

### **Annex III**

#### **Amendments to relevant sections of the summary of product characteristics and package leaflet**

Note:

The relevant sections of the Summary of Product Characteristics and package leaflet are the outcome of the referral procedure.

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

## Metoclopramide-containing products

The following wording should be included in the SmPC of the marketing authorisations to be varied, as relevant:

### Summary of Product Characteristics

#### **4.1 Therapeutic indications**

##### **Parenteral route/IM-IV**

##### Adult population

{Tradename} is indicated in adults for:

- Prevention of post operative nausea and vomiting (PONV)
- Symptomatic treatment of nausea and vomiting, including acute migraine induced nausea and vomiting
- Prevention of radiotherapy induced nausea and vomiting (RINV).

##### Paediatric population

{Tradename} is indicated in children (aged 1-18 years) for:

- Prevention of delayed chemotherapy induced nausea and vomiting (CINV) as a second line option
- Treatment of established post operative nausea and vomiting (PONV) as a second line option

##### **Oral route**

##### Adult population

{Tradename} is indicated in adults for:

- Prevention of delayed chemotherapy induced nausea and vomiting (CINV)
- Prevention of radiotherapy induced nausea and vomiting (RINV).
- Symptomatic treatment of nausea and vomiting, including acute migraine induced nausea and vomiting. Metoclopramide can be used in combination with oral analgesics to improve the absorption of analgesics in acute migraine.

##### Paediatric population

{Tradename} is indicated in children (aged 1-18 years) for:

- Prevention of delayed chemotherapy induced nausea and vomiting (CINV) as a second line option

##### **Rectal route**

##### Adult population

{Tradename} is indicated in adults for:

- Prevention of delayed chemotherapy induced nausea and vomiting (CINV)
- Prevention of radiotherapy induced nausea and vomiting (RINV)

#### **4.2 Posology and method of administration**

##### **Parenteral route**

The solution can be administered intravenously or intramuscularly.  
Intravenous doses should be administered as a slow bolus (at least over 3 minutes).

##### All indications (adult patients)

For prevention of PONV a single dose of 10mg is recommended.

For the symptomatic treatment of nausea and vomiting, including acute migraine induced nausea and vomiting and for the prevention of radiotherapy induced nausea and vomiting (RINV): the recommended single dose is 10 mg, repeated up to three times daily

The maximum recommended daily dose is 30 mg or 0.5mg/kg body weight.

The injectable treatment duration should be as short as possible and transfer to oral or rectal treatment should be made as soon as possible.

All indications (paediatric patients aged 1-18 years)

The recommended dose is 0.1 to 0.15 mg/kg body weight, repeated up to three times daily by intravenous route. The maximum dose in 24 hours is 0.5 mg/kg body weight.

*Dosing table*

Age	Body Weight	Dose	Frequency
1-3 years	10-14 kg	1 mg	Up to 3 times daily
3-5 years	15-19 kg	2 mg	Up to 3 times daily
5-9 years	20-29 kg	2.5 mg	Up to 3 times daily
9-18 years	30-60 kg	5 mg	Up to 3 times daily
15-18 years	Over 60kg	10 mg	Up to 3 times daily

The maximum treatment duration is 48 hours for treatment of established post operative nausea and vomiting (PONV).

The maximum treatment duration is 5 days for prevention of delayed chemotherapy induced nausea and vomiting (CINV).

**Oral route**

All indications (adult patients)

**For immediate release preparations**

The recommended single dose is 10 mg, repeated up to three times daily.

**For prolonged release preparations**

**15mg strength**

The recommended single dose is 15 mg, repeated up to twice daily.

**30mg strength**

The recommended dose is 30mg once daily.

**For all preparations**

The maximum recommended daily dose is 30 mg or 0.5mg/kg body weight.

The maximum recommended treatment duration is 5 days.

Prevention of delayed chemotherapy induced nausea and vomiting (CINV) (paediatric patients aged 1-18 years)

The recommended dose is 0.1 to 0.15 mg/kg body weight, repeated up to three times daily by oral route. The maximum dose in 24 hours is 0.5 mg/kg body weight.

