide, rasagiline, ropinirole, rotigotine, selegiline, tolcapone).

4.4 Special warnings and precautions for use

Central Nervous System

DROPERIDOL EQUITY may enhance CNS depression produced by other CNS-depressant medicines. Any patient subjected to anaesthesia and receiving potent CNS depressant medicines or showing symptoms of CNS depression should be monitored closely.

Concomitant use of metoclopramide and other neuroleptics may lead to an increase in extrapyramidal symptoms and should be avoided (see section 4.5).

Use with caution in patients with epilepsy (or a history of epilepsy) and conditions predisposing to epilepsy or convulsions.

Cardiovascular system

Mild to moderate hypotension and occasionally (reflex) tachycardia have been observed following the administration of droperidol as contained in DROPERIDOL EQUITY. This reaction usually subsides spontaneously. However, should hypotension persist, the possibility of hypovolaemia should be considered, and appropriate fluid replacement administered.

Patients with, or suspected of having, the following risk factors for cardiac dysrhythmia should be carefully evaluated prior to administration of DROPERIDOL EQUITY:

- a history of significant cardiac disease including serious ventricular dysrhythmia, second or third degree atrio-ventricular block, sinus node dysfunction, congestive heart failure, ischemic heart disease and left ventricular hypertrophy;

2025.06.17

- family history of sudden death;
- renal failure (particularly when on chronic dialysis);
- significant chronic obstructive pulmonary disease and respiratory failure;
- risk factors for electrolyte disturbances, as seen in patients taking laxatives, glucocorticoids, potassium-wasting diuretics, in association with the administration of insulin in acute settings, or in patients with prolonged vomiting and/or diarrhoea.

Patients at risk for cardiac dysrhythmia should have serum electrolytes and creatinine levels assessed and the presence of QT prolongation excluded prior to administration of DROPERIDOL EQUITY.

Continuous pulse oximetry should be performed in patients with identified or suspected risk of ventricular dysrhythmia and should continue for 30 minutes following single intravenous administration.

General

To prevent QT prolongation, caution is necessary when patients are taking medicine likely to induce electrolyte imbalance (hypokalaemia and/or hypomagnesaemia) e.g. potassium-wasting diuretics, laxatives and glucocorticoids.

Substances inhibiting the activity of cytochrome P450 iso-enzymes (CYP) CYP1A2, CYP3A4 or both could decrease the rate at which droperidol is metabolised and prolong its pharmacological action. Hence, caution is advised if droperidol is given concomitantly with strong CYP 1A2 and CYP3A4 inhibitors (see section 4.5).

Patients who have, or are suspected of having, a history of alcohol abuse or recent high intakes, should be thoroughly assessed before droperidol is administered.

Taking the following medicines with DROPERIDOL EQUITY, that may induce cardiac rhythm disorders,

2025.06.17

specifically torsades de pointes, is not recommended (see section 4.5):

Arsenic trioxide, antiparasitic medicines likely to induce torsades de pointes (chloroquine, halofantrine, lumefantrine, pentamidine), neuroleptics likely to induce torsades de pointes (chlorpromazine, cyamemazine, flupentixol, fluphenazine, haloperidol, levomepromazine, pimozide, pipamperone, pipotiazine, sulpiride, tiapride, zuclopenthixol), delamanid, crizotinib, hydroxychloroquine, methadone, sulfamethoxazole + trimethoprim.

In case of unexplained hyperthermia, it is essential to discontinue treatment, since this sign may be one of the elements of malignant syndrome reported with neuroleptics.

Cases of venous thromboembolism (VTE) have been reported with antipsychotic medicines. 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 DROPERIDOL EQUITY and preventive measures undertaken.

The dose should be reduced in the elderly and those with impaired renal and hepatic function (see section 4.2).

4.5 Interaction with other medicines and other forms of interaction

Contraindicated for concomitant use

Medicines known to cause torsades de pointes through QT prolongation should not be concomitantly administered with DROPERIDOL EQUITY. For example:

- Class IA anti-dysrhythmics e.g., quinidine, hydroquinidine, disopyramide, procainamide
- Class III anti-dysrhythmics e.g., amiodarone, sotalol, dronedarone
- cocaine
- dopaminergic agents (amantadine, apomorphine, bromocriptine, cabergoline, entacapone, lisuride, piribedil, pramipexole, quinagolide, rasagiline, ropinirole, rotigotine, selegiline, tolcapone).

2025.06.17

Reciprocal antagonism between the dopaminergic agent and the neuroleptic. Use an anti-emetic devoid of extrapyramidal effects.

