PATHWAYS AND GUIDELINES DEVELOPMENT SUBGROUP

Shared Care Protocol

Shared Care Guideline for: **Domperidone for Paediatric Gastro-oesophageal Reflux Disease (GORD)**		Reference Number
Version: 2.0	**Replaces: 1.1**	**Issue date:** dd/mm/yyyy
Author(s)/Originator(s): (please state author name and department) Chris Paget, Senior Specialist Paediatric Pharmacist, Royal Manchester Children's Hospital, CMFT		**To be read in conjunction with the following documents:** Current Summary of Product characteristics (http://www.medicines.org.uk) BNF
Date approved by Pathways and Guidelines Development Subgroup: *dd/mm/yy*	**Date approved by Greater Manchester Medicines Management Group:** *dd/mm/yyyy*	
Date approved by Commissioners: *dd/mm/yyyy*	**Review Date:** *dd/mm/yyyy*	

Please complete all sections

1. Name of Drug, Brand Name, Form and Strength	Domperidone 1mg/mL oral suspension, 10mg tablets
2. Licensed Indications	Domperidone is indicated for the relief of the symptoms of nausea and vomiting. In the paediatric pateint group it is used as a pro-kinetic agent for severe GORD (unlicensed use).
3. Criteria for shared care	Prescribing responsibility will only be transferred when ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated and established by the secondary care specialist. ▪ The patient's initial reaction to and progress on the drug is satisfactory. ▪ The GP has agreed in writing in each individual case that shared care is appropriate. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements.
4. Patients excluded from shared care	• Unstable disease state • >18 years old

5. Therapeutic use & background	In the paediatric population domperidone is used as a pro-kinetic agent for severe GORD unresponsive to Gaviscon and optimised dose of either proton pump inhibitor or H2 antagonist (this is an unlicensed use). However, the evidence for the long-term efficacy of motility stimulants in the management of GORD in children is limited and unconvincing. Studies have shown oral domperidone to increase lower oesophaegeal pressure, improve antroduodenal motility and accelerate gastric emptying. In May 2014 the MHRA released information regarding domperidone and risk of cardiac side effects – this included restricted indications, new contraindications, and reduced dose and duration of use. Dosing of domperidone, as initiated by specialist, should be in line with the new lower dosing recommendations (see dosing in section 7). See: https://www.gov.uk/drug-safety-update/domperidone-risks-of-cardiac-side-effects Treatment with domperidone will be initiated by a specialist in cases where benefit of treatment outweighs risk and initial steps in the management of GORD have been optimised as per NICE guidance, Gastro-oesophageal reflux disease in children and young people: diagnosis and management. Following the MHRA alert additional monitoring will be carried out for patients commenced on domperidone (see sections 10 and 11) NICE NG1 January 2015 - Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people recommends: "Do not offer metoclopramide, domperidone or erythromycin to treat GOR or GORD without seeking specialist advice and taking into account their potential to cause adverse events." The BNFC domperidone entry was also updated in October 2014 to read: "Domperidone for the treatment of gastro-oesophageal reflux disease (GORD)" The MHRA/CHM recently restricted the use of domperidone because it is associated with a small increased risk of serious cardiac side-effects - see section 4.6. As a result, the unlicensed use of domperidone for the treatment of GORD has been reviewed in BNFC. Although evidence on its long-term efficacy in the management of GORD is unconvincing, the Paediatric Formulary Committee recognises that domperidone may be used when other interventions have been tried. If there are any cardiac concerns, an ECG should be obtained before and during treatment. Contra-indications to the use of domperidone include cardiac disease, predisposition to cardiac conduction disorders, concomitant use of other drugs that prolong the QT interval, and concomitant use of potent CYP3A4 inhibitors. Children and their carers should be told how to recognise signs of arrhythmia and advised to seek medical attention if symptoms such as palpitation or syncope develop. The dose of domperidone for the treatment of GORD has also been revised, and treatment should be interrupted occasionally to assess recurrence."
6. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	• Known hypersensitivity to domperidone or any of the excipients • If stimulation of the gastric motility could be harmful, e.g. in patients with gastro-intestinal haemorrhage, mechanical obstruction or perforation. • Moderate or severe hepatic impairment • Known existing prolongation of cardiac conduction intervals, particularly QTc • Patients with significant electrolyte disturbances or underlying cardiac diseases such as congestive heart failure • Prolactin-releasing pituitary tumour (prolactinoma) • Co-administration with QT-prolonging drugs • Co-administration with potent CYP3A4 inhibitors (regardless of their QT prolonging effects)

