

**SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET**

SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

<Motilium and associated names – see Annex I> <strength> <pharmaceutical form>
[To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One orodispersible tablet contains domperidone 10 mg.
One film-coated tablet contains domperidone 10 mg.
One film-coated tablet contains domperidone maleate 12.72 mg equivalent to domperidone 10 mg.
The oral suspension contains domperidone 1 mg per ml.
One suppository contains domperidone 30 mg.

Excipients with known effect

Orodispersible tablets: aspartame

Film-coated tablets: lactose monohydrate

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Domperidone film-coated tablet

White to faintly cream coloured, circular, biconvex tablet.

Domperidone maleate film-coated tablet

Off white, circular, biconvex tablet

Oral suspension

White homogenous suspension.

Orodispersible tablet

White to off white, circular, freeze dried units.

Suppositories

White to slightly yellow suppositories.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Motilium is indicated for the relief of the symptoms of nausea and vomiting.

4.2 Posology and method of administration

Motilium should be used at the lowest effective dose for the shortest duration necessary to control nausea and vomiting.

It is recommended to take oral Motilium before meals. If taken after meals, absorption of the drug is somewhat delayed.

Patients should try to take each dose at the scheduled time. If a scheduled dose is missed, the missed dose should be omitted and the usual dosing schedule resumed. The dose should not be doubled to make up for a missed dose.

Usually, the maximum treatment duration should not exceed one week.

Adults, and adolescents (12 years of age and older and weighing 35 kg or more)

Tablets

One 10 mg tablet up to three times per day with a maximum dose of 30 mg per day.

Orodispersible tablets

One 10 mg tablet up to three times per day with a maximum dose of 30 mg per day.

The orodispersible tablet dissolves rapidly in the mouth with the help of saliva, and can be taken with or without water. When taken without water, the tablet should be placed on the tongue and dissolve in the mouth before swallowing. If convenient, a glass of water can be taken afterwards.

Oral suspension

10 ml (of 1 mg/ml oral suspension) up to three times per day with a maximum dose of 30 ml per day.

Suppositories

One 30 mg suppository inserted into the rectum two times per day.

Neonates, infants, children (less than 12 years of age) and adolescents weighing less than 35 kg

Oral suspension

The dose is 0.25 mg/kg per intake. This should be given at least 4-6 hours apart up to three times per day not to exceed a total amount of 0.75 mg/kg per day. For example, for a child weighing 10 kg, the dose is 2.5 mg per intake and this can be given up to three times per day not to exceed a total amount of 7.5 mg per day.

Motilium oral suspension should be taken before meals/feeding. If taken after meals, absorption of the drug is somewhat delayed.

Tablets, suppositories

Due to the need for accurate dosing, tablets and suppositories are unsuitable for use in children and adolescents weighing less than 35 kg. Use of the oral suspension is recommended in these patients.

Hepatic impairment

Motilium is contraindicated in moderate or severe hepatic impairment (see section 4.3). Dose modification in mild hepatic impairment is however not needed (see section 5.2).

Renal impairment

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, and the dose may need to be reduced.

4.3 Contraindications

Motilium is contraindicated in the following situations:

- known hypersensitivity to domperidone or any of the excipients
- prolactin-releasing pituitary tumour (prolactinoma)
- when stimulation of the gastric motility could be harmful, e.g., in patients with gastro-intestinal haemorrhage, mechanical obstruction or perforation
- in patients with moderate or severe hepatic impairment (see section 5.2)
- in patients who have known existing prolongation of cardiac conduction intervals, particularly QTc, patients with significant electrolyte disturbances or underlying cardiac diseases such as congestive heart failure (see section 4.4)
- co-administration with QT-prolonging drugs (see section 4.5)
- co-administration with potent CYP3A4 inhibitors (regardless of their QT-prolonging effects) (see section 4.5).

4.4 Special warnings and precautions for use

Renal impairment

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, and the dose may need to be reduced.

Cardiovascular effects

Domperidone has been associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance, there have been very rare cases of QT-prolongation and *torsades de pointes* in patients taking domperidone. These reports included patients with confounding risk factors, electrolyte abnormalities and concomitant treatment which may have been contributing factors (see section 4.8).

Epidemiological studies showed that domperidone was associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death (see section 4.8). A higher risk was observed in patients older than 60 years, patients taking daily doses greater than 30 mg, and patients concurrently taking QT-prolonging drugs or CYP3A4 inhibitors.

Domperidone should be used at the lowest effective dose in adults and children.

Domperidone is contraindicated in patients with known existing prolongation of cardiac conduction intervals, particularly QTc, in patients with significant electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia), or bradycardia, or in patients with underlying cardiac diseases such as congestive heart failure due to increased risk of ventricular arrhythmia (see section 4.3). Electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia) or bradycardia are known to be conditions increasing the proarrhythmic risk.

Treatment with domperidone should be stopped if signs or symptoms occur that may be associated with cardiac arrhythmia, and the patients should consult their physician.

Patients should be advised to promptly report any cardiac symptoms.

Paediatric population

Although neurological side effects are rare (see section 4.8), the risk of neurological side effects is higher in young children since metabolic functions and the blood-brain barrier are not fully developed in the first months of life. Therefore, it is recommended that the dose be determined accurately and strictly followed in neonates, infants and children (see section 4.2).

Overdosing may cause extrapyramidal disorders in children, but other causes should be taken into consideration.

Precautions for use

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

The oral suspension contains sorbitol and may be unsuitable for patients with sorbitol intolerance.

The suppositories contain butylated hydroxyanisole which can irritate eyes, skin and the lining of the mouth and nose (mucous membranes).

Use in patients with risk of hyperphenylalaninaemia

The orodispersible tablets contain aspartame. Do not use in patients with a risk of hyperphenylalaninaemia.

4.5 Interaction with other medicinal products and other forms of interaction

When antacids or antisecretory drugs are used concomitantly, they should not be taken simultaneously with oral formulations of Motilium (domperidone base), i.e., they should be taken after meals and not before meals.

Co-administration with levodopa

Although no dosage adjustment of levodopa is deemed necessary, an increase (maximum of 30% - 40%) of plasma concentration has been observed when domperidone was taken concomitantly with levodopa.

The main metabolic pathway of domperidone is through CYP3A4. *In vitro* data suggest that the concomitant use of drugs that significantly inhibit this enzyme may result in increased plasma levels of domperidone.

Increased risk of occurrence of QT interval prolongation, due to pharmacodynamic and/or pharmacokinetic interactions.

Concomitant use of the following substances is contraindicated

QTc-prolonging medicinal products (risk of torsades de points)

- anti-arrhythmics class IA (e.g., disopyramide, hydroquinidine, 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., erythromycin, levofloxacin, moxifloxacin, spiramycin)
- certain antifungal agents (e.g., fluconazole, pentamidine)
- certain antimalarial agents (in particular halofantrine, lumefantrine)
- certain gastro-intestinal medicines (e.g., cisapride, dolasetron, prucalopride)
- certain antihistaminics (e.g., mequitazine, mizolastine)
- certain medicines used in cancer (e.g., toremifene, vandetanib, vincamine)
- certain other medicines (e.g., bepridil, diphemanil, methadone)

(see section 4.3).

