MOTILIUM INSTANTS

PL 13249/0028

UKPAR

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MOTILIUM INSTANTS

PL 13249/0028

LAY SUMMARY

On 23rd February 2010, the MHRA granted McNeil Limited a Marketing Authorisation (licence) for the medicinal product Motilium Instants (PL 13249/0028). This is a Pharmacy Only Medicines (P).

The tablets contain domperidone, which works by helping your stomach to move food contents through your digestive systems normally and in the right direction, so that they don't stay too long in one place. Domperidone also works to relieve feelings of nausea and queasiness.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Motilium Instants outweigh the risks. Hence Marketing Authorisation has been granted.

MOTILIUM INSTANTS

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product Motilium Instants (PL 13249/0028) on the 23rd February 2010. This product is a Pharmacy Only Medicines (P).

This is a standard national abridged application for a line extension to Motilium ™ Tablets 10mg (PL 13249/0014) which had been authorised as a Pharmacy Medicine in the UK by Johnson & Johnson MSD Consumer Pharmaceuticals in May 1997. This product was originally approved in 1983 to Janssen-Cilag Ltd as PL 00242/0100.

Domperidone is a dopamine antagonist and increases gastrointestinal motility. It is used for the relief of functional dyspepsia and nausea and vomiting of various causes. Domperidone has advantage over metoclopramide and the phenothiazines of being less likely to cause central effects such as sedation and dystonic reactions because it does not readily cross the blood-brain barrier. Domperidone acts at the chemoreceptor trigger zone and so is unlikely to be effective in motion sickness and other vestibular disorders.

Motilium Instants is indicated for the relief of post-prandial symptoms of fullness, nausea, epigastric bloating and belching that is occasionally accompanied by epigastric discomfort and heartburn; and for the relief of nausea and vomiting of less than 48 hours duration.

PHARMACEUTICAL ASSESSMENT

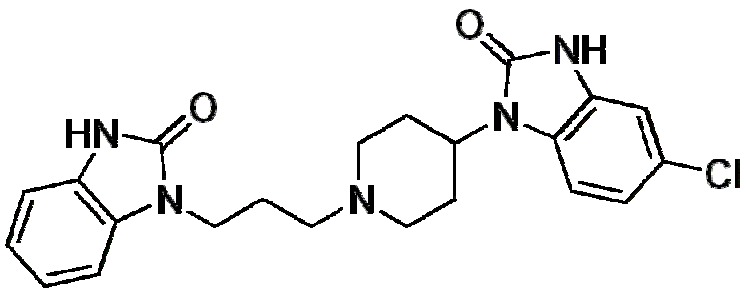
DRUG SUBSTANCE

Nomenclature

rINN: Domperidone

Chemical names: 5-chloro-1-(1-[3-(2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)propyl]piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one

Structure



Molecular formula: $C_{22}H_{24}ClN_5O_2$

Molecular Mass: 425.9 g/mol

All aspects of the manufacture and control of the active substance domperidone are covered by a European Directorate for the Quality of Medicines (EDQM) certificate of suitability.

DRUG PRODUCT

Other ingredients

Other ingredients consist of pharmaceutical excipients, namely mannitol, poloxamer 188, aspartame, mint flavour and gelatine type B.

All excipients used comply with their respective European Pharmacopoeia monograph with the exception of poloxamer 188 which is tested in accordance with USP and mint flavour complies with in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

Pharmaceutical development

Suitable pharmaceutical development data have been provided for this application. Comparable dissolution and impurity profile are provided for these products versus the originator product.

Manufacture
A description and flow-chart of the manufacturing method have been provided. In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation has been carried out on batches of the product. The results appear satisfactory.

Finished product specification
The finished product specification is satisfactory. Test methods have been described and adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis have been provided for any working standards used.

Container Closure System
Product is packaged in Blister packs comprising PVDC/LDPE/PVC foil and heat seal lacquer/aluminium/PET/Kraft paper. Specifications and Certificates of Analysis for all packaging types used have been provided. These are satisfactory. All primary product packaging complies with EU legislation regarding contact with food.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 2 years with storage conditions of 'Do not store above 25degree C. Store in the original container' is set and this is acceptable.

Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL) and Labelling
The SPC, PIL and labelling are pharmaceutically satisfactory.

The applicant has submitted results of PIL user testing. The results indicate that the PIL is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA Form
The MAA form is pharmaceutically satisfactory.

Expert Report
The pharmaceutical expert report is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
It is recommended that Marketing Authorisation is granted for this application.

PRECLINICAL ASSESSMENT

The preclinical data was assessed previously for the originator product (Domperidone Maleate Tablets 10mg). No new preclinical data have been supplied with this application and none are required for an application of this type.

A preclinical expert report has been provided, written by an appropriately qualified person. This is satisfactory.

CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY

Pharmacodynamics

Domperidone is a dopamine antagonist and increases gastrointestinal motility. It does not reach brain dopamine receptors, probably because it does not readily cross the blood brain barrier.

Pharmacokinetics

Domperidone is absorbed from the gastrointestinal tract and metabolised in the liver. It is secreted in the bile mainly as inactive metabolites.

Bioequivalence

An open, single dose three way randomised cross-over study was, performed on 24 healthy male and female subjects at Heymans Institute of Pharmacology of the University of Ghent, Ghent, Belgium. The study compared Motilium instant tablets (BN 4CFD163/B a pilot scale batch), domperidone malate tablets (BN 94H021/609) and domperidone base tablets(BN 94/H02/575), each taken as a single dose of 2*10 mg tablets with a wash out period of seven days between each study period. Subjects fasted from 22.00 hours the night before dosing. The dose was administered with a glass of water in the case of the conventional dosage forms and without water for the Zydis formulation. Blood samples were taken before drug administration and at frequent intervals during the study and 24, 32 & 48 hours post dosing.

Domperidone was assayed using a HPLC/fluorescence method and the analytical work performed in accordance with GLP guidelines. The main pharmacokinetic parameters are summarised in Tables below.

	Zydis (A)	**Maleate (B)**	**Base (C)**
Cmax (ng/ml)	33.1 ± 12.9 (30.6 ± 1.6)	35.3 ± 12.6 (33.1 ± 1.4)	35.2 ±15.8 (31.8 ± 1.6)
Tmax (h)	0.9 ± 0.6	0.9 ± 0.3	0.8 ± 0.3
AUC (o-8h) (ng.h/ml)	72.0 ± 21.3 (68.7 ± 14.)	69.4 ± 19.7 (66.7 ± 1.3)	68.1 ± 25.8 (63.4 ± 1.5)
AUC (o-∞)	**111 ± 37 (106 ± 1)**	**108 ± 33 (104 ± 1)**	**106 ± 37 (99.5 ± 1.4)**

	90% Confidence interval		
Parameter	A v B	A v C	B v C
Cmax (ng/ml)	80-105	24-111	91-121
AUC (o-∞))	94-111	98-115	96-113

Results obtained for 90% CI for Cmax and AUC are within the conventionally accepted bioequivalence of 80 – 125% confidence intervals.

EFFICACY

No new efficacy data are provided or required. However, the applicant has submitted copies of several publications with a summary review of the literature confirming the effectiveness of Domperidone.

SAFETY

No new safety data are provided or needed. However, the applicant has provided several copies of publications with a safety review from the literature. No new safety issues have been detected.

EXPERT REPORT
A satisfactory clinical expert report has been submitted with appropriate CV.

SUMMARY OF PRODUCT CHARACTERISTICS
This is satisfactory.

PATIENT INFORMATION LEAFLET
This is satisfactory.

LABELLING
These are satisfactory.

DISCUSSION
Dopamine antagonists, including Domperidone, have been available in the UK for more than ten years. Their use is well established with recognised efficacy and acceptable safety.

With regards to current application, sufficient clinical information has been submitted. When used as indicated, Motilium Instants Tablets have a favourable benefit-to-risk ratio.

CONCLUSION
Marketing authorisation can be granted.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Motilium Instants are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

No new data have been submitted and none are required for an application of this type.

