
MOTILIUM[®]

domperidone

DATASHEET

1. PRODUCT NAME

Motilium 10 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10 mg domperidone base.

Excipients with known effect:

Each film-coated tablet contains 54.2 mg of lactose monohydrate

For the full list of excipients, see **6.1 List of excipients**.

3. PHARMACEUTICAL FORM

Film-coated tablets

MOTILIUM 10 mg tablets are white, circular, film-coated, biconvex tablets with m/10 imprinted on one side and JANSSEN on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults and children weighing ≥ 35 kg

Symptomatic treatment of the dyspeptic symptom complex that may be associated with delayed gastric emptying such as epigastric sense of fullness, abdominal distension or swelling, or epigastric pain or discomfort.

Treatment of acute symptoms of nausea and vomiting.

There is insufficient evidence to support the use of domperidone in childhood gastro-oesophageal reflux disease. Domperidone may not be suitable for chemotherapy- or radiotherapy-induced nausea and vomiting or post-operative nausea and vomiting.

4.2 Dose and method of administration

General

MOTILIUM should be taken 15-30 minutes before meals and, if necessary, before retiring. If taken after meals, absorption is somewhat delayed.

Adults and adolescents ≥ 12 years of age and weighing ≥ 35 kg, and children < 12 years of age and weighing ≥ 35 kg

1 tablet three to four times daily.

The dose of MOTILIUM should be the lowest effective dose for the individual situation (typically 30 mg/day). The dose may be increased, if necessary, to a maximum daily oral dose of 40 mg (1 tablet four times daily).

Usually, the maximum treatment duration should not exceed one week for the treatment of acute nausea and vomiting. If nausea and vomiting persists for longer than one week, patients should consult their physician. For other indications, the initial duration of treatment is up to four weeks. If treatment exceeds four weeks, patients should be re-evaluated and the need for continued treatment re-assessed.

For children, the total daily dose has been determined as 0.25 mg/kg three to four times per day with a maximum **daily** dose of 1.0 mg/kg. However, the MOTILIUM tablet formulation is unsuitable for treatment in children weighing less than 35 kg. Use in children under 2 years of age is contraindicated (see **section 4.3 Contraindications**). Overdosing may cause nervous system disorders in children (see **section 4.9 Overdose**).

Adults and adolescents (≥ 12 years of age) and weighing < 35 Kg

MOTILIUM tablets are unsuitable for use in adults and adolescents weighing less than 35 kg.

Infants and children < 12 years of age and weighing < 35 kg

Use in children under 2 years of age is contraindicated (see **section 4.3 Contraindications**).

The efficacy of MOTILIUM has not been established in infants and children < 12 years of age and weighing < 35 kg (see **section 5.1 Pharmacodynamic properties - Clinical Studies - Infants and children ≤ 12 years of age**).

Use in renal impairment

It is unlikely that the dose needs to be adjusted for single administration in patients with renal insufficiency. However, since the elimination half-life of domperidone is prolonged in severe renal impairment, on repeated administration the dosing frequency of MOTILIUM should be reduced to once or twice daily depending on the severity of the impairment (see **section 4.4 Special warnings and precautions for use**). Generally, patients on prolonged therapy should be reviewed regularly.

Hepatic impairment

MOTILIUM is contraindicated for patients with moderate or severe hepatic impairment (see **section 4.3 Contraindications**).

4.3 Contraindications

MOTILIUM is contraindicated in the following situations:

- Known hypersensitivity to domperidone or any of the excipients
- Prolactin-releasing pituitary tumour (prolactinoma)
- Use in children under 2 years of age.
- Co-administration with potent CYP3A4 inhibitors has been shown to increase domperidone concentrations to the point where QT interval prolongation may occur. Examples of potent CYP3A4 inhibitors include some azole antifungals (eg, itraconazole, voriconazole, posaconazole), some macrolide antibiotics (eg, clarithromycin, telithromycin), and some protease inhibitors (ritonavir, saquinavir, telaprevir).
- Co-administration with medicines that prolong the QTc interval.
- MOTILIUM should not be used whenever stimulation of gastrointestinal motility might be dangerous such as in the presence of gastrointestinal haemorrhage, mechanical obstruction, or perforation.

- In patients with moderate or severe hepatic impairment (see **section 5.2 Pharmacokinetic properties**).