*Dosing table*

Age	Body Weight	Dose	Frequency
1-3 years	10-14 kg	1 mg	Up to 3 times daily
3-5 years	15-19 kg	2 mg	Up to 3 times daily
5-9 years	20-29 kg	2.5 mg	Up to 3 times daily
9-18 years	30-60 kg	5 mg	Up to 3 times daily

15-18 years	Over 60kg	10 mg	Up to 3 times daily
-------------	-----------	-------	---------------------

[Appropriate measuring device must be provided with the product, and instructions for use must be included in the SmPC]

The maximum treatment duration is 5 days for prevention of delayed chemotherapy induced nausea and vomiting (CINV).

For tablets/capsules/granules

Appropriate additional information regarding posologies adaptation should be implemented in the SmPC depending on the strength of the formulations

For formulations which cannot be used to administer a 5mg dose

Tablets/capsules/granules are not suitable for use in children weighing less than 61 kg.

Other pharmaceutical forms/strengths may be more appropriate for administration to this population.

For formulations which can be used to administer a 5mg dose

Tablets/capsules/granules are not suitable for use in children weighing less than 30 kg.

Other pharmaceutical forms/strengths may be more appropriate for administration to this population

Rectal route

All indications (adult patients)

The recommended single dose is 10 mg, repeated up to three times daily.

The maximum recommended daily dose is 30 mg or 0.5mg/kg body weight.

The maximum recommended treatment duration is 5 days.

All routes of administration at the exception prolonged release preparations

Method of administration:

A minimal interval of 6 hours between two administrations is to be respected, even in case of vomiting or rejection of the dose (see section 4.4).

15mg strength prolonged release preparations

Method of administration:

A minimal interval of 12 hours between two administrations is to be respected, even in case of vomiting or rejection of the dose (see section 4.4).

30 mg strength prolonged release preparations

Method of administration:

A minimal interval of 24 hours between two administrations is to be respected, even in case of vomiting or rejection of the dose (see section 4.4).

All routes of administration

Special population

Elderly

In elderly patients a dose reduction should be considered, based on renal and hepatic function and overall frailty.

Renal impairment:

In patients with end stage renal disease (Creatinine clearance  $\leq$  15 ml/min), the daily dose should be reduced by 75%.

In patients with moderate to severe renal impairment (Creatinine clearance 15-60 ml/min), the dose should be reduced by 50% (see section 5.2).

Hepatic impairment:

In patients with severe hepatic impairment, the dose should be reduced by 50% (see section 5.2).

*Appropriate additional information regarding posologies adaptation should be implemented in the SmPC depending on the formulations for these specific populations:*

<Other pharmaceutical forms/strengths may be more appropriate for administration to this/these population(s)>

<This formulation is not suitable for administration to this/these population(s)>

#### *Paediatric population*

Metoclopramide is contraindicated in children aged less than 1 year (see section 4.3).

### **4.3 Contraindications**

#### **For all formulations**

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Gastrointestinal haemorrhage, mechanical obstruction or gastro-intestinal perforation for which the stimulation of gastrointestinal motility constitutes a risk
- Confirmed or suspected pheochromocytoma, due to the risk of severe hypertension episodes
- History of neuroleptic or metoclopramide-induced tardive dyskinesia
- Epilepsy (increased crises frequency and intensity)
- Parkinson's disease
- Combination with levodopa or dopaminergic agonists (see section 4.5)
- Known history of methaemoglobinaemia with metoclopramide or of NADH cytochrome-b5 deficiency.
- Use in children less than 1 year of age due to an increased risk of extrapyramidal disorders (see section 4.4)

#### **For rectal formulations**

- Recent history of proctitis or rectal bleeding
- Use in children below 18 years of age

### **4.4 Special warnings and precautions for use**

#### **For all routes of administration at the exception of prolonged release preparations**

#### **Neurological Disorders**

Extrapyramidal disorders may occur, particularly in children and young adults, and/or when high doses are used. These reactions occur usually at the beginning of the treatment and can occur after a single administration. Metoclopramide should be discontinued immediately in the event of extrapyramidal symptoms. These effects are generally completely reversible after treatment discontinuation, but may require a symptomatic treatment (benzodiazepines in children and/or anticholinergic anti-Parkinsonian medicinal products in adults).