The 90% confidence intervals for the test/reference lie within the acceptance criteria specified in the CPMP/EWP/QWP/1401/98 *Notes for Guidance on the Investigation of Bioavailability and Bioequivalence*. Bioequivalence of the test product to the reference formulation has been satisfactorily demonstrated in accordance with CHMP criteria.

No new safety data are supplied or required for this line extension application. Domperidone has well-established side-effect profiles and are generally well-tolerated.

The SPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s product and the innovator product are interchangeable. Extensive clinical experience with Motilium Instants is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

MOTILIUM INSTANTS

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1	The MHRA received the marketing authorisation applications on 15th April 2005
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 4th May 2005
3	Following assessment of the applications the MHRA requested further information on 10th March 2006 and 1st April 2008 for the quality part and on 2nd April 2008 for the clinical parts of the dossier
4	The applicant responded to the MHRA's requests, providing further information on 19th March 2008 and 7th October 2008 for the quality sections, and 7th October 2008 for the Clinical section.
5	The application was determined on 23rd February 2010

MOTILIUM INSTANTS

PL 13249/0028

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
MOTILIUM INSTANTS

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One tablet contains 10 mg domperidone.
Excipients include 0.75mg aspartame.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Orodispersible tablet.
White to off-white circular tablet.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the relief of post-prandial symptoms of fullness, nausea, epigastric bloating and belching that is occasionally accompanied by epigastric discomfort and heartburn.

For the relief of nausea and vomiting of less than 48 hours duration.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
For the relief of symptoms of post prandial stomach discomfort

Adults and children 16 years of age and older
Up to 10 mg three times daily and at night.
Maximum duration of course of treatment 2 weeks.

For the relief of nausea and vomiting
Adults and children 16 years of age and older
Up to 10 mg three times daily and at night.
Maximum duration of course of treatment 48 hours.

Use in children under 16 years of age
Not recommended.

Method of administration

For oral use

Allow the tablet to disintegrate on the tongue then swallow the medication.

4.3 CONTRAINDICATIONS
- Known hypersensitivity to domperidone or any of the excipients.
- Prolactin-releasing pituitary tumour (prolactinoma).
- When stimulation of the gastric motility could be harmful: gastro-intestinal haemorrhage, mechanical obstruction or perforation.
- Hepatic and/or renal impairment.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Motilium Instants should only be taken according to the above posology (See 4.2). Patients who find they have post-prandial symptoms that persist, and are having to take domperidone continuously for more than 2 weeks should be referred to their GP.

Patients who find that their nausea and vomiting persist for more than 48 hours should be referred to their doctor.
The patient should be advised that Motilium Instants is not recommended for the treatment of motion sickness.

Motilium Instants contain aspartame (E951) a source of phenylalanine. May be harmful for people with phenylketonuria.

Use with Potent CYP3A4 Inhibitors

Co-administration with oral ketoconazole, erythromycin or other potent CYP3A4 inhibitors that prolong the QTc interval should be avoided (see section 4.5 Interaction with other medicinal products and other forms of interaction).

The label will include; Do not take if you are pregnant.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

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.

Separate *in vivo pharmacokinetic/pharmacodynamic* interaction studies with oral ketoconazole or oral erythromycin in healthy subjects confirmed a marked inhibition of domperidone's CYP3 A4 mediated first pass metabolism by these drugs.With the combination of oral domperidone 10mg four times daily and ketoconazole 200mg twice daily, a mean QTc prolongation of 9.8 msec was seen over the observation period, with changes at individual time points ranging from 1.2 to 17.5 msec. With the combination of domperidone 10mg four times daily and oral erythromycin 500mg three times daily, mean QTc over the observation period was prolonged by 9.9 msec, with changes at individual time points ranging from 1.6 to 14.3 msec. Both the Cmax and AUC of domperidone at steady state were increased approximately three-fold in each of these interaction studies. In these studies domperidone monotherapy at 10mg given orally four times daily resulted in increases in mean QTc of 1.6 msec (ketoconazole study) and 2.5 msec (erythromycin study), while ketoconazole monotherapy (200 mg twice daily) and erythromycin monotherapy (500 mg three times daily) led to increases in QTc of 3.8 and 4.9 msec, respectively, over the observation period.