Potent CYP3A4 inhibitors (regardless of their QT-prolonging effects), i.e.,

- protease inhibitors (e.g., ritonavir, saquinavir, telaprevir)
- systemic azole antifungals (e.g., itraconazole, ketoconazole, posaconazole, voriconazole)
- certain macrolide antibiotics (e.g., clarithromycin, telithromycin)

(see section 4.3).

Concomitant use of the following substances is not recommended

- Moderate CYP3A4 inhibitors i.e., diltiazem, verapamil and some macrolides.

Concomitant use of the following substances requires caution with use

Caution with bradycardia and hypokalaemia-inducing drugs, as well as with the following macrolides involved in QT interval prolongation: azithromycin and roxithromycin (clarithromycin is contraindicated as it is a potent CYP3A4 inhibitor).

The above list of substances is representative and not exhaustive.

4.6 Pregnancy and 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.

Breast-feeding

Domperidone is excreted in human milk and breast-fed infants receive less than 0.1% of the maternal weight-adjusted dose. Occurrence of adverse effects, in particular cardiac effects cannot be excluded after exposure *via* breast milk. A decision should be made whether to discontinue breast-feeding or to discontinue/abstain from domperidone therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. Caution should be exercised in case of QTc-prolongation risk factors in breast-fed infants.

4.7 Effects on ability to drive and use machines

Dizziness and somnolence have been observed following use of domperidone (see section 4.8). 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

The safety of domperidone was evaluated in clinical trials and in post-marketing experience. The clinical trials included 1,275 patients with dyspepsia, gastro-oesophageal reflux disorder (GERD), Irritable Bowel Syndrome (IBS), nausea and vomiting or other related conditions in 31 double-blind, placebo-controlled studies. All patients were at least 15 years old and received at least one dose of Motilium (domperidone base). The median total daily dose was 30 mg (range 10 to 80 mg), and median duration of exposure was 28 days (range 1 to 28 days). Studies in diabetic gastroparesis or symptoms secondary to chemotherapy or parkinsonism were excluded.

The following terms and frequencies are applied: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1000$), and very rare ($< 1/10,000$). Where frequency can not be estimated from clinical trials data, it is recorded as "Not known".

System Organ Class	Adverse Drug Reaction Frequency		
	Common	Uncommon	Not known
Immune system disorders			Anaphylactic reaction (including anaphylactic shock)
Psychiatric disorders		Loss of libido Anxiety Agitation Nervousness	
Nervous system disorders		Dizziness Somnolence Headache Extrapyramidal disorder	Convulsion Restless legs syndrome*
Eye disorders			Oculogyric crisis
Cardiac disorders			Ventricular arrhythmias QTc prolongation Torsade de Pointes Sudden cardiac death (see section 4.4)
Gastrointestinal disorders	Dry mouth	Diarrhoea	
Skin and subcutaneous tissue disorder		Rash Pruritus Urticaria	Angioedema
Renal and urinary disorders			Urinary retention
Reproductive system		Galactorrhoea	Gynaecomastia

and breast disorders		Breast pain Breast tenderness	Amenorrhoea
General disorders and administration site conditions		Asthenia	
Investigations			Liver function test abnormal Blood prolactin increased

*exacerbation of restless legs syndrome in patients with Parkinson's disease

In 45 clinical studies where domperidone was used at higher dosages, for longer duration and for additional indications including diabetic gastroparesis, the frequency of adverse events (apart from dry mouth) was considerably higher. This was particularly evident for pharmacologically predictable events related to increased prolactin. In addition to the reactions listed above, akathisia, breast discharge, breast enlargement, breast swelling, depression, hypersensitivity, lactation disorder, and irregular menstruation were also noted.

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

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

Symptoms

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. In the event of overdose, standard symptomatic treatment should be given immediately. ECG monitoring should be undertaken, because of the possibility of QTc interval prolongation. Gastric lavage as well as the administration of activated charcoal, may be useful. Close medical supervision and supportive therapy is recommended. Anticholinergic, anti-parkinson drugs may be helpful in controlling the extrapyramidal disorders.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Propulsives, ATC code: A03F A03

Domperidone is a dopamine antagonist with anti-emetic properties. Domperidone does not readily cross the blood-brain barrier. In domperidone users, especially in adults, extrapyramidal disorders are very rare, but domperidone promotes the release of prolactin from the pituitary. Its anti-emetic effect may be due to a combination of peripheral (gastrokinetic) effects and antagonism of dopamine receptors in the chemoreceptor trigger zone, which lies outside the blood-brain barrier in the area postrema. Animal studies, together with the low concentrations found in the brain, indicate a predominantly peripheral effect of domperidone on dopamine receptors. Studies in man have shown oral domperidone to increase lower oesophageal pressure, improve antroduodenal motility and accelerate gastric emptying. There is no effect on gastric secretion.

In accordance with ICH-E14 guidelines, a thorough QT study was performed. This study included a placebo, an active comparator and a positive control and was conducted in healthy subjects with up to

80 mg per day (10 or 20 mg administered four times a day) of domperidone. This study found a maximal difference of QTc between domperidone and placebo in LS-means in the change from baseline of 3.4 msec for 20 mg domperidone administered four times a day on Day 4. The 2-sided 90% CI (1.0 to 5.9 msec) did not exceed 10 msec. No clinically relevant QTc effects were observed in this study when domperidone was administered at up to 80 mg/day (i.e., more than twice the maximum recommended dosing).

However, two previous drug-drug interaction studies showed some evidence of QTc-prolongation when domperidone was given as monotherapy (10 mg administered four times a day). The largest time-matched mean difference of QTcF between domperidone and placebo was 5.4 msec (95% CI: -1.7 to 12.4) and 7.5 msec (95% CI: 0.6 to 14.4), respectively.

5.2 Pharmacokinetic properties

Absorption

Domperidone is rapidly absorbed after oral administration, with peak plasma concentrations occurring at approximately 1 hr after dosing. The C_{max} and AUC values of domperidone increased proportionally with dose in the 10 mg to 20 mg dose range. A 2- to 3-fold accumulation of domperidone AUC was observed with repeated four times daily (every 5 hr) dosing of domperidone for 4 days.

Although domperidone's bioavailability is enhanced in normal subjects when taken after a meal, patients with gastro-intestinal complaints should take domperidone 15-30 minutes before a meal. Reduced gastric acidity impairs the absorption of domperidone. Oral bioavailability is decreased by prior concomitant administration of cimetidine and sodium bicarbonate.

