VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Metoclopramide is indicated for the treatment of nausea and vomiting, for example in connection with migraine, gastro-oesophageal reflux, for conditions of impaired motility of the gastrointestinal tract (meteorism, hiccups, gastric retention, intestinal atony) and for X-ray examination of the small intestine.

The listed indications occur commonly and without any particular pattern and not specific to any particular patient population.

VI.2.2 Summary of treatment benefits

Taking into account the published information on the use and dosage of metoclopramide, it can be concluded that the use of this medicinal product in the proposed indication and according to the dosage recommendations given in the SmPC is fully justified. Safety and efficacy of metoclopramide in treatment of the proposed indication is sufficiently evident from its approved clinical use.

VI.2.3 Unknowns relating to treatment benefits

None.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
• Serious high blood pressure events (Severe hypertensive events)	Confirmed or suspected pheochromocytoma, due to the risk of severe hypertension episodes is a known contraindication and patients with risk of severe hypertensive events should therefore not use Metoclopramide Orifarm.	There is no specific measure to prevent the risk. The risk is mentioned as a contraindication in the summary of Product Characteristics and patient information leaflet. The risk can be reduced by not allowing the product to be used in patients who are at risk of angle-closure glaucoma.
• Increased uncontrollable movements (Increased extrapyramidal reactions)	There is an increased risk of extrapyramidal reactions in children less than 1 year of age and Metoclopramide Orifarm should therefore not be used in this population. 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). Extrapyramidal disorders are listed as a common undesirable effect in section 4.8 of the SmPC.	There is no specific measure to prevent the risk. The risk is mentioned as a contraindication in the summary of Product Characteristics and patient information leaflet. The risk can be reduced by not allowing the product to be used in patients under 1 year. The risk is mentioned as a warning in the summary of Product Characteristics and patient information leaflet.
• Hypersensitivity reactions	Hypersensitivity to the active substance or to any of the excipients is a known contraindication and patients with this risk should therefore	There is no specific measure to prevent the risk. The risk is mentioned as a contraindication in the summary of Product

Risk	What is known	Preventability
	not use Metoclopramide Orifarm. Common undesirable effect in section 4.8: Hypersensitivity is a uncommon undesirable effect listed in section 4.8 of the SmPC.	Characteristics and patient information leaflet. The risk can be reduced by not allowing the product to be used in patients who are at risk of hypersensitivity reactions.
• Tardive dyskinesia (Involuntary muscle spasms)	History of neuroleptic or metoclopramide-induced tardive dyskinesia is a known contraindication and patients with this risk should therefore not use Metoclopramide Orifarm. 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. Tardive dyskinesia which may be persistent, during or after prolonged treatment, particularly in elderly patients (see section 4.4) is an undesirable effect listed in section 4.8 of the SmPC.	There is no specific measure to prevent the risk. The risk is mentioned as a contraindication in the summary of Product Characteristics and patient information leaflet. The risk can be reduced by not allowing the product to be used in patients who are at risk of tardive dyskinesia.
• Worsening of existing gastrointestinal disorders.	Gastrointestinal haemorrhage, mechanical obstruction or gastro-intestinal perforation for which the stimulation of gastrointestinal motility constitutes a risk is a known contraindication and patients with this risk should therefore not use Metoclopramide Orifarm.	There is no specific measure to prevent the risk. The risk is mentioned as a contraindication in the summary of Product Characteristics and patient information leaflet. The risk can be reduced by not allowing the product to be used in patients who has existing gastrointestinal disorders.
• Decreased effect when used concomitantly with levodopa, anticholinergic agents and/or morphine	Combination with levodopa or dopaminergic agonists is a known contraindication and patients who receive levodopa	There is no specific measure to prevent the risk. The risk is mentioned as a contraindication in the

Risk	What is known	Preventability
derivatives.	should therefore not use Metoclopramide Orifarm. Levodopa or dopaminergic agonists and metoclopramide have a mutual antagonism. Anticholinergics and morphine derivatives may have both a mutual antagonism with metoclopramide on the digestive tract motility.	summary of Product Characteristics and patient information leaflet. The risk can be reduced by not allowing the product to be used in patients who receive levodopa. Caution should be exercised when metoclopramide is co-administered with anticholinergics and/or morphine derivatives.
• Hyperprolactinemia (Raised levels of a hormone called prolactin in the blood)	Endocrine disorders during prolonged treatment in relation with hyperprolactinaemia (amenorrhoea, galactorrhoea, gynaecomastia) can occur as an undesirable effect when treated with metoclopramide.	There is no specific measure to prevent the risk. The risk is mentioned as an undesirable effect in the summary of Product Characteristics and patient information leaflet.
• Methaemoglobinaemia (Abnormal blood pigment level)	Known history of methaemoglobinaemia with metoclopramide or of NADH cytochrome-b5 deficiency is a known contraindication and patients with this risk should therefore not use Metoclopramide Orifarm. Methaemoglobinaemia, which could be related to NADH cytochrome b5 reductase deficiency, particularly in neonates can occur as an undesirable effect when treated with metoclopramide.	There is no specific measure to prevent the risk. The risk is mentioned as a warning in the summary of Product Characteristics and patient information leaflet. The risk can be reduced by not allowing the product to be used in patients with known history of methaemoglobinaemia with metoclopramide or of NADH cytochrome-b5 deficiency.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
• Seizure risk in epileptics	Epilepsy (increased crises frequency and intensity) is a known contraindication and patients with this risk should therefore not use Metoclopramide Orifarm. Convulsion especially in epileptic patients can occur as an undesirable effect when treated with metoclopramide.
• Neuroleptic malignant syndrome (Life-threatening neurological disorder)	Neuroleptic malignant syndrome has been reported with metoclopramide in combination with neuroleptics as well as with metoclopramide monotherapy. Metoclopramide should be discontinued immediately in the event of symptoms of neuroleptic malignant syndrome and appropriate treatment

Risk	What is known (Including reason why it is considered a potential risk)
	should be initiated. Neuroleptic malignant syndrome can occur as an undesirable effect when treated with metoclopramide.

Missing information

None.

VI.2.5 Summary of additional risk minimisation measures by safety concern

Routine Pharmacovigilance is used for the safety concerns, which are all listed in the SmPC.

There are no specific risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Metoclopramide Orifarm can be found in Annex 2.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

None.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable as this is the initial risk management plan.