The time interval of at least 6 hours specified in the section 4.2 should be respected between each metoclopramide administration, even in case of vomiting and rejection of the dose, in order to avoid overdose.

Prolonged treatment with metoclopramide may cause tardive dyskinesia, potentially irreversible, especially in the elderly. Treatment should not exceed 3 months because of the risk of tardive dyskinesia (see section 4.8). Treatment must be discontinued if clinical signs of tardive dyskinesia appear.

Neuroleptic malignant syndrome has been reported with metoclopramide in combination with neuroleptics as well as with metoclopramide monotherapy (see section 4.8). Metoclopramide should be discontinued immediately in the event of symptoms of neuroleptic malignant syndrome and appropriate treatment should be initiated.

Special care should be exercised in patients with underlying neurological conditions and in patients being treated with other centrally-acting drugs (see section 4.3)

Symptoms of Parkinson's disease may also be exacerbated by metoclopramide.

#### **For the 15 mg strength prolonged release preparations**

##### Neurological Disorders

Extrapyramidal disorders may occur, particularly in children and young adults, and/or when high doses are used. These reactions occur usually at the beginning of the treatment and can occur after a single administration. Metoclopramide should be discontinued immediately in the event of extrapyramidal symptoms. These effects are generally completely reversible after treatment discontinuation, but may require a symptomatic treatment (benzodiazepines in children and/or anticholinergic anti-Parkinsonian medicinal products in adults).

The time interval of at least 12 hours specified in the section 4.2 should be respected between each metoclopramide administration, even in case of vomiting and rejection of the dose, in order to avoid overdose.

Prolonged treatment with metoclopramide may cause tardive dyskinesia, potentially irreversible, especially in the elderly. Treatment should not exceed 3 months because of the risk of tardive dyskinesia (see section 4.8). Treatment must be discontinued if clinical signs of tardive dyskinesia appear.

Neuroleptic malignant syndrome has been reported with metoclopramide in combination with neuroleptics as well as with metoclopramide monotherapy (see section 4.8). Metoclopramide should be discontinued immediately in the event of symptoms of neuroleptic malignant syndrome and appropriate treatment should be initiated.

Special care should be exercised in patients with underlying neurological conditions and in patients being treated with other centrally-acting drugs (see section 4.3)

Symptoms of Parkinson's disease may also be exacerbated by metoclopramide.

#### **For the 30 mg strength prolonged release preparations**

##### Neurological Disorders

Extrapyramidal disorders may occur, particularly in children and young adults, and/or when high doses are used. These reactions occur usually at the beginning of the treatment and can occur after a single administration. Metoclopramide should be discontinued immediately in the event of extrapyramidal symptoms. These effects are generally completely reversible after treatment discontinuation, but may require a symptomatic treatment (benzodiazepines in children and/or anticholinergic anti-Parkinsonian medicinal products in adults).

The time interval of at least 24 hours specified in the section 4.2 should be respected between each metoclopramide administration, even in case of vomiting and rejection of the dose, in order to avoid overdose.

Prolonged treatment with metoclopramide may cause tardive dyskinesia, potentially irreversible, especially in the elderly. Treatment should not exceed 3 months because of the risk of tardive dyskinesia (see section 4.8). Treatment must be discontinued if clinical signs of tardive dyskinesia appear.

Neuroleptic malignant syndrome has been reported with metoclopramide in combination with neuroleptics as well as with metoclopramide monotherapy (see section 4.8). Metoclopramide should be discontinued immediately in the event of symptoms of neuroleptic malignant syndrome and appropriate treatment should be initiated.

Special care should be exercised in patients with underlying neurological conditions and in patients being treated with other centrally-acting drugs (see section 4.3)

Symptoms of Parkinson's disease may also be exacerbated by metoclopramide.

#### **For all routes of administration**

### Methaemoglobinemia

Methemoglobinemia which could be related to NADH cytochrome b5 reductase deficiency has been reported. In such cases, metoclopramide should be immediately and permanently discontinued and appropriate measures initiated (such as treatment with methylene blue).

### Cardiac Disorders

There have been reports of serious cardiovascular undesirable effects including cases of circulatory collapse, severe bradycardia, cardiac arrest and QT prolongation following administration of metoclopramide by injection, particularly via the intravenous route (see section 4.8).