4.4 Special warnings and precautions for use

Cardiovascular effects

MOTILIUM should be used with caution in older patients or those with current or history of cardiac disease. An increase in the risk of serious ventricular arrhythmias and sudden cardiac death has been reported in epidemiology studies (see **section 4.8 Undesirable Effects**). Those studies suggest this increased risk may be higher in patients older than 60 years or at total daily doses of more than 30mg. Therefore, MOTILIUM should be used with caution in older patients. MOTILIUM should be used at the lowest effective dose in adults and children. Treatment with domperidone should be stopped if signs or symptoms occur that may be associated with cardiac arrhythmia, and the patient should consult their physician.

Use of MOTILIUM and other drugs which prolong QTc intervals requires that caution be exercised in patients who have existing prolongation of cardiac conduction intervals, particularly QTc, patients with significant electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia), or bradycardia, or in patients with underlying cardiac diseases such as congestive heart failure. Electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia) and bradycardia are known to be conditions increasing the proarrhythmic risk. Other risk factors for sudden cardiac arrest include a family history of coronary artery disease, high blood pressure, high blood cholesterol, obesity, diabetes, smoking and excessive alcohol consumption. It is desirable to optimise electrolyte levels prior to starting domperidone.

Drug interaction potential

The main metabolic pathway of domperidone is through CYP3A4. *In vitro* and human data show that the concomitant use of drugs that significantly inhibit this enzyme may result in increased plasma levels of domperidone. Co-administration of domperidone with potent CYP3A4 inhibitors which have been shown to cause QT interval prolongation is contraindicated (see **section 4.3 Contraindications**).

Caution should be exercised when domperidone is co-administered with potent CYP3A4 inhibitors which have not been shown to cause QT interval prolongation such as indinavir and patients should be monitored closely for signs or symptoms of adverse reactions (see **section 4.8 Undesirable Effects**).

Caution should be exercised when domperidone is co-administered with drugs which have been shown to cause QT interval prolongation and patients should be monitored closely for signs or symptoms of cardiovascular adverse reactions (see **section 4.8 Undesirable Effects**). Examples include:

- anti arrhythmics class IA (e.g., disopyramide, quinidine)
- anti arrhythmics class III (e.g., amiodarone, dofetilide, dronedarone, ibutilide, sotalol)
- certain antipsychotics (e.g., haloperidol, pimozide, sertindole)
- certain antidepressants (e.g., citalopram, escitalopram)
- certain antibiotics (e.g., levofloxacin, moxifloxacin)
- certain antifungal agents (e.g., pentamidine)
- certain antimalarial agents (e.g., halofantrine)
- certain azole antifungals, (e.g., itraconazole, ketoconazole, voriconazole)
- certain calcium antagonists, (e.g., diltiazem, verapamil)
- certain gastro intestinal drugs (e.g., dolasetron)

- certain HIV protease inhibitors (e.g., amprenavir, atazanavir, fosamprenavir, indinavir, nelfinavir, ritonavir, saquinavir)
- certain drugs used in cancer (e.g., toremifene, vandetanib)
- certain macrolide antibiotics (e.g., clarithromycin, erythromycin)
- certain other drugs (e.g., aprepitant, bepridil, methadone, nefazodone, telithromycin)

Antacids or antisecretory agents should not be taken simultaneously with MOTILIUM, as they lower the oral bioavailability of domperidone (see **section 4.5 Interactions with other medicines and other forms of interactions**). When used concomitantly, MOTILIUM should be taken before meals and antacids or antisecretory agents after meals.

Intolerance to lactose

The film-coated tablets contain lactose and may be unsuitable for patients with lactose intolerance, galactosemia or glucose/galactose malabsorption.

Prolactin levels

MOTILIUM produces an increase in plasma prolactin. The raised level persists with chronic administration but falls to normal on discontinuing the medicine. During chronic oral administration of 30 mg daily for two weeks the plasma prolactin level measured 90 minutes after medicine intake remained fairly constant at 25 ng/mL in males (normal value was 5 ng/mL) whilst in females the level of 117 ng/mL after the first dose decreased to 56 ng/mL after 14 doses (pretreatment normal value was 9 ng/mL).

Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin-dependent *in vitro*, a factor of potential importance if the administration of domperidone is contemplated in a patient with a past history of breast cancer. Although disturbances such as galactorrhoea, amenorrhoea, gynaecomastia and impotence have been reported with other prolactin-elevating medicines, the clinical significance of elevated serum prolactin levels is unknown. An increase in mammary neoplasms has been found in rodents after chronic administration of domperidone and other prolactin-stimulating medicines.

Neither clinical studies nor epidemiological studies conducted to date have shown an association between chronic administration of these medicines and mammary tumorigenesis. Domperidone does not affect plasma growth hormone or aldosterone levels.

Renal impairment

Since the elimination half-life of domperidone is prolonged in severe renal impairment, the dosing frequency of MOTILIUM should to be reduced to once or twice daily depending on the severity of the impairment. The dose may also need to be reduced. Such patients with severe renal impairment should be reviewed regularly (see **sections 5.2 Pharmacokinetic properties and 4.2 Dose and method of administration**).

Hepatic Impairment

MOTILIUM is contraindicated for patients with moderate or severe hepatic impairment (see **section 4.3 Contraindications**). Dose adjustment is not required for patients with mild hepatic impairment (see **section 5.2 Pharmacokinetic properties**).

Infants

MOTILIUM tablets are unsuitable for use in children <12 years of age and weighing less than 35 kg. (see section **4.2 Dose and method of administration**).

4.5 Interactions with other medicines and other forms of interactions

Concomitant administration of anticholinergic drugs may antagonise the anti-dyspeptic effect of MOTILIUM.

If administered prior to atropine, domperidone reduces the relaxant effect of atropine upon the lower oesophageal sphincter, but has no reversing effect if atropine is administered first. The main metabolic pathway of domperidone is through the cytochrome P450 isoenzyme CYP3A4. *In vitro* and human data show that the concomitant use of drugs that significantly inhibit this enzyme may result in increased plasma levels of domperidone.

When domperidone was co-administered with potent CYP3A4 inhibitors which have been shown to cause QT interval prolongation, clinically relevant changes in QT intervals were observed. Therefore, co-administration of domperidone with certain drugs is contraindicated (see **section 4.3 Contraindications**).

Caution should be exercised when domperidone is co-administered with potent CYP3A4 inhibitors which have not been shown to cause QT interval prolongation or drugs which have been shown to cause QT interval prolongation (see **section 4.4 Special warnings and precautions for use**).

Theoretically, since MOTILIUM has gastro-kinetic effects, it could influence the absorption of concomitantly orally administered drugs, particularly those with sustained-release or enteric-coated formulations. However, in patients already stabilised on digoxin or paracetamol, concomitant administration of domperidone did not influence the blood levels of these drugs.

Domperidone has been used with:

- neuroleptics, without potentiation of their activity,
- dopaminergic agonists (bromocriptine, L-dopa) for suppression of unwanted peripheral effects such as digestive disorders, nausea and vomiting, without affecting their central activity.

4.6 Fertility, pregnancy & lactation

Pregnancy

There are limited post-marketing data on the use of domperidone in pregnant women. A study in rats has shown reproductive toxicity at a high, maternally toxic dose. The potential risk for humans is unknown. Therefore, MOTILIUM should only be used during pregnancy when justified by the anticipated therapeutic benefit.

Lactation

The amount of domperidone that could be ingested by an infant through breast milk is low. The maximal relative infant dose (%) is estimated to be about 0.1% of the maternal weight-adjusted dosage. It is not known whether this is harmful to the newborn. Therefore breast-feeding is not recommended for women who are taking MOTILIUM.

4.7 Effects on Ability to Drive and Use Machines

Dizziness and somnolence have been observed following use of domperidone (see **section 4.8 Undesirable Effects**). Therefore, patients should be advised not to drive or use machinery or engage in other activities requiring mental alertness and coordination until they have established how MOTILIUM affects them.

4.8 Undesirable Effects

Clinical Trial Data

The safety of MOTILIUM was evaluated in 1221 patients with gastroparesis, dyspepsia, gastro-oesophageal reflux disorder (GERD), or other related conditions in 45 clinical trials included in the safety database. All patients were ≥ 15 years old and received at least one dose of oral MOTILIUM (domperidone base). Slightly fewer than one-half (553/1221) of patients were diabetic. The median total daily dose was 80 mg (range 10 to 160 mg), with 230 patients receiving a dose greater than 80 mg. Median duration of exposure was 56 days (range 1 to 2248 days).