Based on the C_{max} resulting from administering multiple twice daily doses of 60 mg suppository, a 30 mg suppository given twice daily is expected to provide peak plasma levels similar to those of a 10 mg oral dose administered four times a day.

Distribution

Domperidone is 91-93% bound to plasma proteins. Distribution studies with radiolabelled drug in animals have shown wide tissue distribution, but low brain concentration. Small amounts 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.

Excretion

Urinary and faecal excretions amount to 31 and 66% of the oral dose, respectively. The proportion of the drug 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.

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. Motilium is contraindicated in patients with moderate or severe hepatic impairment (see section 4.3).

Renal impairment

In subjects with severe renal impairment (creatinine clearance < 30 ml/min/1.73 m²), the elimination half-life of domperidone was increased from 7.4 to 20.8 hours, but plasma drug levels were lower than in healthy volunteers. Since very little unchanged drug (approximately 1%) is excreted *via* the kidneys, it is unlikely that the dose of a single administration needs to be adjusted in patients with renal impairment. However, on repeated administration, the dosing frequency should be reduced to once or twice daily depending on the severity of the impairment, and the dose may need to be reduced.

Paediatric population

No pharmacokinetic data are available in the paediatric population.

5.3 Preclinical safety data

Electrophysiological *in vitro* and *in vivo* studies indicate an overall moderate risk of domperidone to prolong the QTc interval in humans. In *in vitro* experiments on isolated cells transfected with hERG and on isolated guinea pig myocytes, exposure ratios ranged between 26- to 47-fold, based on IC₅₀ values inhibiting currents through IKr ion channels in comparison to the free plasma concentrations in humans after administration of the maximum daily dose of 10 mg administered three times a day. Safety margins for prolongation of action potential duration in *in vitro* experiments on isolated cardiac tissues exceeded the free plasma concentrations in humans at maximum daily dose (10 mg administered three times a day) by 45-fold. Safety margins in *in vitro* pro-arrhythmic models (isolated Langendorff perfused heart) exceeded the free plasma concentrations in humans at maximum daily dose (10 mg administered three times a day) by 9- up to 45-fold. In *in vivo* models, the no effect levels for QTc-prolongation in dogs and induction of arrhythmias in a rabbit model sensitised for *torsade de points* exceeded the free plasma concentrations in humans at maximum daily dose (10 mg administered three times a day) by more than 22-fold and 435-fold, respectively. In the anaesthetised guinea pig model following slow intravenous infusions, there were no effects on QTc at total plasma concentrations of 45.4 ng/ml, which are 3-fold higher than the total plasma levels in humans at maximum daily dose (10 mg administered three times a day). The relevance of the latter study for humans following exposure to orally administered domperidone is uncertain.

In the presence of inhibition of the metabolism *via* CYP3A4, free plasma concentrations of domperidone can rise up to 3-fold.

At a high, maternally toxic dose (more than 40 times the recommended human dose), teratogenic effects were seen in the rat. No teratogenicity was observed in mice and rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[To be completed nationally]

6.2 Incompatibilities

[To be completed nationally]

6.3 Shelf life

Domperidone film-coated tablet:
3 years.

Oral suspension:
3 years. In-use shelf life after first opening: 3 months

Other formulations:
[To be completed nationally]

6.4 Special precautions for storage

[To be completed nationally]

6.5 Nature and contents of container

[See Annex I - To be completed nationally]

6.6 Special precautions for disposal and other handling

Oral suspension:

Mix the contents of the bottle completely using a gentle tilting motion to avoid the formation of foam.

Other formulations: [To be completed nationally]

7. MARKETING AUTHORISATION HOLDER

[See Annex I - to be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

This version of the SmPC was approved.

[To be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Motilium 10 mg film-coated tablets
domperidone maleate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 12.72 mg domperidone maleate (equivalent to 10 mg domperidone)

3. LIST OF EXCIPIENTS

Also contains lactose.
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

30 tablets
100 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use
Read the package leaflet before use.

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

Do not store above 30°C

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

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Motilium 10 mg tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Motilium 10 mg film-coated tablets
domperidone maleate (equivalent to 10 mg domperidone)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Motilium 10 mg film-coated tablets
domperidone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 10 mg domperidone

3. LIST OF EXCIPIENTS

Also contains lactose.
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

30 tablets
100 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use
Read the package leaflet before use.

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

Do not store above 30°C

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

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Motilium 10 mg tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Motilium 10 mg film-coated tablets
domperidone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Motilium 10 mg orodispersible tablets
domperidone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each orodispersible tablet contains 10 mg domperidone

3. LIST OF EXCIPIENTS

Also contains aspartame (E951), mannitol (E421).
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

10 orodispersible tablets
20 orodispersible tablets
30 orodispersible tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use
Read the package leaflet before use.

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

Do not store above 25°C

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

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

Do not press tablets through the foil as this will crush them.

16. INFORMATION IN BRAILLE

Motilium 10 mg orodispersible tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Motilium 10 mg orodispersible tablets
domperidone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND IMMEDIATE PACKAGING

CARTON AND BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT

Motilium 1 mg/ml oral suspension
domperidone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 mg domperidone per ml

3. LIST OF EXCIPIENTS

Also contains sorbitol (E420), methylhydroxybenzoate (E218) and propylhydroxybenzoate (E216).
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

100 ml oral suspension
200 ml oral suspension

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use
Read the package leaflet before use.

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

Mix the contents of the bottle completely using a gentle tilting motion to avoid the formation of foam.

8. EXPIRY DATE

EXP
Shelf life after first opening the bottle: 3 months

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Do not refrigerate or freeze. Protect from light.

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

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

Before use, mix the contents of the bottle completely using a gentle tilting motion to avoid the formation of foam.

16. INFORMATION IN BRAILLE

Motilium 1 mg/ml oral suspension (carton only)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Motilium 30 mg suppositories
domperidone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each suppository contains 30 mg domperidone

3. LIST OF EXCIPIENTS

Also contains butylated hydroxyanisole (E320).
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

6 suppositories

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For rectal administration only. Do not take orally.
Read the package leaflet before use.

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

Do not store above 25°C.

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

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

Remove suppositories from wrapper before use.

16. INFORMATION IN BRAILLE

Motilium 30 mg suppository

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

FOIL

1. NAME OF THE MEDICINAL PRODUCT

Motilium 30 mg suppositories
domperidone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER

PACKAGE LEAFLET

Package leaflet: Information for the user

MOTILIUM®

10 mg film-coated tablets

(12.72 mg domperidone maleate = 10 mg domperidone per tablet)

10 mg film-coated tablets

(10 mg domperidone per tablet)

10 mg orodispersible tablets

(10 mg domperidone per tablet)

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What MOTILIUM is and what it is used for
2. What you need to know before you take MOTILIUM
3. How to take MOTILIUM
4. Possible side effects
5. How to store MOTILIUM
6. Contents of the pack and other information

1. What MOTILIUM is and what it is used for

This medicine is used to treat nausea (feeling sick) and vomiting (being sick) in adults and adolescents (12 years of age and older and weighing 35 kg or more).