4.6 PREGNANCY AND LACTATION

There are limited post-marketing data on the use of domperidone in pregnant women. Therefore, Motilium Instants should only be used during pregnancy when justified by the anticipated therapeutic benefit. Studies have shown that domperidone enters breast milk. It is not known whether this is harmful to the newborn. Therefore, breast feeding is not recommended for mothers who are taking Motilium Instants.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Motilium Instants have no or negligible influence on the ability to drive and use machines.

4.8 UNDESIRABLE EFFECTS

At the dosages and duration recommended here domperidone is generally very well tolerated with few undesirable effects.

Immune system disorder: Very rare; allergic reactions including anaphylaxis, anaphylactic shock, anaphylactic reaction, urticaria and angioedema. .
Endocrine disorder: Rare; increased prolactin levels.
Nervous system disorders: Very rare; extrapyramidal side effects.
Cardiac disorders: QTc prolongation (frequency not known). Very rare (<1/10,000): ventricular arrhythmias.

Gastrointestinal disorders: Rare; gastrointestinal disorders, including very rare transient intestinal cramps. Very rare: diarrhoea.
Skin and subcutaneous tissue disorders: Very rare; pruritus, rash.
Reproductive system and breast disorders: Rare; galactorrhoea, gynaecomastia, amenorrhoea.

As the hypophysis is outside the blood brain barrier, domperidone may cause an increase in prolactin levels. In rare cases, this hyperprolactinaemia may lead to neuro endocrinological side effects such as galactorrhoea, gynaecomastia and amenorrhoea.
Extrapyramidal side effects are exceptional in adults. These side effects reverse spontaneously and completely as soon as treatment is stopped.

4.9 OVERDOSE

Symptoms

Symptoms of overdosage may include drowsiness, disorientation and extrapyramidal reactions, especially in children.

Treatment

There is no specific antidote to domperidone; but in the event of overdose, gastric lavage as well as the administration of activated charcoal may be useful. Close medical supervision and supportive therapy are recommended. Anticholinergic, anti-parkinson drugs may be helpful in controlling the extrapyramidal reactions.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Propulsives. ATC Code: A03F A 03

Domperidone is a dopamine antagonist with anti-emetic properties. Domperidone does not readily cross the blood-brain barrier. In domperidone users, especially adults, extrapyramidal side effects 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.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

In fasting subjects, domperidone is rapidly absorbed after oral administration, with peak plasma concentrations at 30 to 60 minutes. The low absolute bioavailability of oral domperidone (approximately 15%) is due to an extensive first-pass metabolism in the gut wall and liver. 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. The time of peak absorption is slightly delayed and the AUC somewhat increased when domperidone is taken after a meal.

Distribution

Oral Domperidone does not appear to accumulate or to induce its own metabolism; a peak plasma level after 90 minutes of 21 ng/ml after two weeks oral administration of 30mg per day was almost the same as that of 18 ng/ml after the first dose. 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.

5.3 PRECLINICAL SAFETY DATA

Electrophysiological in vitro and in vivo studies indicate an overall moderate risk of domperidone to prolong the QT interval in humans. In in vitro experiments on isolated cells transfected with HERG and on isolated guinea pig myocytes, exposure ratios ranged between 5- and 30-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 20mg q.i.d. Exposure 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 (20mg q.i.d.) by 17-fold. However, safety margins in in vitro and in in vivo pro-arrhythmic models (isolated Langendorff perfused heart) and in in vivo models (dog, guinea pig, rabbits sensitised for torsades de points) exceeded the free plasma concentrations in humans at maximum daily dose (20mg q.i.d) by more than 17-fold. In the presence of inhibition of the metabolism via CYP3A4 free plasma concentrations of domperidone can rise up to 10-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 rats.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Gelatin
Mannitol
Poloxamer 188
Aspartame
Mint flavour

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

2 years.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25°C. Store in the original container.

6.5 NATURE AND CONTENTS OF CONTAINER

Blister packs comprising PVDC/LDPE/PVC foil and heat seal lacquer/aluminium/PET/Kraft paper.
Pack size: 10 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements.