Table 1. Adverse - Reactions Reported by $\geq 1\%$ of MOTILIUM-Treated Patients in 45 Clinical Trials

System/Organ Class Adverse Reaction	MOTILIUM (n=1221) %
Psychiatric Disorders	
Depression	2.5
Anxiety	1.6
Libido Decreased/Loss of Libido	1.5
Nervous System Disorders	
Headache	5.6
Somnolence	2.5
Akathisia	1.0
Gastrointestinal Disorders	
Diarrhoea	5.2
Skin and Subcutaneous Tissue Disorders	
Rash	2.8
Pruritus	1.7
Reproductive System and Breast Disorders	
Breast Enlargement/Gynaecomastia	5.3
Breast Tenderness	4.4
Galactorrhoea	3.3
Amenorrhoea	2.9
Breast Pain	2.3
Menstruation Irregular	2.0
Lactation Disorder	1.6
General Disorders and Administration Site Conditions	
Asthenia	1.9

ADRs that occurred in $< 1\%$ of Domperidone-treated patients in the 45 clinical trials (n=1221) are listed below in **Table 2**.

Table 2. Adverse Drug Reactions Reported by $<1\%$ of MOTILIUM -Treated Patients in 45 Clinical Trials

System/Organ Class Adverse Reaction	MOTILIUM (n=1221) %
Immune System Disorders	
Hypersensitivity	0.2
Skin and Subcutaneous Tissue Disorders	
Urticaria	0.7
Reproductive System and Breast Disorders	
Breast Discharge	0.8

System/Organ Class	MOTILIUM (n=1221)
Adverse Reaction	%
Breast Swelling	0.5

The following adverse reaction has been reported with over-the-counter use: dry mouth.

Postmarketing

In addition to the adverse effects reported during clinical studies and listed above, the following adverse drug reactions have been reported. In each table, the frequencies are provided according to the following convention:

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

In **Table 3**, ADRs are presented by frequency category based on spontaneous reporting rates, when known.

Table 3. Adverse Drug Reactions Identified During Postmarketing Experience with MOTILIUM by Frequency Category Estimated from Spontaneous Reporting Rates

Immune System Disorders	
<i>Very rare</i>	Anaphylactic Reaction (including Anaphylactic Shock)
Psychiatric Disorders	
<i>Very rare</i>	Agitation, Nervousness
Nervous System Disorders	
<i>Very rare</i>	Dizziness, Extrapyramidal Disorder, Convulsion
Cardiac Disorders	
<i>Very rare</i>	Sudden Cardiac Death*, Serious Ventricular Arrhythmias*
Skin and Subcutaneous Tissue Disorders	
<i>Very rare</i>	Angioedema, Urticaria
Renal and Urinary Disorders	
<i>Very rare</i>	Urinary Retention
Reproductive System and Breast Disorders	
<i>Rare</i>	Gynaecomastia, Amenorrhoea
Investigations	
<i>Very rare</i>	Liver Function Test Abnormal, Blood Prolactin Increased

* Based on epidemiology data (see below)

Very rare case reports of QTc prolongation, ventricular arrhythmia, and sudden death have occurred with domperidone use. Although most reported cases have occurred in patients receiving the intravenous form of domperidone, or in patients with other risk factors, an association with oral domperidone cannot be completely ruled out. Therefore, domperidone should be used with caution in patients with other risk factors for QTc prolongation including hypokalaemia, severe hypomagnesaemia, structural heart disease, the concomitant administration of QTc prolonging medicines, or an underlying genetic predisposition.

Extrapyramidal disorder occurs primarily in neonates and infants. Other central nervous system-related effects of convulsion and agitation also are reported primarily in infants and children.

An increase in the risk of serious ventricular arrhythmias and sudden cardiac death has been reported in some epidemiology studies. The risk may be higher in patients older than 60 years

or at total daily doses of more than 30mg. Domperidone should be used at the lowest effective dose in adults and children. Due to the limitations of these data, the exact frequency of these adverse reactions could not be defined.

Paediatric population

In postmarketing experience, there were no differences in the safety profile of adults and children., with the exception of extrapyramidal disorder which occurred primarily in neonates and infants (up to one year of age), and other central nervous system-related effects of convulsion and agitation which were reported primarily in infants and children.

4.9 Overdose

Symptoms and signs

Overdose has been reported primarily in infants and children. Symptoms of overdosage may include agitation, altered consciousness, convulsion, disorientation, somnolence and extrapyramidal reactions.