2. What you need to know before you take MOTILIUM

Do not take MOTILIUM if you:

- are allergic (hypersensitive) to domperidone or any of the other ingredients of MOTILIUM
- have stomach bleeding or if you regularly have severe abdominal pain or persistent black stools (poo)
- have a blocked or perforated gut
- have a tumour of the pituitary gland (prolactinoma)
- have a disorder known as phenylketonuria (a metabolic disorder) orodispersible tablets should not be used as they contain aspartamine
- have a moderate or severe liver disease
- have an ECG (electrocardiogram) that shows a heart problem called “prolonged QT interval”
- have or had a problem where your heart cannot pump the blood around your body as well as it should (condition called heart failure)
- have a problem that gives you a low level of potassium or magnesium, or a high level of potassium in your blood
- are taking certain medicines (see “Taking other medicines”).

Warnings and precautions

These medicinal products are not suitable for neonates, infants and children less than 12 years of age or adolescents weighing less than 35 kg. If MOTILIUM is for a child, ask your doctor for the children's formulation.

Before taking this medicine contact your doctor if you:

- suffer from liver problems (liver function impairment or failure) (see "Do not take MOTILIUM")
- suffer from kidney problems (kidney function impairment or failure). It is advisable to ask your doctor for advice in case of prolonged treatment as you may need to take a lower dose or take this medicine less often, and your doctor may want to examine you regularly.

Domperidone may be associated with an increased risk of heart rhythm disorder and cardiac arrest. This risk may be more likely in those over 60 years old or in those taking doses higher than 30 mg per day. The risk also increases when domperidone is given together with some drugs. Tell your doctor or pharmacist if you are taking drugs to treat infection (fungal infections or bacterial infection) and/or if you have heart problems or AIDS/HIV (see "Taking other medicines").

MOTILIUM should be used at the lowest effective dose in adults and children.

While taking MOTILIUM, contact your doctor if you experience heart rhythm disorders such as palpitations, trouble breathing, loss of consciousness. Treatment with MOTILIUM should be stopped.

Taking other medicines

Do not take MOTILIUM if you are taking medicine to treat:

- fungal infections, e.g., pentamidine or azole anti-fungals, specifically itraconazole, oral ketoconazole, fluconazole, posaconazole or voriconazole
- bacterial infections, specifically erythromycin, clarithromycin, telithromycin, levofloxacin, moxifloxacin, spiramycin (these are antibiotics)
- heart problems or high blood pressure (e.g., amiodarone, dronedarone, ibutilide, disopyramide, dofetilide, sotalol, hydroquinidine, quinidine)
- psychoses (e.g., haloperidol, pimozide, sertindole)
- depression (e.g., citalopram escitalopram)
- gastro-intestinal disorders (e.g., cisapride, dolasetron, prucalopride)
- allergy (e.g., mequitazine, mizolastine)
- malaria (in particular halofantrine, lumefantrine)
- AIDS/HIV such as ritonavir or saquinavir (these are protease inhibitors)
- Hepatitis C (e.g., telaprevir)
- cancer (e.g., toremifene, vandetanib, vincamine).

Do not take MOTILIUM if you are taking certain other medicines (e.g., bepridil, diphemanil, methadone).

Tell your doctor or pharmacist if you are taking drugs to treat infection, heart problems, AIDS/HIV or Parkinson's disease.

It is important to ask your doctor or pharmacist if MOTILIUM is safe for you when you are taking any other medicines, including medicines obtained without prescription.

Taking MOTILIUM with food and drink

Take MOTILIUM before meals, as when taken after meals, the absorption of the medicine is slightly delayed.

Pregnancy

It is not known whether the use of MOTILIUM is harmful during pregnancy. If you are pregnant or think you may be you should inform your doctor who will decide if you can take MOTILIUM.

Breast-feeding

Small amounts of domperidone have been detected in breast milk. MOTILIUM may cause unwanted side effects affecting the heart in a breast-fed baby. MOTILIUM should be used during breast-feeding only if your doctor considers this clearly necessary. Ask your doctor for advice before taking this medicine.

Driving and using machines

Some patients have reported feeling dizzy or sleepy after taking MOTILIUM. Do not drive or use machinery while taking MOTILIUM until you know how MOTILIUM affects you.

Important information about some of the ingredients of MOTILIUM:

- The orodispersible tablets contain aspartame and therefore should not be used by patients with phenylketonuria.
- The film-coated tablets contain lactose (a type of sugar). If you have been told you have an intolerance to some sugars, consult your doctor before taking this medicine.

3. How to take MOTILIUM

Follow these instructions closely unless your doctor has advised you otherwise.

Take Motilium before meals, as when taken after meals, the absorption of the medicine is slightly delayed.

Duration of treatment

Symptoms usually resolve with 3-4 days of taking this medicine. Do not take MOTILIUM for longer than 7 days without consulting your doctor.

Adults and adolescents 12 years of age and older and with a body weight of 35 kg or more

Tablets

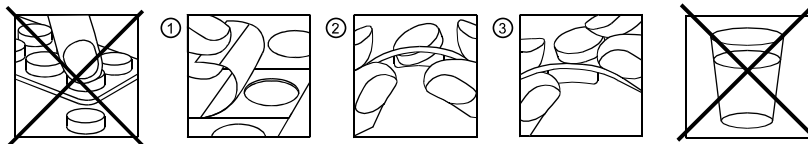
The usual dose is one tablet taken up to three times per day, if possible before meals. Take the tablet with some water or other liquid. Do not chew the tablet. Do not take more than three tablets per day.

Orodispersible tablets

The usual dose is one tablet taken up to three times per day, if possible before meals. Do not take more than three tablets per day.

Since the orodispersible tablets are fragile, do not press them through the foil, as this would break or damage the tablet. To remove the tablet from the blister:

- Do not press the tablet through the foil.
- Pull up the edge of the foil and remove the foil completely (diagram 1).
- Push up the tablet (diagram 2).
- Take the tablet out of the blister (diagram 3).
- The orodispersible tablet is then placed on the tongue, melts automatically and is swallowed with saliva. It is not necessary to drink any liquid.



Neonates, infants, children less than 12 years of age and adolescents weighing less than 35 kg

Tablets and orodispersible tablets are not suitable for children less than 12 years of age or adolescents weighing less than 35 kg. If MOTILIUM is for a child, ask your doctor which formulation is appropriate.

If you take more MOTILIUM than you should

If you have used or taken too much MOTILIUM, contact your doctor, pharmacist or the poison centre immediately, in particular if a child has taken too much. In the event of overdose, symptomatic treatment could be implemented. An ECG monitoring could be undertaken, because of the possibility of a heart problem called “prolonged QT interval”.

Information for the doctor: close observation of the patient, gastric lavage, administration of activated charcoal and general supportive measures are recommended. Anticholinergic anti-Parkinson medication may help to counteract the extrapyramidal disorders.