Special care should be taken when administering metoclopramide, particularly via the intravenous route to the elderly population, to patients with cardiac conduction disturbances (including QT prolongation), patients with uncorrected electrolyte imbalance, bradycardia and those taking other drugs known to prolong QT interval.

Intravenous doses should be administered as a slow bolus (at least over 3 minutes) in order to reduce the risk of adverse effects (e.g. hypotension, akathisia).

### Renal and Hepatic Impairment

In patients with renal impairment or with severe hepatic impairment, a dose reduction is recommended (see section 4.2).

### Additional statements related to excipients

[To be completed nationally, if necessary]

## **4.5 Interaction with other medicinal products and other forms of interaction**

### All routes of administration

#### **Contraindicated combination**

Levodopa or dopaminergic agonists and metoclopramide have a mutual antagonism (see section 4.3).

#### **Combination to be avoided**

Alcohol potentiates the sedative effect of metoclopramide.

#### **Combination to be taken into account**

Due to the prokinetic effect of metoclopramide, the absorption of certain drugs may be modified.

#### *Anticholinergics and morphine derivatives*

Anticholinergics and morphine derivatives may have both a mutual antagonism with metoclopramide on the digestive tract motility.

#### *Central nervous system depressants (morphine derivatives, anxiolytics, sedative H1 antihistamines, sedative antidepressants, barbiturates, clonidine and related)*

Sedative effects of Central Nervous System depressants and metoclopramide are potentiated.

#### *Neuroleptics*

Metoclopramide may have an additive effect with other neuroleptics on the occurrence of extrapyramidal disorders.

#### *Serotonergic drugs*

The use of metoclopramide with serotonergic drugs such as SSRIs may increase the risk of serotonin syndrome.

#### *Digoxin*

Metoclopramide may decrease digoxin bioavailability. Careful monitoring of digoxin plasma concentration is required.

#### *Cyclosporine*

Metoclopramide increases cyclosporine bioavailability (C<sub>max</sub> by 46% and exposure by 22%). Careful monitoring of cyclosporine plasma concentration is required. The clinical consequence is uncertain.

#### *Mivacurium and suxamethonium*

Metoclopramide injection may prolong the duration of neuromuscular block (through inhibition of plasma cholinesterase).

#### *Strong CYP2D6 inhibitors*

Metoclopramide exposure levels are increased when co-administered with strong CYP2D6 inhibitors such as fluoxetine and paroxetine. Although the clinical significance is uncertain, patients should be monitored for adverse reactions.

#### **4.6 Fertility, pregnancy and lactation**

##### **All routes of administration**

###### *Pregnancy*

A large amount of data on pregnant women (more than 1000 exposed outcomes) indicates no malformative toxicity nor foetotoxicity. Metoclopramide can be used during pregnancy if clinically needed. Due to pharmacological properties (as other neuroleptics), in case of metoclopramide administration at the end of pregnancy, extrapyramidal syndrome in newborn cannot be excluded. Metoclopramide should be avoided at the end of pregnancy. If metoclopramide is used, neonatal monitoring should be undertaken.

###### *Breastfeeding*

Metoclopramide is excreted in breast milk at low level. Adverse reactions in the breast-fed baby cannot be excluded. Therefore metoclopramide is not recommended during breastfeeding. Discontinuation of metoclopramide in breastfeeding women should be considered.

#### **4.7 Effects on ability to drive and use machines**

##### **All routes of administration**

Metoclopramide may cause drowsiness, dizziness, dyskinesia and dystonias which could affect the vision and also interfere with the ability to drive and operate machinery.

#### **4.8 Undesirable effects**

##### **All routes of administration**

Adverse reactions listed by System Organ Class. Frequencies are defined using the following convention: very common ( $\geq 1/10$ ), common ( $\geq 1/100$ ,  $< 1/10$ ), uncommon ( $\geq 1/1000$ ,  $< 1/100$ ), rare ( $\geq 1/10000$ ,  $< 1/1000$ ), very rare ( $< 1/10000$ ), not known (cannot be estimated from the available data).