7. Prescribing in pregnancy and lactation	This drug can be prescribed in the pregnant patient, however, only to be prescribed by specialist in cases where benefit of treatment is considered to outweigh risk. This would be initiated by specialist and is not covered under the scope of the shared care arrangement.	
8. Dosage regimen for continuing care	***Route of administration***	Oral, NG
	Preparations available: 1mg/mL oral suspension 10mg tablets	
	Please prescribe: Child 1 month to 18 years: 250 micrograms/kg (max 10 mg) TDS. If response inadequate, dose can be increased if necessary up to 400 micrograms/kg (max 20 mg) TDS. Any dose adjustments should be directed by the specialist. (This dose is as per BNF-C) To continue if therapeutic benefit is seen until stopped following specialist review.	
	Is titration required	**No**
	Adjunctive treatment regime: Alginate e.g. Gaviscon Proton pump inhibitor or H_2 antagonist	
	Conditions requiring dose reduction: Domperidone is contraindicated in patients with moderate or severe hepatic impairment. Since the elimination half-life of domperidone is prolonged in severe renal impairment, on repeated administration, the dosing frequency of domperidone should be reduced to once or twice daily depending on the severity of the impairment, and the dose may need to be reduced. Such patients on prolonged therapy should be reviewed regularly	
	Usual response time : Within first few days of commencing treatment	
	Duration of treatment: On-going if response seen	
	Treatment to be terminated by: Specialist	
	NB. All dose adjustments will be the responsibility of the initiating specialist care unless directions have been specified in the medical letter to the GP.	

9.Drug Interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics

Concomitant use of the following substances is contraindicated:

QTc prolonging medicinal products
- anti-arrhythmics class IA (e.g., disopyramide, hydroquinidine, quinidine)
- anti-arrhythmics class III (e.g., amiodarone, dofetilide, dronedarone, ibutilide, sotalol)
- certain anti-psychotics (e.g., haloperidol, pimozide, sertindole)
- certain anti-depressants (e.g., citalopram, escitalopram)
- certain antibiotics (e.g. , erythromycin, levofloxacin, moxifloxacin, spiramycin)
- certain antifungal agents (e.g., 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)

Potent CYP3A4 inhibitors (**regardless of their QT prolonging effects**), i.e.:
- protease inhibitors
- systemic azole antifungals
- some macrolides (erythromycin, clarithromycin, telithromycin)

Concomitant use of the following substances is not recommended:

- Moderate CYP3A4 inhibitors i.e. diltiazem, verapamil and some macrolides.
- Caution with bradycardia and hypokalaemia-inducing drugs, as well as with the following macrolides involved in QT-interval prolongation: azithromycin and roxithromycin (clarithromycin is contra-indicated as it is a potent CYP3A4 inhibitor).

10. Adverse drug reactions

For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF

Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

Adverse event System – symptom/sign	**Action to be taken** Include whether drug should be stopped prior to contacting secondary care specialist	**By whom**
Gastrointestinal: Dry mouth Diarrhoea	Stop if pateint unable to tolerate side-effets	GP-inform specialist
Cardiac disorders Ventricular arrhythmias Sudden cardiac death QTc prolongation	Stop immediately if symptoms suggestive of cardiac arrhythmias	GP-refer to specialist for review
Skin and subcutaneous tissue disorders (uncommon): Rash	If skin disorder considered to be due to domperidone stop treatment	GP-inform specialist

	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.	Stop treatment	GP-inform specialist

The patient should be advised to report any of the following signs or symptoms to their GP without delay:

Any signs/symptoms suggestive of arrhythmias.