- hydroxyzine
- levodopa
- anti-cancer medicine such as toremifene, vandetanib
- vincamine
- macrolide antibiotics e.g., erythromycin, clarithromycin, spiramycin
- fluoroquinolone antibiotics e.g., sparfloxacin, moxifloxacin
- antihistamines e.g., astemizole, terfenadine, mequitazine
- certain antipsychotic medications e.g., chlorpromazine, haloperidol, pimozide, thioridazine, risperidone, sertindole
- anti-malaria medicine e.g., chloroquine, halofantrine, piperaquine
- cisapride, domperidone, methadone, pentamidine, bepridil
- tricyclic antidepressants (such as amitriptyline, citalopram, escitalopram)
- certain tetracyclic antidepressants (such as maprotiline)

Concomitant use of medicines that induce extrapyramidal symptoms, e.g., metoclopramide and other neuroleptics, may lead to an increased incidence of these symptoms and should therefore be avoided.
Since droperidol blocks dopamine receptors, it may inhibit the action of dopamine agonists, such as bromocriptine, lisuride, and of L-dopa (see section 4.3).

Concomitant use is not recommended (see section 4.4):

- alcoholic beverages and medicines containing alcohol. Caution is also advised when DROPERIDOL EQUITY is used in patients who have, or are suspected of having, a history of alcohol abuse or recent high intakes, as the risk of dysrhythmia is increased.
- arsenic trioxide
- anti-parasitic medicine e.g., lumefantrine, pentamidine, hydroxychloroquine

2025.06.17

- neuroleptic medicine e,g., cyamemazine, flupentixol, fluphenazine, levomepromazine, pipamperone, pipotiazine, sulpiride, tiapride, zuclopenthixol
- crizotinib
- delamanid
- sodium oxybate
- sulfamethoxazole + trimethoprim

Caution is advised for concomitant use

Caution is advised when DROPERIDOL EQUITY is used with any other medication known to prolong the QT interval. This includes:

- anagrelide
- azithromycin, roxithromycin
- beta-blockers in heart failure
- bradycardia-inducing agents
- ciprofloxacin, levofloxacin, norfloxacin
- glasdegib

To reduce the risk of QT prolongation, caution is necessary when patients are taking medicines likely to induce electrolyte imbalance (hypokalaemia and/or hypomagnesaemia) e.g., potassium-wasting diuretics, laxatives and glucocorticoids.

Caution is advised for concomitant use of DROPERIDOL EQUITY with lithium and ondansetron.

DROPERIDOL EQUITY may potentiate the action of sedatives. This includes barbiturates, benzodiazepines, morphine derivatives (analgesics, antitussives and substitution treatments), neuroleptics, anxiolytics other than benzodiazepines (for example meprobamate), hypnotic agents, sedative antidepressants (amitriptyline, doxepin, mianserine, mirtazapine, trimipramine), sedative H1 antihistamines, central-acting antihypertensive agents, baclofen and thalidomide.

2025.06.17

Droperidol as contained in DROPERIDOL EQUITY, may potentiate respiratory depression caused by opioids.

Substances inhibiting the activity of cytochrome P450 iso-enzymes (CYP) CYP1A2, CYP3A4 or both could decrease the rate at which droperidol is metabolised and prolong its pharmacological action. Hence, caution is advised if DROPERIDOL EQUITY is given concomitantly with CYP1A2 inhibitors (e.g., ciprofloxacin, ticlopidine), CYP3A4 inhibitors (e.g., diltiazem, erythromycin, fluconazole, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, verapamil) or both (e.g., cimetidine, mibefradil).

Concomitant use to be taken into consideration

- aripiprazole
- dapoxetine
- medicines that cause male hypogonadism (abiraterone, apalutamide, bicalutamide, cyproterone, degarelix, dutasteride, enzalutamide, finasteride, flutamide, gosereline, leuprorelin, nilutamide, triptorelin)
- orlistat

Medicines that cause orthostatic hypotension

In addition to antihypertensive agents, many medicines can cause orthostatic hypotension. This is specifically the case of nitrate derivatives, type 5 phosphodiesterase inhibitors, alpha-blockers for urological purposes, imipraminic antidepressants and phenothiazine neuroleptics, dopaminergic agonists and levodopa. Therefore, their joint use with DROPERIDOL EQUITY risks increasing the frequency and intensity of this undesirable effect. Refer to the interactions specific to each group, with the corresponding constraint levels.