Treatment

There is no specific antidote to domperidone. Anticholinergics, anti-Parkinsonian agents may be helpful in controlling the extrapyramidal reactions. Close observation and supportive therapy is recommended.

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: Propulsives, ATC code: A03F A 03

Mechanism of Actions

Domperidone is a dopamine antagonist with antiemetic properties. Domperidone does not readily cross the blood-brain barrier. It seldom causes extrapyramidal side effects, but does cause a rise in prolactin levels. Its antiemetic effect may be due to a combination of peripheral (gastrokinetic) effects and antagonism of central dopamine receptors in the chemoreceptor trigger zone which lies in the area postrema and is regarded as being outside the blood-brain barrier.

It also antagonises the behavioural effects of dopamine much more effectively when administered intracerebrally than when given systemically. These findings, together with the low concentrations found in the brain, indicate a predominantly peripheral effect of domperidone on dopamine receptors.

Studies in humans have shown intravenous and oral domperidone to increase lower oesophageal pressure, improve antroduodenal motility and accelerate gastric emptying. Domperidone has no effect on gastric secretion.

Effect on QT/QTc Interval and Cardiac Electrophysiology

In accordance with ICH—E14 guidelines, a thorough QT study was performed in healthy subjects. This study included a placebo, active comparator and positive control and was conducted using recommended therapeutic doses (10 or 20 mg administered 4 times a day). This study found a maximal difference of QTc between domperidone and placebo in LS-means in the change from baseline was 3.4 msec for 20 mg domperidone administered 4 times a day on Day 4, and the 2-sided 90% CI (1.0 - 5.9 msec) did not exceed 10 msec. The QT

prolongation observed in this study when domperidone was administered according to the recommended dosing is not clinically relevant.

This lack of clinical relevance is corroborated by pharmacokinetics and QTc interval data from two older studies which involved a 5-day treatment of 20 mg and 40 mg domperidone administered 4 times a day. ECGs were recorded prior to the study, on Day 5 at 1 hour (approximately at t_{max}) after the morning dose, and 3 days later. In both studies, no difference between QTc after active treatment and placebo was observed. It was therefore concluded that concentrations of domperidone after 80 and 160 mg daily had no clinically significant effect on QTc in healthy subjects.

Clinical Studies

Infants and children ≤ 12 years of age

A multicenter, double-blind, randomized, placebo-controlled, parallel-group, prospective study was conducted to evaluate the safety and efficacy of domperidone in 292 children with acute gastroenteritis aged 6 months to 12 years (median age 7 years). In addition to oral rehydration treatment (ORT), randomized subjects received domperidone oral suspension at 0.25 mg/kg (up to a maximum of 30 mg domperidone/day), or placebo, 3 times a day, for up to 7 days. This study did not achieve the primary objective, which was to demonstrate that domperidone suspension plus ORT is more effective than placebo plus ORT at reducing the percentage of subjects with no vomiting episodes during the first 48 hours after the first treatment administration.

5.2 Pharmacokinetic properties

Absorption

In fasting subjects, domperidone is rapidly absorbed following oral administration with peak plasma concentrations occurring at approximately 30 to 60 minutes.

The low oral bioavailability (approximately 15%) is due to extensive first pass metabolism in the gut wall and liver. Although the bioavailability of domperidone is enhanced in normal subjects when taken after a meal, patients with gastro-intestinal complaints should take domperidone 15 to 30 minutes before a meal. Oral bioavailability of domperidone base is decreased by prior concomitant administration of cimetidine and sodium bicarbonate (see **section 4.5 Interactions with other medicines and other forms of interactions**). The time of peak absorption is slightly delayed and the AUC somewhat increased when the oral medicine is taken after a meal.

Distribution

Oral domperidone does not appear to accumulate or induce its own metabolism; a peak plasma level after 90 minutes of 21 ng/mL after two weeks oral administration of 30 mg per day was almost the same as that of 18 ng/mL after the first dose. Domperidone is 91 to 93% bound to plasma proteins. Distribution studies with radiolabelled drug in animals have shown wide tissue distribution, but low brain concentration. Small amount of drug cross the placenta in rats.