If you forget to take MOTILIUM

Take your medicine as soon as you remember. If it is almost time for your next dose, wait until that is due and then continue as normal. Do not take a double dose to make up for a forgotten dose.

4. Possible side effects

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

Uncommon (may affect up to 1 in 100 people):

- Involuntary movements of the face or arms and legs, excessive trembling, excessive muscle stiffness or muscle spasm

Not known (frequency cannot be estimated from the available data):

- Seizures
- A type of reaction that may occur soon after administration and is recognised by skin rash, itching, shortness of breath, and/or a swollen face
- A severe hypersensitivity reaction that may occur soon after administration that is characterised by hives, itching, flushing, fainting, and difficulty breathing among other possible symptoms
- Disorders of the cardiovascular system: heart rhythm disorders (rapid or irregular heart beat) have been reported; if this happens, you should stop the treatment immediately. Domperidone may be associated with an increased risk of heart rhythm disorder and cardiac arrest. This risk may be more likely in those over 60 years old or taking doses higher than 30 mg per day. Domperidone should be used at the lowest effective dose in adults and children.

Stop treatment with MOTILIUM and contact your doctor immediately if you experience any of the unwanted events described above.

Other unwanted effects that have been observed with MOTILIUM are listed below:

Common (may affect up to 1 in 10 people):

- Dry mouth

Uncommon (may affect up to 1 in 100 people):

- Anxiety
- Agitation
- Nervousness
- Loss of interest in sex or diminished interest in sex
- Headache
- Sleepiness
- Diarrhoea
- Rash
- Itchiness
- Hives
- Painful or tender breasts
- Milk discharge from breasts

- A general feeling of weakness
- Feeling dizzy

Not known (frequency cannot be estimated from the available data):

- Upward movement of the eyes
- Stopped menstrual periods in women
- Enlarged breasts in men
- Inability to urinate
- Changes in certain laboratory test results
- Restless legs syndrome (uncomfortable feeling, with an irresistible urge to move your legs, and sometimes arms and other parts of your body)

Some patients who have used MOTILIUM for conditions and dosages requiring medical oversight have experienced the following unwanted effects:

Restlessness; swollen or enlarged breasts, unusual discharge from breasts, irregular menstrual periods in women, difficulty breastfeeding, depression, hypersensitivity.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. 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 MOTILIUM

- Keep the medicine out of the sight and reach of children.
- Do not use MOTILIUM after the expiry date which is stated on the pack. The expiry date “exp.” refers to the last day of the month shown where the first two figures indicate the month, the next the year.
- Do not store the tablets above 30 C.
- Do not store the orodispersible tablets above 25 C.

Medicines should not be disposed of *via* wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What MOTILIUM contains

The active substance is domperidone.

The other ingredients are:

- Film-coated tablets (domperidone maleate): lactose, maize starch, microcrystalline cellulose, polyvidone, potato starch, magnesium stearate, silicon dioxide, polysorbate 20, hydroxypropyl methyl cellulose, propylene glycol.
- Film-coated tablets (domperidone): lactose, maize starch, microcrystalline cellulose, potato starch, polyvidone, magnesium stearate, vegetable oil, sodium lauryl sulphate, hypromellose.
- Orodispersible tablets: gelatin, mannitol (E421), aspartame (E951), mint flavoring, poloxamer 188.

What MOTILIUM looks like and contents of the pack

- The tablets are available in a blister pack containing 30 or 100 tablets.
- The orodispersible tablets are available in a blister pack containing 10, 20 or 30 tablets.
- Not all formulations and pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

[To be completed nationally].

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

Manufacturer

Film-coated tablets

Janssen-Cilag, Domaine de Maigremont, 27100 Val de Reuil, France

Orodispersible tablets

Janssen Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse, Belgium

or

Janssen-Cilag SPA, Via C. Janssen, Borgo San Michele, 04100 Latina, Italy

or

Janssen-Cilag, Domaine de Maigremont, 27100 Val de Reuil, France

Marketing Authorisation Numbers

Film-coated tablets (domperidone maleate): *[To be completed nationally]*

Film-coated tablets (domperidone): *[To be completed nationally]*

Orodispersible tablets: *[To be completed nationally]*

Name of the Member State	Name of the medicinal product	Name of the Member State	Name of the medicinal product
Austria	Motilium	Italy	Motilium
Belgium	Motilium, Motilium Instant	Luxembourg	Motilium, Motilium Instant
Denmark	Motilium	Netherlands	Motilium
France	Motilium, Motilyo	Portugal	Motilium
Greece	Cilroton	Spain	Nauzelín
Ireland	Motilium		

This package insert was last revised in

Package leaflet: Information for the user

MOTILIUM® 1mg/ml oral suspension (1 mg domperidone per 1ml suspension)

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What MOTILIUM is and what it is used for
2. What you need to know before you take MOTILIUM
3. How to take MOTILIUM
4. Possible side effects
5. How to store MOTILIUM
6. Contents of the pack and other information

1. What MOTILIUM is and what it is used for

This medicine is used to treat nausea (feeling sick) and vomiting (being sick) in adults and children.

Please read the section “How to take MOTILIUM” to see which doses should be used in adults and which should be used in children.

2. What you need to know before you take MOTILIUM

Do not take MOTILIUM if you

- are allergic (hypersensitive) to domperidone or any of the other ingredients of MOTILIUM
- have stomach bleeding or if you regularly have severe abdominal pain or persistent black stools (poo)
- have a blocked or perforated gut
- have a tumour of the pituitary gland (prolactinoma)
- have a moderate or severe liver disease
- have an ECG (electrocardiogram) that shows a heart problem called “prolonged QT interval”
- have or had a problem where your heart cannot pump the blood around your body as well as it should (condition called heart failure)
- have a problem that gives you a low level of potassium or magnesium, or a high level of potassium in your blood
- are taking certain medicines (see “Taking other medicines”).

Warnings and precautions

Before taking this medicine contact your doctor if you:

- suffer from liver problems (liver function impairment or failure) (see “Do not take MOTILIUM”)

- suffer from kidney problems (kidney function impairment or failure). It is advisable to ask your doctor for advice in case of prolonged treatment as you may need to take a lower dose or take this medicine less often, and your doctor may want to examine you regularly.

Domperidone may be associated with an increased risk of heart rhythm disorder and cardiac arrest. This risk may be more likely in those over 60 years old or in those taking doses higher than 30 mg per day. The risk also increases when domperidone is given together with some drugs. Tell your doctor or pharmacist if you are taking drugs to treat infection (fungal infections or bacterial infection) and/or if you have heart problems or AIDS/HIV (see “Taking other medicines”).

MOTILIUM should be used at the lowest effective dose in adults and children.

While taking MOTILIUM, contact your doctor if you experience heart rhythm disorders such as palpitations, trouble breathing, loss of consciousness. Treatment with MOTILIUM should be stopped.