<b>Systeme Organ Class</b>	<b>Frequency</b>	<b>Adverse reactions</b>
<b>Blood and lymphatic system disorders</b>		
	Not known	Methaemoglobinaemia, which could be related to NADH cytochrome b5 reductase deficiency, particularly in neonates (see section 4.4) Sulphaemoglobinaemia, mainly with concomitant administration of high doses of sulphur-releasing medicinal products
<b>Cardiac disorders</b>		
	Uncommon	Bradycardia, particularly with intravenous formulation
	Not known	Cardiac arrest, occurring shortly after injectable use, and which can be subsequent to bradycardia (see section 4.4); Atrioventricular block, Sinus arrest particularly with intravenous formulation; Electrocardiogram QT prolonged; Torsade de Pointes;
<b>Endocrine disorders*</b>		
	Uncommon	Amenorrhoea, Hyperprolactinaemia,
	Rare	Galactorrhoea
	Not known	Gynaecomastia
<b>Gastrointestinal disorders</b>		
	Common	Diarrhoea
<b>General disorders and administration site conditions</b>		
	Common	Asthenia



<b>Immune system disorders</b>		
	Uncommon	Hypersensitivity
	Not known	Anaphylactic reaction (including anaphylactic shock particularly with intravenous formulation)
<b>Nervous system disorders</b>		
	Very common	Somnolence
	Common	Extrapyramidal disorders (particularly in children and young adults and/or when the recommended dose is exceeded, even following administration of a single dose of the drug) (see section 4.4), Parkinsonism, Akathisia
	Uncommon	Dystonia, Dyskinesia, Depressed level of consciousness
	Rare	Convulsion especially in epileptic patients
	Not known	Tardive dyskinesia which may be persistent, during or after prolonged treatment, particularly in elderly patients (see section 4.4), Neuroleptic malignant syndrome (see section 4.4)
<b>Psychiatric disorders</b>		
	Common	Depression
	Uncommon	Hallucination
	Rare	Confusional state
<b>Vascular disorder</b>		
	Common:	Hypotension, particularly with intravenous formulation
	Not known	Shock, syncope after injectable use Acute hypertension in patients with pheochromocytoma (see section 4.3)

\* Endocrine disorders during prolonged treatment in relation with hyperprolactinaemia (amenorrhoea, galactorrhoea, gynaecomastia).

The following reactions, sometimes associated, occur more frequently when high doses are used:

- Extrapyramidal symptoms: acute dystonia and dyskinesia, parkinsonian syndrome, akathisia, even following administration of a single dose of the medicinal product, particularly in children and young adults (see section 4.4).
- Drowsiness, decreased level of consciousness, confusion, hallucination.

#### **4.9 Overdose**

##### **All routes of administration**

##### Symptoms

Extrapyramidal disorders, drowsiness, decreased level of consciousness, confusion, hallucination, and cardio-respiratory arrest may occur.

##### Management

In case of extrapyramidal symptoms related or not to overdose, the treatment is only symptomatic (benzodiazepines in children and/or anticholinergic anti-parkinsonian medicinal products in adults).

A symptomatic treatment and a continuous monitoring of the cardiovascular and respiratory functions should be carried out according to clinical status.

#### **5.2 Pharmacokinetic properties**

### All routes of administration

#### Renal impairment

The clearance of metoclopramide is reduced by up to 70% in patients with severe renal impairment, while the plasma elimination half-life is increased (approximately 10 hours for a creatinine clearance of 10-50 mL/minute and 15 hours for a creatinine clearance <10 mL/minute).

#### Hepatic impairment

In patients with cirrhosis of the liver, accumulation of metoclopramide has been observed, associated with a 50% reduction in plasma clearance.

## Package Leaflet

### 1. What Tradename is and what it is used for

Tradename is an antiemetic. It contains a medicine called "metoclopramide". It works on a part of your brain that prevents you from feeling sick (nausea) or being sick (vomiting).