Metabolism

Domperidone undergoes rapid and extensive hepatic metabolism by hydroxylation and *N*-dealkylation. *In vitro* metabolism experiments with diagnostic inhibitors revealed that CYP3A4 is a major form of cytochrome P-450 involved in the *N*-dealkylation of domperidone, whereas CYP3A4, CYP1A2 and CYP2E1 are involved in domperidone aromatic hydroxylation (see **section 4.5 Interactions with other medicines and other forms of interactions**).

Elimination

Urinary and faecal excretion amounts to 31 and 66%, respectively, of the oral dose. The proportion of the medicine excreted unchanged is small (10% of faecal excretion and approximately 1% of urinary excretion). The plasma half-life after a single oral dose is 7-9 hours in healthy subjects but is prolonged in patients with severe renal insufficiency.

Special Populations

Hepatic Impairment

In subjects with moderate hepatic impairment (Pugh score 7 to 9, Child-Pugh rating B), the AUC and C_{max} of domperidone is 2.9- and 1.5-fold higher, respectively, than in healthy subjects. The unbound fraction is increased by 25%, and the terminal elimination half-life is prolonged from 15 to 23 hours. Subjects with mild hepatic impairment have a somewhat lower systemic exposure than healthy subjects based on C_{max} and AUC, with no change in protein binding or terminal half-life. Subjects with severe hepatic impairment were not studied (see **section 4.3 Contraindications**).

Renal impairment

In studies with severe renal insufficiency (serum creatinine > 6 mg/100 mL, i.e., > 0.6 mmol/L) the half-life of domperidone is increased from 7.4 to 20.8 hours, but plasma drug levels are lower than in subjects with normal renal function. Very little unchanged drug (approximately 1%) is excreted via the kidneys (see **section 4.4 Special warnings and precautions for use**).

5.3 Preclinical safety data

Carcinogenicity, Mutagenicity, Teratogenicity

MOTILIUM was administered to mice for 18 months and rats for 24 months in carcinogenicity studies. No dose-related effects were observed except for an increased incidence of malignant mammary tumours at 25 times the maximum human dose in female mice and rats and an increased incidence of pituitary tumours at 25 times the human dose in male rats.

No evidence for mutagenic potential was seen in dominant lethal studies in male and female mice, micronucleus tests in female mice and female rats, a study of chromosomal aberrations in human lymphocytes, a sex-linked recessive lethal test on *Drosophila melanogaster*, and in the Ames metabolic activation test with *Salmonella typhimurium*. Minor teratogenic effects were seen in one study where MOTILIUM was administered to rats orally at approximately 125 times the maximum human dose level. These findings were not confirmed by another study where the medicine was administered orally to rats at dosage levels as high as 400 times than that given to man.

Embryotoxicity without maternal toxicity was encountered when MOTILIUM was administered intravenously to rats (> 6 times the maximum human dose level) and orally to mice (44 times the maximum human dose level). Concurrent embryotoxicity and maternal toxicity were inconsistently found at oral dose levels approximately 6 times the maximum human level in rabbits and in rats and approximately 24 times the maximum human dose level.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose

Maize starch

Microcrystalline cellulose

Pregelatinized potato starch
Povidone
Magnesium stearate
Hydrogenated cottonseed oil
Sodium lauryl sulfate
Hypromellose.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years

6.4 Special Precautions for Storage

Stored at or below 30°C. Protect from light. Store at room temperature.

6.5 Nature and contents of container

Blister packs of 100 tablets.

6.6 Special precautions for disposal

No special requirements.

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

28 June 1984

10. DATE OF REVISION OF THE TEXT

01 June 2018

Summary table of changes

Section changes	Summary of new information
All	- Datasheet reformat and editorial updates
4.2	- Revision of sub-heading to clarify children < 12 years of age and weighing ≥ 35 kg;

	<ul style="list-style-type: none">- Add sub-heading and information for adults and adolescents (≥ 12 years of age) and weighing < 35kg;- Add sub-heading and information for infants and children < 12 years of age and weighing < 35 kg;- Added warning for use in hepatic impairment
4.4	<ul style="list-style-type: none">- Update warning for cardiac effects
4.9	<ul style="list-style-type: none">- Deletion of guidance on use of gastric lavage and activated charcoal for treatment of overdose
5.1	<ul style="list-style-type: none">- Add updated clinical study information for infants and children ≤ 12 years of age
5.2	<ul style="list-style-type: none">- Deletion of statement regarding pharmacokinetic data in preterm neonates