Other important co morbidities (e.g. Chickenpox exposure). Include advice on management and prevention and who will be responsible for this in each case:
No specific advice.

Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the "Yellow Card" scheme.

11.Baseline investigations to be arranged by initiating specialist

List of investigations / monitoring undertaken by secondary care

ECG prior to commencing treatment
ECG within one month of starting treatment

12. Ongoing monitoring requirements to be arranged by initiating specialist

Is monitoring required?	**Yes - done by specialist**			
Monitoring	**Frequency**	**Results**	**Action**	**By whom**
ECG	Annually	Normal Abnormal	No Action Stop domperidone	Specialist

13. Pharmaceutical aspects

e.g. special storage requirements, washout periods Or where there are "no special considerations"
Oral liquid formulations of domperidone should only be given via appropriately designed, graduated measuring devices (e.g. oral syringes for children and cups for adults and adolescents) to ensure dose accuracy.

14. Responsibilities of initiating specialist

- Initiate treatment and prescribe until dose is stable.
- Patient has had interventions including advice regarding reducing feeds to smaller and more frequent amounts, has been tried with thickeners, alginates and H2 antagonists or PPIs and failed to show a response before domperidone is being considered – as per NICE NG1 guidance.
- Undertake baseline monitoring.
- Dose adjustments.
- Monitor patient's initial reaction to and progress on the drug.
- The consultant team will write formally to the GP to request shared care using the GMMMG agreed process. Failure to supply all the required information will result in the refusal of the request until all information has been supplied
- Patients will only be transferred to the GP once the GP has agreed.
- Ensure that the patient has an adequate supply of medication until GP supply can be arranged.
- Continue to monitor and supervise the patient according to this protocol, while the

	patient remains on this drug, and agree to review the patient promptly if contacted by the GP • Provide GP with diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. • Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient or inform GP if the patient does not attend appointment. • Provide GP with advice on when to stop this drug. • Act upon communication from the GP in a timely manner. • Provide patient with relevant drug information to enable Informed consent to therapy. • Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action. • Provide patient with relevant drug information to enable understanding of the role of monitoring. • Be available to provide patient specific advice and support to GPs as necessary.
15. Responsibilities of the GP	• Continue treatment as directed by the specialist. • Act upon communication from the specialist in a timely manner. • GPs should reply to request for shared care to either accept or decline within 14 days. A form is available on the GMMMG website to facilitate this, if you so wish. • Ensure no drug interactions with concomitant medicines. • To monitor and prescribe in collaboration with the specialist according to this protocol. • Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. • If the GP does not feel it is appropriate to take on the prescribing then the prescribing responsibilities will remain with the specialist. The GP should indicate the reason for declining. • Enter a READ code (e.g. 8BM5.00) on to the patient record to highlight the existence of shared care for the patient.
16. Responsibilities of the patient	• To take medication as directed by the prescriber, or to contact the GP if not taking medication • To attend hospital and GP clinic appointments • Failure to attend will result in medication being stopped (on specialist advice). • To report adverse effects to their Specialist or GP.

17.Additional Responsibilities e.g. Failure of patient to attend for monitoring, Intolerance of drugs, Monitoring parameters outside acceptable range, Treatment failure, Communication failure	**List any special considerations**	**Action required**	**By whom**	**Date**
	n/a			

18. Supporting documentation	The SCG must be accompanied by a patient information leaflet. Available at: http://www.medicinesforchildren.org.uk/domperidone-gastro-oesophageal-reflux
19. Patient monitoring booklet	N/A
20. Contact details	See Appendix 1