#### Parenteral route/IM-IV

##### Adult population

{Tradename} is used in adults:

- to prevent nausea and vomiting that may occur after surgery
- to treat nausea and vomiting including nausea and vomiting which may occur with a migraine
- to prevent nausea and vomiting caused by radiotherapy

##### Paediatric population

{Tradename} is used in children (aged 1-18 years) only if other treatment does not work or cannot be used:

- to prevent delayed nausea and vomiting that may occur after chemotherapy
- to treat nausea and vomiting that has occurred after surgery

#### Oral route

##### Adult population

{Tradename} is used in adults:

- to prevent delayed nausea and vomiting that may occur after chemotherapy
- to prevent nausea and vomiting caused by radiotherapy
- to treat nausea and vomiting including nausea and vomiting which may occur with a migraine. Metoclopramide can be taken with oral painkillers in case of migraine to help painkillers work more effectively.

##### Paediatric population

{Tradename} is indicated in children (aged 1-18 years) if other treatment does not work or cannot be used to prevent delayed nausea and vomiting that may occur after chemotherapy

#### Rectal route

##### Adult population

{Tradename} is indicated in adults:

- to prevent delayed nausea and vomiting that may occur after chemotherapy
- to prevent nausea and vomiting caused by radiotherapy

### 2. What you need to know before you are given {Tradename}

#### **Do not take {Tradename} if:**

##### For all formulations

- you are allergic to metoclopramide or any of the other ingredients of this medicine (listed in section 6).
- you have bleeding, obstruction or a tear in your stomach or gut.
- you have or may have a rare tumour of the adrenal gland, which sits near the kidney (pheochromocytoma).
- you have ever had involuntary muscle spasms (tardive dyskinesia), when you have been treated with a medicine.
- you have epilepsy
- you have Parkinson's disease

- you are taking levodopa (a medicine for Parkinson's disease) or dopaminergic agonists (see below "Other medicines and Tradename")
- you have ever had an abnormal blood pigment levels (methaemoglobinemia) or NADH cytochrome-b5 deficiency

Do not give {Tradename} to a child less than 1 year of age (see below "Children and adolescents").

#### For rectal formulation

- you have recently experienced inflammation and/or bleeding from your back passage (anus/rectum)
- you are below 18 years of age.

Do not take {Tradename} if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before you take Tradename.

### Warnings and precautions

#### For all routes of administration

Talk to your doctor, pharmacist or nurse before taking {Tradename} if:

- you have a history of abnormal heart beats (QT interval prolongation) or any other heart problems
- you have problems with the levels of salts in your blood, such as potassium, sodium and magnesium.
- you are using other medicines known to affect the way your heart beats
- you have any neurological (brain) problems
- you have liver or kidney problems. The dose may be reduced (see section 3).

Your doctor may perform blood tests to check your blood pigment levels. In cases of abnormal levels (methaemoglobinemia), the treatment should be immediately and permanently stopped.

#### For immediate release oral formulations

You must wait at least 6 hours between each metoclopramide dose, even in case of vomiting and rejection of the dose, in order to avoid overdose.

#### For 15mg prolonged release oral formulations

You must wait at least 12 hours between each metoclopramide dose, even in case of vomiting and rejection of the dose, in order to avoid overdose.

#### For 30mg prolonged release oral formulations

You must wait at least 24 hours between each metoclopramide dose, even in case of vomiting and rejection of the dose, in order to avoid overdose.

Do not exceed 3-month treatment because of the risk of involuntary muscle spasms.

### Children and adolescents

#### For all formulations

Uncontrollable movements (extrapyramidal disorders) may occur in children and young adults. This medicine must not be used in children below 1 year of age because of the increased risk of the uncontrollable movements (see above "Do not take {Tradename} if").

### Other medicines and {Tradename}

#### For all routes of administration

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. This is because some medicines can affect the way {Tradename} works or {Tradename} can affect how other medicines work. These medicines include the following:

- levodopa or other medicines used to treat Parkinson's disease (see above "Do not take {Tradename} if")
- anticholinergics (medicines used to relieve stomach cramps or spasms)
- morphine derivatives (medicines used to treat severe pain)
- sedative medicines
- any medicines used to treat mental health problems
- digoxin (medicine used to treat heart failure)
- cyclosporine (medicine used to treat certain problems with the immune system)
- mivacurium and suxamethonium (medicines used to relax muscles)

- fluoxetine and paroxetine (medicine used to treat depression)

**{ Tradename } with alcohol**

For all routes of administration

Alcohol should not be consumed during treatment with metoclopramide because it increases the sedative effect of { Tradename }.