Taking other medicines

Do not take MOTILIUM if you are taking medicine to treat:

- fungal infections, e.g., pentamidine or azole anti-fungals, specifically itraconazole, oral ketoconazole, fluconazole, posaconazole or voriconazole
- bacterial infections, specifically erythromycin, clarithromycin, telithromycin, levofloxacin, moxifloxacin, spiramycin (these are antibiotics)
- heart problems or high blood pressure (e.g., amiodarone, dronedarone, ibutilide, disopyramide, dofetilide, sotalol, hydroquinidine, quinidine)
- psychoses (e.g., haloperidol, pimozide, sertindole)
- depression (e.g., citalopram escitalopram)
- gastro-intestinal disorders (e.g., cisapride, dolasetron, prucalopride)
- allergy (e.g., mequitazine, mizolastine)
- malaria (in particular halofantrine, lumefantrine)
- AIDS/HIV such as ritonavir or saquinavir (these are protease inhibitors)
- Hepatitis C (e.g., telaprevir)
- cancer (e.g., toremifene, vandetanib, vincamine).

Do not take MOTILIUM if you are taking certain other medicines (e.g., bepridil, diphemanil, methadone).

Tell your doctor or pharmacist if you are taking drugs to treat infection, heart problems, AIDS/HIV or Parkinson’s disease.

It is important to ask your doctor or pharmacist if MOTILIUM is safe for you when you are taking any other medicines, including medicines obtained without prescription.

Taking MOTILIUM with food and drink

Take MOTILIUM before meals, as when taken after meals, the absorption of the medicine is slightly delayed.

Pregnancy

It is not known whether the use of MOTILIUM is harmful during pregnancy. If you are pregnant or think you may be you should inform your doctor who will decide if you can take MOTILIUM.

Breast-feeding

Small amounts of domperidone have been detected in breast milk. MOTILIUM may cause unwanted side effects affecting the heart in a breast-fed baby. MOTILIUM should be used during breast-feeding only if your doctor considers this clearly necessary. Ask your doctor for advice before taking this medicine.

Driving and using machines

Some patients have reported feeling dizzy or sleepy after taking MOTILIUM. Do not drive or use machinery while taking MOTILIUM until you know how MOTILIUM affects you.

Important information about some of the ingredients of MOTILIUM

- MOTILIUM suspension contains less than 1 mmol sodium, so can be considered sodium-free.
- MOTILIUM suspension contains sorbitol (E 420). Sorbitol may have a mild laxative effect. Also, if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this product.
- MOTILIUM suspension also contains methyl parahydroxy benzoate (E218) and propyl parahydroxy benzoate (E216). These substances may cause allergic reactions (possibly delayed), and exceptionally, bronchospasm.

3. How to take MOTILIUM

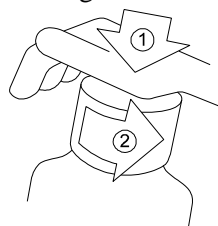
Follow these instructions closely unless your doctor has advised you otherwise.

Take MOTILIUM before meals because when taken after meals, the absorption of the medicine is slightly delayed.

Duration of treatment

Symptoms usually resolve with 3-4 days of taking this medicine. Do not take MOTILIUM for longer than 7 days without consulting your doctor.

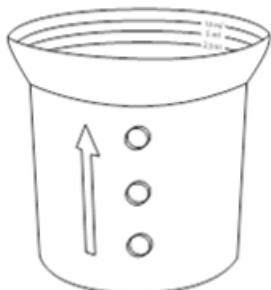
The bottle is protected by a childproof cap. To open the bottle, press down the plastic screw cap whilst turning it counter clockwise as shown below.



Mix the contents of the bottle completely using a gentle tilting motion to avoid the formation of foam.

Adults and adolescents 12 years of age and older and with a body weight of 35 kg or more

- A dosing cup is supplied with this medicine. This cup has three lines: 2.5 ml, 5 ml and 10 ml, (for example it will hold 10 ml of oral suspension when filled to the top line)
- Use the measuring cup just as it sits on the bottle. Make sure that the side with the graduations (the side that holds less) is uppermost; that is the side you have to fill. When the arrow on the side points up, the correct side is uppermost



- Measure the amount required into the dosing cup
- Do not dilute MOTILIUM and do not mix with other liquids
- The usual dose is 10 ml taken up to three times per day, if possible before meals. Do not take more than 30 ml per day (this is equal to 3 dosing cups filled to the top line)

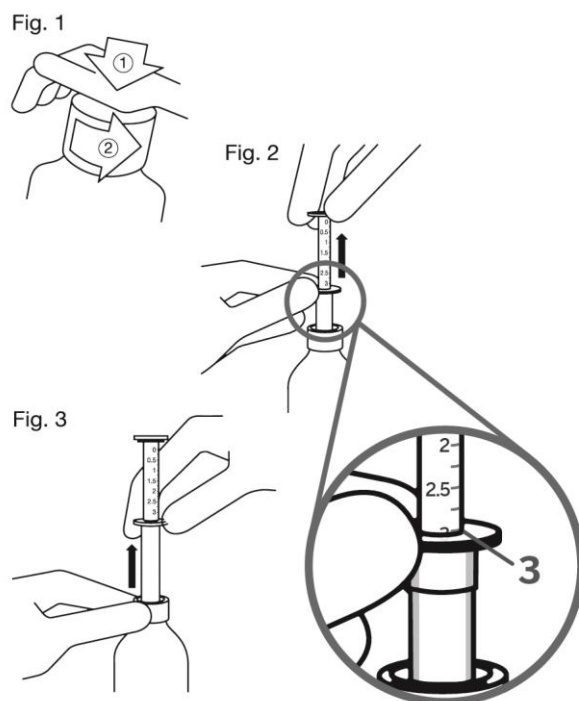
- Clean the dosing cup after use.

Neonates, infants, children less than 12 years of age and adolescents with a body weight of less than 35 kg

- Your doctor will explain to you exactly how much of this medicine to give to the child, and how often.
- Give MOTILIUM to children using the pipette supplied with the medicine. In children, the dose is dependent on body weight. For example, for a child weighing 10 kg, the dose per intake is obtained by pulling the piston up to the graduation mark corresponding to the body weight of the children i.e., 10 kg.
- Give the dose a maximum of three times a day at least 4-6 hours apart, if possible before meals/feeding. Do not give more than three times in a 24 hour time period.

How to use the pipette to prepare the correct dose for children

- Remove the plastic screw cap from the top of the bottle (Fig. 1).
- Place the pipette in the bottle.
- Hold the lower ring of the pipette.
- Draw the medicine into the pipette by pulling up the upper ring to the mark corresponding to the child's weight in kilograms (unless told otherwise by your doctor) (Fig. 2).
- Remove the whole pipette from the bottle (Fig. 3).
- Give the medicine by emptying the pipette into the child's mouth.
- Clean the pipette in water.
- Seal the bottle with the plastic screw cap.