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

7 MARKETING AUTHORISATION HOLDER

McNeil Ltd.
Saunderton
High Wycombe
Buckinghamshire HP14 4HJ
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 13249/0028

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/02/2010

10 DATE OF REVISION OF THE TEXT

23/02/2010

PATIENT INFORMATION LEAFLET

motilium®
domperidone
instants

- This medicine is used for **two** reasons, which have **different treatment durations**. See Section 1 ▶
- This medicine is for use by adults and children aged 16 years and over.
- **Do not take this medicine:**
  - There are some people who should not use this medicine. *To find out if you are one of them. See Section 2* ▶
  - If you have ever had a **bad reaction** to any of the ingredients. *For the list of ingredients. See Section 6* ▶
- **Speak to your doctor:**
  - If you suffer from any of the conditions mentioned in *Section 2* ▶
  - If you are taking any **other medicines**. *See Section 2* ▶
- **Follow the dosage instructions carefully**. These are shown in the dosage table. *See Section 3* ▶

Now read this whole leaflet carefully before you use this medicine. Keep the leaflet: you might need it again.

1 What the medicine is for

Motilium Instants is a medicine which is used for **two** reasons, which have **different treatment durations**.

- To treat short lived episodes of **nausea** (feeling sick or queasy) and **vomiting** (being sick) of less than **48 hours** duration.
- To relieve **nausea, fullness, belching, heavy bloated stomach, trapped wind and heartburn** which can happen after a meal for treatment periods of up to **2 weeks**. This may be because the stomach's digestive rhythm has slowed down and is not moving food contents in the right direction through the digestive system as efficiently as it needs to.

The tablets contain domperidone, which works by helping your stomach to move food contents through your digestive system normally and in the right direction, so that they don't stay too long in one place.

This medicine is for use in adults and children aged 16 years and over.

2 Before taking this medicine

This medicine is suitable for most adults and children aged 16 years and over, but a few people should not use it. If you are in any doubt, talk to your doctor or pharmacist.

Do not take this medicine...

- If you have ever had a **bad reaction** to any of the ingredients.
- If you have a **disease of the pituitary gland** (prolactinoma).
- If you have an underlying illness affecting the **digestive system**, for example:
  - A **stomach** or **duodenal ulcer.**
  - A **blocked** or **perforated gut.**
  - Your **bowel motions (stools)** are often black.
  - You frequently have **severe stomach cramps.**
- If you have **kidney** or **liver problems.**
- If you are taking any of the following **medicines**:
  - *Oral ketoconazole* (an **antifungal** medicine when taken by mouth).
  - *Oral erythromycin* (an **antibiotic**).

If any of these apply to you, **get advice from a doctor or pharmacist without taking Motilium Instants.**

Talk to your doctor or pharmacist...

- If you suffer from **phenylketonuria.**
- If you are taking any **other medicines.**

If you are not sure about any of the medicines you are taking, show the bottle or pack to your pharmacist.

If any of these bullet points apply to you now or in the past, **talk to a doctor or pharmacist**.

If you are pregnant or breast-feeding

- Do not take if you are pregnant or think you might be pregnant.
- Do not take this medicine if you are breast-feeding unless your doctor or another health care professional has told you to.

Some of the ingredients can cause problems

- Aspartame (E951) contains a source of phenylalanine which may be harmful for people with phenylketonuria.

Special warnings about use in travel sickness

- This product should not be used to treat travel sickness. Speak to your doctor or pharmacist about suitable treatments.

3 How to take this medicine

Check the tables that follow to see how much medicine to take.

- Peel back the lid and tip the tablet out. Do not push the tablet through the lid.
- Let the tablet melt on the tongue then swallow.
- For oral use only.
- Do not use more than the stated dose shown in the tables.
- The tablets are for **short term treatment** only.
- If symptoms of nausea (feeling sick) and vomiting (being sick) persist for more than **48 hours**, talk to your doctor.
- If symptoms of stomach discomfort which occur after a meal persist for more than **2 weeks**, talk to your doctor.

Children under 16 years old

Do not give to children under 16 years old.