Medicines that lower the seizure threshold

Concomitant use of proconvulsant medicines, or that lower the seizure threshold, should be carefully considered, due to the severity of the risk involved. These medicines are represented in particular by the majority of antidepressants (imipraminic, selective serotonin uptake inhibitors), neuroleptics (phenothiazines

2025.06.17

and butyrophenones), mefloquine, chloroquine, fluoroquinolones, bupropion and tramadol.

4.6 Fertility, pregnancy and lactation

Pregnancy

A limited amount of clinical data has shown no increase of malformative risk.

Droperidol has not been shown to be teratogenic in rats. Animal studies are insufficient with respect to the effects on pregnancy and embryonal/foetal, parturition and postnatal development.

In newborn babies from mothers under long-term treatment and high doses of neuroleptics, temporary neurological disturbances of extrapyramidal nature have been described.

As a precaution, it is best not to administer DROPERIDOL EQUITY during pregnancy. If it is necessary to administer DROPERIDOL EQUITY in late pregnancy, it is recommended to monitor the neurological functions of the newborn.

Breastfeeding

Neuroleptics of the butyrophenone type are known to be excreted in breast milk; treatment with DROPERIDOL EQUITY should be limited to a single administration. Repeated administration is not recommended.

Fertility

The clinical effect of DROPERIDOL EQUITY on fertility has not been established.

4.7 Effects on ability to drive and use machines

DROPERIDOL EQUITY has an important influence on the ability to drive and use machines.

Patients should not drive or operate a machine for 24 hours after DROPERIDOL EQUITY administration.

2025.06.17

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported events during clinical experience are incidents of drowsiness and sedation. In addition, less frequent reports of hypotension, cardiac dysrhythmias, neuroleptic malignant syndrome (NMS) and symptoms associated with NMS, plus movement disorders, such as dyskinesias, plus incidents of anxiety or agitation have occurred.

Tabulated list of adverse reactions

Blood and lymphatic systems disorders	
Less frequent	Blood dyscrasias
Immune system disorders	
Less frequent	Anaphylactic reaction, angioneurotic oedema, hypersensitivity
Metabolism and nutrition disorders	
Frequency unknown	Inappropriate anti-diuretic hormone secretion
Psychiatric disorders	
Less frequent	Anxiety, restlessness/akathisia, confusional states, agitation, dysphoria
Frequency unknown	hallucinations
Nervous system disorders	
Frequent	Drowsiness
Less frequent	Dystonia, oculogyration, extrapyramidal disorder, convulsions, tremor
Frequency unknown	Epileptic fits, Parkinson's disease; psychomotor hyperactivity, coma
Cardiac disorders	
Less frequent	Tachycardia, dizziness, cardiac dysrhythmias, including ventricular dysrhythmias, cardiac arrest Torsade de pointes, electrogram QT prolongation
Vascular disorders	

2025.06.17

Frequent	Hypotension
Frequency unknown	Syncope
Respiratory, thoracic and mediastinal disorders	
Frequency unknown	Bronchospasm, laryngospasm
Skin and subcutaneous system disorders	
Less frequent	Rash
General disorders and administration site conditions	
Less frequent	Neuroleptic malignant syndrome (NMS), sudden death

Symptoms potentially associated with NMS have been reported i.e., changes in body temperature, stiffness and fever. An alteration in mental status with confusion or agitation and altered consciousness, have been seen. Autonomic instability may manifest as tachycardia, fluctuating blood pressure, excessive sweating/salivation and tremor. In extreme cases NMS may lead to coma, or renal and/or hepato-biliary problems.

Isolated cases of amenorrhoea, galactorrhoea, gynaecomastia, hyperprolactinaemia, and oligomenorrhoea have been associated with prolonged exposure in psychiatric indications.

Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis have been reported with antipsychotic medicines - frequency unknown.

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. Health care providers are requested to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

2025.06.17

4.9 Overdose

Symptoms

The manifestations of DROPERIDOL EQUITY overdose are an extension of its pharmacologic actions. Symptoms of accidental overdose are psychic indifference with a transition to sleep, sometimes in association with lowered blood pressure.

At higher doses or in sensitive patients, extrapyramidal disorders may occur (salivation, abnormal movements, sometimes muscle rigidity). Convulsions may occur at toxic doses.

Cases of QT-interval prolongation, ventricular dysrhythmias and sudden death have been reported rarely.

Treatment

No specific antidote is known. However, when extrapyramidal reactions occur, an anticholinergic should be administered.

Patients with DROPERIDOL EQUITY overdose should be closely monitored for signs of QT interval prolongation. Factors which predispose to torsades de pointes, e.g., electrolyte disturbances (especially hypokalaemia or hypomagnesaemia) and bradycardia should be taken into consideration.