If you take more MOTILIUM than you should

If you have used or taken too much MOTILIUM, contact your doctor, pharmacist or the poison centre immediately, in particular if a child has taken too much. In the event of overdose, symptomatic treatment could be implemented. An ECG monitoring could be undertaken, because of the possibility of a heart problem called “prolonged QT interval”.

Information for the doctor: close observation of the patient, gastric lavage, administration of activated charcoal and general supportive measures are recommended. Anticholinergic anti-Parkinson medication may help to counteract the extrapyramidal disorders.

If you forget to take MOTILIUM

Take your medicine as soon as you remember. If it is almost time for your next dose, wait until that is due and then continue as normal. Do not take a double dose to make up for a forgotten dose.

4. Possible side effects

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

Uncommon (may affect up to 1 in 100 people):

- Involuntary movements of the face or arms and legs, excessive trembling, excessive muscle stiffness or muscle spasm

Not known (frequency cannot be estimated from the available data):

- Seizures
- A type of reaction that may occur soon after administration and is recognised by skin rash, itching, shortness of breath, and/or a swollen face
- A severe hypersensitivity reaction that may occur soon after administration that is characterised by hives, itching, flushing, fainting, and difficulty breathing among other possible symptoms
- Disorders of the cardiovascular system: heart rhythm disorders (rapid or irregular heart beat) have been reported; if this happens, you should stop the treatment immediately. Domperidone may be associated with an increased risk of heart rhythm disorder and cardiac arrest. This risk may be more likely in those over 60 years old or taking doses higher than 30 mg per day. Domperidone should be used at the lowest effective dose in adults and children.

Stop treatment with MOTILIUM and contact your doctor immediately if you experience any of the unwanted events described above.

Other unwanted effects that have been observed with MOTILIUM are listed below:

Common (may affect up to 1 in 10 people):

- Dry mouth

Uncommon (may affect up to 1 in 100 people):

- Anxiety
- Agitation
- Nervousness
- Loss of interest in sex or diminished interest in sex
- Headache
- Sleepiness
- Diarrhoea
- Rash
- Itchiness
- Hives
- Painful or tender breasts
- Milk discharge from breasts
- A general feeling of weakness
- Feeling Dizzy

Not known (frequency cannot be estimated from the available data):

- Upward movement of the eyes
- Stopped menstrual periods in women

- Enlarged breasts in men
- Inability to urinate
- Changes in certain laboratory test results
- Restless legs syndrome (uncomfortable feeling, with an irresistible urge to move your legs, and sometimes arms and other parts of your body)

Some patients who have used MOTILIUM for conditions and dosages requiring medical oversight have experienced the following unwanted effects:

Restlessness; swollen or enlarged breasts, unusual discharge from breasts, irregular menstrual periods in women, difficulty breastfeeding, depression, hypersensitivity.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. 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 MOTILIUM

- Keep the medicine out of the sight and reach of children.
- Do not use MOTILIUM after the expiry date which is stated on the pack. The expiry date “exp.” refers to the last day of the month shown where the first two figures indicate the month, the next the year.
- MOTILIUM suspension should not be used for longer than 3 months after the bottle has first been opened.

Medicines should not be disposed of *via* wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What MOTILIUM contains

The active substance is domperidone.

The other ingredients are:

Sorbitol 70% w/w non-crystallised solution, microcrystalline cellulose, sodium carboxymethylcellulose, methyl hydroxybenzoate (E218), propyl hydroxybenzoate (E216), sodium saccharin, polysorbate 20, sodium hydroxide and purified water.

What MOTILIUM looks like and contents of the pack

[To be completed nationally]

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

[To be completed nationally]

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

Manufacturer

Janssen-Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse, Belgium

Marketing Authorisation Number

[To be completed nationally]

Name of the Member State	Name of the medicinal product	Name of the Member State	Name of the medicinal product
Austria	Motilium	Italy	Motilium
Belgium	Motilium	Luxembourg	Motilium
France	Motilium	Netherlands	Motilium
Greece	Cilroton	Portugal	Motilium
Ireland	Motilium	Spain	Nauzelín

This package insert was last approved in

Package leaflet: Information for the user

MOTILIUM®

30 mg suppositories

(30 mg domperidone per suppository)

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What MOTILIUM is and what it is used for
2. What you need to know before you use MOTILIUM
3. How to use MOTILIUM
4. Possible side effects
5. How to store MOTILIUM
6. Contents of the pack and other information.

1. What MOTILIUM is and what it is used for

This medicine is used to treat nausea (feeling sick) and vomiting (being sick) in adults and adolescents (12 years of age and older and weighing 35 kg or more).

2. What you need to know before you use MOTILIUM

Do not use MOTILIUM if you:

- are allergic (hypersensitive) to domperidone or any of the other ingredients of MOTILIUM
- have stomach bleeding or if you regularly have severe abdominal pain or persistent black stools (poo)
- have a blocked or perforated gut
- have a tumour of the pituitary gland (prolactinoma)
- have a moderate or severe liver disease
- have an ECG (electrocardiogram) that shows a heart problem called “prolonged QT interval”
- have or had a problem where your heart cannot pump the blood around your body as well as it should (condition called heart failure).
- have a problem that gives you a low level of potassium or magnesium, or a high level of potassium in your blood
- are taking certain medicines (see “Taking other medicines”).

This medicinal product is not suitable for neonates, infants and children less than 12 years of age and adolescents weighing less than 35 kg. If MOTILIUM is for a child, ask your doctor which formulation is appropriate.

Warnings and precautions

Before using this medicine contact your doctor if you:

- suffer from liver problems (liver function impairment or failure) (see “Do not take MOTILIUM”)
- suffer from kidney problems (kidney function impairment or failure). It is advisable to ask your doctor for advice in case of prolonged treatment as you may need to use a lower dose or use this medicine less often, and your doctor may want to examine you regularly.

Domperidone may be associated with an increased risk of heart rhythm disorder and cardiac arrest. This risk may be more likely in those over 60 years old or in those taking doses higher than 30 mg per day. The risk also increases when domperidone is given together with some drugs. Tell your doctor or pharmacist if you are taking drugs to treat infection (fungal infections or bacterial infection) and/or if you have heart problems or AIDS/HIV (see “Taking other medicines”).

MOTILIUM should be used at the lowest effective dose in adults and children.

While using MOTILIUM, contact your doctor if you experience heart rhythm disorders such as palpitations, trouble breathing, loss of consciousness. Treatment with MOTILIUM should be stopped.