**Pregnancy, breast-feeding**

For all routes of administration

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before being given this medicine. If necessary, { Tradename } may be taken during pregnancy. Your doctor will decide whether or not you should be given this medicine.

{ Tradename } is not recommended if you are breast-feeding because metoclopramide passes into breast milk and may affect your baby.

**Driving and using machines**

For all routes of administration

You may feel drowsy, dizzy or have uncontrollable twitching, jerking or writhing movements and unusual muscle tone causing distortion of the body after taking { Tradename }. This may affect your vision and also interfere with your ability to drive and use machines.

**Additional statements related to excipients**

[To be completed nationally, if necessary]

**3. How to take { Tradename }**

**Parenteral route**

The medicine will normally be given to you by a doctor or a nurse. It will be given as a slow injection into a vein (over at least 3 minutes) or by injection into a muscle.

In adults patients

For the treatment of nausea and vomiting including nausea and vomiting which may occur with a migraine and for the prevention of nausea and vomiting caused by radiotherapy: the recommended single dose is 10 mg, repeated up to 3 times daily.

The maximum recommended dose per day is 30 mg or 0.5 mg/kg body weight.

For the prevention of nausea and vomiting that may occur after surgery prevention: a single dose of 10mg is recommended.

All indications (paediatric patients aged 1-18 years)

The recommended dose is 0.1 to 0.15 mg/kg body weight, repeated up to 3 times daily, given by slow injection into a vein.

The maximum dose in 24 hours is 0.5 mg/kg body weight.

*Dosing table*

Age	Body Weight	Dose	Frequency
1-3 years	10-14 kg	1 mg	Up to 3 times daily
3-5 years	15-19 kg	2 mg	Up to 3 times daily
5-9 years	20-29 kg	2.5 mg	Up to 3 times daily
9-18 years	30-60 kg	5 mg	Up to 3 times daily

15-18 years	Over 60kg	10 mg	Up to 3 times daily
-------------	-----------	-------	---------------------

The treatment should not exceed 48 hours for treatment of nausea and vomiting that has occurred after surgery.

The treatment should not exceed 5 days for prevention of delayed nausea and vomiting that may occur after chemotherapy.

#### Oral route

##### All indications (adult patients)

##### For immediate release preparations

The recommended single dose is 10 mg, repeated up to three times daily.

##### For prolonged release preparations

##### 15mg strength

The recommended single dose is 15 mg, repeated up to twice daily.

##### 30mg strength

The recommended dose is 30mg once daily.

The maximum recommended dose per day is 30 mg or 0.5 mg/kg body weight.

The maximum recommended treatment duration is 5 days.

##### To prevent delayed nausea and vomiting that may occur after chemotherapy (children aged 1-18 years)

The recommended dose is 0.1 to 0.15 mg/kg body weight, repeated up to 3 times daily, taken by mouth (oral route).

The maximum dose in 24 hours is 0.5 mg/kg body weight.

#### Dosing table

Age	Body Weight	Dose	Frequency
1-3 years	10-14 kg	1 mg	Up to 3 times daily
3-5 years	15-19 kg	2 mg	Up to 3 times daily
5-9 years	20-29 kg	2.5 mg	Up to 3 times daily
9-18 years	30-60 kg	5 mg	Up to 3 times daily
15-18 years	Over 60kg	10 mg	Up to 3 times daily

#### Device / instruction for use

You should not take this medicine for more than 5 days to prevent delayed nausea and vomiting that may occur after chemotherapy.

##### For tablets/capsules/granules

*Appropriate additional information regarding posologies adaptation should be implemented in the SmPC depending on the strength of the formulations*

##### For formulations which cannot be used to administer a 5mg dose

{Tradename} is not suitable for use in children weighing less than 61 kg.

Other pharmaceutical forms/strengths may be more appropriate for administration.

##### For formulations which can be used to administer a 5mg dose

{Tradename} is not suitable for use in children weighing less than 30 kg.

Other pharmaceutical forms/strengths may be more appropriate for administration.

## Rectal route

### All indications (adult patients)

The recommended single dose is 10 mg, repeated up to 3 times daily.  
The maximum recommended dose per day is 30 mg or 0.5mg/kg body weight.