Pronounced hypotension should be treated by boosting circulation volume and taking other appropriate measures. Clear airways and adequate oxygenation should be maintained; an oropharyngeal airway or endotracheal tube might be indicated.

If required, the patient should be observed carefully for 24 hours or longer; body warmth and adequate fluid intake should be maintained.

5. PHARMACOLOGICAL PROPERTIES

2025.06.17

5.1 Pharmacodynamic properties

A.2.6.5 Central nervous system depressants. Miscellaneous structures.

Pharmacotherapeutic group: Butyrophenone derivates. ATC code: N05AD08.

Droperidol is a butyrophenone neuroleptic. Its pharmacologic profile is characterised mainly by dopamine-blocking and weak α1-adrenolytic effects. Droperidol is devoid of anticholinergic and antihistaminic activity.

It has a marked tranquillising and sedative effect, alleviates apprehension and causes a state of mental detachment and indifference while maintaining a state of reflex alertness.

Droperidol produces an antiemetic effect. It lowers the incidence of nausea and vomiting during surgical procedures and provides anti-emetic protection in the post-operative period.

Droperidol potentiates other central nervous system depressants. It induces mild α1-adrenergic blockade and peripheral vascular dilation and reduces the pressor effect of adrenaline. It can cause hypotension and decreased peripheral vascular resistance and may decrease pulmonary arterial pressure (particularly if it is abnormally high). It may also reduce the incidence of adrenaline-induced dysrhythmia, but. it does not prevent other forms of cardiac dysrhythmia.

5.2 Pharmacokinetic properties

The action of a single intravenous dose commences 2-3 minutes following administration. The tranquillising and sedative effects tend to persist for 2 to 4 hours, although alertness may be affected for up to 12 hours.

Distribution

Following intravenous administration, plasma concentrations fall rapidly during the first 15 minutes; this is metabolism independent, redistribution of the drug. Plasma protein binding amounts to 85 – 90 %. The distribution volume is approximately 1,5 L/kg.

2025.06.17

Biotransformation

Droperidol is extensively metabolised in the liver, and undergoes oxidation, dealkylation, demethylation and hydroxylation by cytochrome P450 isoenzymes 1A2 and 3A4, and to a lesser extent by 2C 19. The metabolites are devoid of neuroleptic activity.

Elimination

Elimination occurs mainly through metabolism; 75 % is excreted via the kidneys. Only 1 % of the active substance is excreted unchanged in the urine, and 11 % in the faeces. Plasma clearance is 0,8 (0,4 – 1,8) L/min. The elimination half-life ($t_{1/2\,ß}$) is 134 ± 13 min.

Paediatric population

In a study including 12 children (aged 3.5 to 12 years), the values for distribution volume and clearance were lower than those observed in the adult population (0.58 ± 0.29 L/kg and 4.66 ± 2.28 mL/kg*min, respectively) and decreased simultaneously. The elimination half-life (101.5 ± 26.4 min) was similar to that observed in adults.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol

Tartaric acid (acidifier and pH adjuster)

Sodium hydroxide (for pH adjustment)

Water for injection

6.2 Incompatibilities

Incompatible with barbiturates. This medicine must not be mixed with other medicines except those mentioned in section 6.6.

2025.06.17

6.3 Shelf life

Unopened: 36 months

After first opening: For immediate use.

After dilution: Compatibility of DROPERIDOL EQUITY with 0,9 % sodium chloride in plastic syringes has been demonstrated for 48 hours at 25 °C. From a microbiological point of view, DROPERIDOL EQUITY should be used immediately.

From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light.

Store the ampoules in the original package until required for use.

For storage conditions after dilution of the medicine, see section 6.3.

6.5 Nature and contents of container

DROPERIDOL EQUITY is packaged in 1 ml one point cut ampoules made of brown type I glass.

The ampoules are packaged in thermoformed blister strips or in paper racks and then inserted in cardboard boxes, 10 ampoules per box.

6.6 Special precautions for disposal and other handling

For single use only. Any unused solution should be discarded.

The solution should be inspected visually prior to use. Only clear and colourless solutions free from visible

2025.06.17

particles should be used.

For use in patient-controlled analgesia (PCA): Draw DROPERIDOL EQUITY and morphine into a syringe and make up the volume with 0,9 % sodium chloride for injection.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Equity Pharmaceuticals (Pty) Ltd.

100 Sovereign Drive

Route 21 Corporate Park

Nellmapius Drive

Irene, Pretoria

8. REGISTRATION NUMBER(S)

57/2.6.5/0556

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 June 2025

10. DATE OF REVISION OF THE TEXT

2025.06.17