Taking other medicines

Do not use MOTILIUM if you are taking medicine to treat:

- fungal infections, e.g., pentamidine or azole anti-fungals, specifically itraconazole, oral ketoconazole, fluconazole, posaconazole or voriconazole
- bacterial infections, specifically erythromycin, clarithromycin, telithromycin, levofloxacin, moxifloxacin, spiramycin (these are antibiotics)
- heart problems or high blood pressure (e.g., amiodarone, dronedarone, ibutilide, disopyramide, dofetilide, sotalol, hydroquinidine, quinidine)
- psychoses (e.g., haloperidol, pimozide, sertindole)
- depression (e.g., citalopram escitalopram)
- gastro-intestinal disorders (e.g., cisapride, dolasetron, prucalopride)
- allergy (e.g., mequitazine, mizolastine)
- malaria (in particular halofantrine, lumefantrine)
- AIDS/HIV such as ritonavir or saquinavir (these are protease inhibitors)
- Hepatitis C (e.g., telaprevir)
- cancer (e.g., toremifene, vandetanib, vincamine).

Do not use MOTILIUM if you are taking certain other medicines (e.g., bepridil, diphemanil, methadone).

Tell your doctor or pharmacist if you are taking drugs to treat infection, heart problems, AIDS/HIV or Parkinson’s disease.

It is important to ask your doctor or pharmacist if MOTILIUM is safe for you when you are taking any other medicines, including medicines obtained without prescription.

Using MOTILIUM with food and drink

The absorption of MOTILIUM Suppositories is not affected by food or drink.

Pregnancy

It is not known whether the use of MOTILIUM is harmful during pregnancy. If you are pregnant or think you may be you should inform your doctor who will decide if you can use MOTILIUM.

Breast-feeding

Small amounts of domperidone have been detected in breast milk. MOTILIUM may cause unwanted side effects affecting the heart in a breast-fed baby. MOTILIUM should be used during breast-feeding only if your doctor considers this clearly necessary. Ask your doctor for advice before using this medicine.

Driving and using machines

Some patients have reported feeling dizzy or sleepy after taking MOTILIUM. Do not drive or use machinery while taking MOTILIUM until you know how MOTILIUM affects you.

Important information about some of the ingredients of MOTILIUM:

- MOTILIUM suppositories contain an ingredient called butylated hydroxyanisole which can irritate eyes, skin and the lining of the mouth and nose (mucous membranes). If you think you have such a reaction please tell your doctor.

3. How to use MOTILIUM

Follow these instructions closely unless your doctor has advised you otherwise.

Duration of treatment

Symptoms usually resolve with 3-4 days of using this medicine. Do not use MOTILIUM for longer than 7 days without consulting your doctor.

Adults and adolescents (12 years of age and older and weighing 35 kg or more)

The usual dose is one suppository two times a day. Do not use more than two suppositories per day.

Inserting the suppositories

- First wash your hands.
- The suppository should be moistened and then inserted into the bottom as far as possible.
- Once this has been done tense your muscles to prevent the suppository coming out.

Neonates, infants, children less than 12 years of age and adolescents weighing less than 35 kg

Suppositories are not suitable for neonates, infants or children less than 12 years of age or adolescents weighing less than 35 kg. If MOTILIUM is for a child, ask your doctor for the children's formulation.

If you use more MOTILIUM than you should

If you have used too much MOTILIUM, contact your doctor, pharmacist or the poison centre immediately, in particular if a child has used too much. In the event of overdose, symptomatic treatment could be implemented. An ECG monitoring could be undertaken, because of the possibility of a heart problem called "prolonged QT interval".

Information for the doctor: close observation of the patient, gastric lavage, administration of activated charcoal and general supportive measures are recommended. Anticholinergic anti-Parkinson medication may help to counteract the extrapyramidal disorders.

If you forget to use MOTILIUM

Use your medicine as soon as you remember. If it is almost time for your next dose, wait until that is due and then continue as normal. Do not use a double dose to make up for a forgotten dose.

4. Possible side effects

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

Uncommon (may affect up to 1 in 100 people):

- Involuntary movements of the face or arms and legs, excessive trembling, excessive muscle stiffness or muscle spasm

Not known (frequency cannot be estimated from the available data):

- Seizures
- A type of reaction that may occur soon after administration and is recognised by skin rash, itching, shortness of breath, and/or a swollen face

- A severe hypersensitivity reaction that may occur soon after administration that is characterised by hives, itching, flushing, fainting, and difficulty breathing among other possible symptoms
- Disorders of the cardiovascular system: heart rhythm disorders (rapid or irregular heart beat) have been reported; if this happens, you should stop the treatment immediately. Domperidone may be associated with an increased risk of heart rhythm disorder and cardiac arrest. This risk may be more likely in those over 60 years old or taking doses higher than 30 mg per day. Domperidone should be used at the lowest effective dose in adults and children.

Stop treatment with MOTILIUM and contact your doctor immediately if you experience any of the unwanted events described above.

Other unwanted effects that have been observed with MOTILIUM are listed below:

Common (may affect up to 1 in 10 people):

- Dry mouth

Uncommon (may affect up to 1 in 100 people):

- Anxiety
- Agitation
- Nervousness
- Loss of interest in sex or diminished interest in sex
- Headache
- Sleepiness
- Diarrhoea
- Rash
- Itchiness
- Hives
- Painful or tender breasts
- Milk discharge from breasts
- A general feeling of weakness
- Feeling Dizzy

Not known (frequency cannot be estimated from the available data):

- Upward movement of the eyes
- Stopped menstrual periods in women
- Enlarged breasts in men
- Inability to urinate
- Changes in certain laboratory test results
- Restless legs syndrome (uncomfortable feeling, with an irresistible urge to move your legs, and sometimes arms and other parts of your body)

Some patients who have used MOTILIUM for conditions and dosages requiring medical oversight have experienced the following unwanted effects:

Restlessness; swollen or enlarged breasts, unusual discharge from breasts, irregular menstrual periods in women, difficulty breastfeeding, depression, hypersensitivity.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. 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 MOTILIUM

- Keep the medicine out of the sight and reach of children.
- Do not use MOTILIUM after the expiry date which is stated on the pack. The expiry date “exp.” refers to the last day of the month shown where the first two figures indicate the month, the next the year.
- Do not store MOTILIUM above 25°C.
- Store the suppositories in a dry place.

Medicines should not be disposed of *via* wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What MOTILIUM contains

The active substance is domperidone.

The other ingredients are: Tartaric acid, macrogol 4000, macrogol 1000, macrogol 400, butyl hydroxyanisol.

What MOTILIUM looks like and contents of the pack

[To be completed nationally]

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

[To be completed nationally]

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

Manufacturer

Cilag AG, Hochstrasse 201, CH-8205 Schaffhausen

Or for 30 mg suppositories only:

Lusomedicamenta Sociedade Técnica Farmacêutica, S.A.
Queluz,
Portugal

Marketing Authorisation Number

[To be completed nationally]

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

Name of the Member State	Name of the medicinal product
Austria	Motilium
Belgium	Motilium
Denmark	Motilium
Ireland	Motilium
Luxembourg	Motilium
Netherlands	Motilium

This package insert was last approved in