Adults and children aged 16 years and over

To treat nausea (feeling sick) and vomiting (being sick) of less than 48 hours duration

Age	Dose
Adults and children aged 16 years and over	Take **one tablet** up to 3 times a day and one tablet at night.

- Do not take more than 4 tablets in any 24 hour period.
- If your symptoms get worse or the tablets have no effect, talk to your doctor.
- If symptoms of nausea and vomiting persist for more than **48 hours**, talk to your doctor.

Adults and children aged 16 years and over

To treat stomach discomfort and nausea experienced after food and drink for up to 2 weeks

Age	Dose
Adults and children aged 16 years and over	Take **one tablet** up to 3 times a day and one tablet at night.

- Do not take more than 4 tablets in any 24 hour period.
- If your symptoms get worse or the tablets have no effect, talk to your doctor.
- If symptoms of stomach discomfort which occurs after a meal persist for more than **2 weeks**, talk to your doctor.

If anyone takes too much

If anyone takes too many Motilium Instants tablets, contact a doctor or your nearest Accident and Emergency department (Casualty) taking this leaflet and pack with you.

If you forget to take the medicine

You should only take this medicine as required following the dosage instructions above carefully. If you forget to take a dose, take the next dose when needed as long as you do not take more than 4 tablets in any 24 hour period.
Do not take a double dose.

4 Possible side-effects

Motilium Instants tablets can have side-effects, like all medicines, although these don't affect everyone and are usually mild.

If you experience any of the following, stop using the medicine and seek immediate medical help:

Very rarely:

- Allergic reactions such as skin rash, itching, shortness of breath, wheezing and/or swollen face.
- Heart rhythm disorders.

If you experience any of the following, stop using the medicine and talk to your doctor:

Very rarely:

- Abnormal muscle movements or tremor (shaking).
- Trembling and muscle stiffness.
- Itchiness or hives.

Rarely:

- Sore or swollen breasts (even in men).
- Fluid leaking from the nipples.
- Stop in menstrual periods.

Other effects which may occur include:

Very rarely:

- Diarrhoea.

Rarely:

- Stomach cramps which are usually of short duration. If they last more than a day, consult your doctor or pharmacist.

If you experience any side-effects not included in this leaflet or are not sure about anything, **talk to your doctor or pharmacist**.

5 Storing this medicine

Keep the product out of the reach and sight of children.

Do not store above 25°C. Store in the original container to protect from moisture.

Do not use your medicine after the date shown as the expiry date on the packaging.

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 protect the environment.

6 Further information

What's in this medicine?

The active ingredient in Motilium Instants is: Domperidone 10 mg.
Other ingredients are: Gelatin, mannitol (E421), poloxamer 188, aspartame (E951) and mint flavour.

What the medicine looks like

Motilium Instants are off-white, melt in the mouth (orodispersible) tablets available in packs of 10 tablets.

Product Licence holder: McNeil Ltd, Saunderton, High Wycombe, Bucks HP14 4HJ.

Manufacturer: Janssen Pharmaceutica NV, Turnhoutseweg 30, B-2340 Beerse, Belgium or Janssen-Cilag SpA, Via C. Janssen, Borgo San Michele, Latina, Italy.

This leaflet was revised November 2009.
Motilium Instants is a registered trade mark.

7 What you can do to help stop these symptoms

The type of nausea or upset stomach treated by Motilium Instants can be caused or aggravated by:

- Overeating, or very large meals.
- Eating too quickly.
- Certain 'triggers' such as coffee, fatty foods, or alcohol.

There are things you can do to help stop future attacks of this type of stomach problem:

Keep away from your 'triggers'. If there are certain foods, drinks or situations that you know bring on your symptoms try to cut them out or cut down.

Go easy on snacks. Snack foods often contain a lot of fat, and can make your symptoms worse.

Eat regularly. Have three or four meals a day, at the same times, and don't rush your meals.

McNeil

07-1201

LABELLING

Braille Reads:

motilium
instants


motilium® instants domperidone
McNeil
DO NOT PUSH THROUGH
PEEL▼HERE
AW_47270
Expiry:
Mfg Date:
Batch Nr.:
XXXXXXXX