The maximum recommended treatment duration is 5 days.

## All routes of administration

### Method of administration

#### For immediate release oral formulations

You must wait at least 6 hours between each metoclopramide dose, even in case of vomiting and rejection of the dose, in order to avoid overdose.

#### For 15mg prolonged release oral formulations

You must wait at least 12 hours between each metoclopramide dose, even in case of vomiting and rejection of the dose, in order to avoid overdose.

#### For 30mg prolonged release oral formulations

You must wait at least 24 hours between each metoclopramide dose, even in case of vomiting and rejection of the dose, in order to avoid overdose.

## All routes of administration

### Older people

The dose may need to be reduced depending on kidney problems, liver problems and overall health.

*Appropriate additional information regarding posologies adaptation should be implemented in the PIL depending on the formulations:*

<Other pharmaceutical forms/strengths may be more appropriate for administration>

<This formulation is not suitable for administration>

### Adults with kidney problems

Talk to your doctor if you have kidney problems. The dose should be reduced if you have moderate or severe kidney problems.

*Appropriate additional information regarding posologies adaptation should be implemented in the PIL depending on the formulations:*

<Other pharmaceutical forms/strengths may be more appropriate for administration>

<This formulation is not suitable for administration>

### Adults with liver problems

Talk to your doctor if you have liver problems. The dose should be reduced if you have severe liver problems.

*Appropriate additional information regarding posologies adaptation should be implemented in the PIL depending on the formulations:*

<Other pharmaceutical forms/strengths may be more appropriate for administration>

<This formulation is not suitable for administration>

### Children and adolescents

Metoclopramide must not be used in children aged less than 1 year (see section 2).

## For all routes of administration

### If you take more {Tradename} than you should

Contact your doctor or pharmacist straight away. You may experience uncontrollable movements (extrapyramidal disorders), feel drowsy, have some troubles of consciousness, be confused, have hallucination and heart problems. Your doctor may prescribe you a treatment for these signs if necessary.

#### For all routes of administration

#### **If you forget to take {Tradename}**

Do not take a double dose to make up for a forgotten dose.

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

#### **4. Possible side effects**

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

#### For all formulations

Stop the treatment and talk straight away to your doctor, pharmacist or nurse if you experience one of the following signs while having this medicine:

- uncontrollable movements (often involving head or neck). These may occur in children or young adults and particularly when high doses are used. These signs usually occur at the beginning of treatment and may even occur after one single administration. These movements will stop when treated appropriately.
- high fever, high blood pressure, convulsions, sweating, production of saliva. These may be signs of a condition called neuroleptic malignant syndrome.
- Itching or skin rashes, swelling of the face, lips or throat, difficulty in breathing. These may be signs of an allergic reaction, which may be severe.

#### **Very common** (may affect more than 1 in 10 people)

- feeling drowsy.

#### **Common** (may affect up to 1 in 10 people)

- depression
- uncontrollable movements such as tics, shaking, twisting movements or muscle contracture (stiffness, rigidity)
- symptoms similar to Parkinson disease (rigidity, tremor)
- feel restless
- blood pressure decrease (particularly with intravenous route)
- diarrhoea
- feeling weak.

#### **Uncommon** (may affect up to 1 in 100 people)

- raised levels of a hormone called prolactin in the blood which may cause: milk production in men, and women who are not breast-feeding
- irregular periods
- hallucination
- decreased level of consciousness
- slow heartbeat (particularly with intravenous route)
- allergy

#### **Rare** (may affect up to 1 in 1,000 people)

- confusional state
- convulsion (especially in patients with epilepsy).

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

- abnormal blood pigment levels: which may change the colour of your skin
- abnormal development of breasts (gynaecomastia)
- involuntary muscle spasms after prolonged use, particularly in elderly patients
- high fever, high blood pressure, convulsions, sweating, production of saliva. These may be signs of a condition called neuroleptic malignant syndrome
- changes in heart beat, which may be shown on an ECG test



- cardiac arrest (particularly with injection route)
- shock (severe decrease of heart pressure) (particularly with injection route)
- fainting (particularly with intravenous route)
- allergic reaction which may be severe (particularly with intravenous route)
- very high blood pressure.

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any side effects not listed in this leaflet.