Appendix 1 – Local Contact Details

Lead author contact information	**Name:** Chris Paget, Senior Specialist Paediatric Pharmacist, Royal Manchester Children's Hospital, CMFT
	Email: chris.paget@cmft.nhs.uk
	Contact number: *0161 701 4331 bleep 9045*
	Organisation: *Central Manchester Foundation Trust*

Commissioner contact information	**Name:** *[insert text here]*
	Email: *[insert text here]*
	Contact number: *[insert text here]*
	Organisation: *[insert text here]*

Secondary care contact information	**If stopping medication or needing advice please contact:**
	Dr
	Contact number:
	Fax:*[insert text here]*
	Hospital: *[insert text here]*

Shared Care Guideline Summary:
DOMPERIDONE for the treatment of *PAEDIATRIC GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)*

Drug	Domperidone 1mg/mL oral suspension, 10 mg tablets
Indication	In paediatrics domperidone is used as a prokinetic agent for severe GORD (unlicensed use).
Overview	In the paediatric population domperidone is used as a pro-kinetic agent for severe GORD unresponsive to Gaviscon and optimised dose of either proton pump inhibitor or H2 antagonist (this is an unlicensed use). However, the evidence for the long-term efficacy of motility stimulants in the management of GORD in children is limited and unconvincing.
Specialist's Responsibilities	**Initial investigations:** Assessment of the patient and diagnosis of severe GORD unresponsive to previous interventions including advice regarding reducing feeds to smaller and more frequent amounts, has been tried with thickeners, alginates and H2 antagonists or PPIs and failed to show a response – as per NICE NG1 guidance. Discuss benefits and side-effects of treatment with the patient/carer. Prior to commencing therapy the specialist team will check an ECG. **Initial regimen:** Child 1 month to 18 years: 250 micrograms/kg (max 10 mg) TDS. If response inadequate, dose can be increased if necessary up to 400 micrograms/kg (max 20 mg) TDS. Any dose adjustments should be directed by the specialist. To continue if therapeutic benefit is seen until stopped following specialist review. **Clinical monitoring:** The specialist team will undertake monitoring of the patient. **Safety monitoring:** The specialist team will arrange for an ECG within one month of starting treatment and on an annual basis thereafter. Monitoring for response and adverse drug reactions (ADRs) during initiation period. Evaluating ADRs raised by the GP and evaluating any concerns arising from reviews undertaken by GP. **Prescribing details:** Specialist initiated. Transferred to GP once stabilised. The consultant and hospital are responsible for at least the first months of treatment and monitoring. To stop the drug or provide GP with advice on when to stop this drug. **Documentation:** The consultant team will write formally to the GP to request shared care using the GMMMG agreed process. Patients will only be transferred to the GP once the GP has agreed. Provide GP with diagnosis, relevant clinical information, treatment plan, duration of treatment with 14 days of seeing the patient or inform GP if the patient does not attend appointment.
GP's Responsibilities	**Maintenance prescription:** Prescribe domperidone in accordance with the specialist's recommendations. Child 1 month to 18 years: 250 micrograms/kg (max 10 mg) TDS. If response inadequate, dose can be increased if necessary up to 400 micrograms/kg (max 20 mg) TDS. Any dose adjustments should be directed by the specialist. To continue if therapeutic benefit is seen until stopped following specialist review. **Clinical monitoring:** To report to and seek advice from the specialist on any aspect of patient care which is of concern to the GP and may affect treatment. **Safety monitoring:** Monitor patient for side-effects.

	Duration of treatment: Stop treatment on advice of specialist. **Documentation:** GPs should reply to request for shared care to either accept or decline within 14 days. A form is available on the GMMMG website to facilitate this, if you so wish.
Adverse Events	See table below
Contra-indications Cautions Drug Interactions	Please refer to the BNF and/or SPC for information.
Other Information	Patient information leaflet. Available at: http://www.medicinesforchildren.org.uk/domperidone-gastro-oesophageal-reflux
Contact Details	**Name:** *[insert text here]* **Address:** *[insert text here]* **Telephone:** *[insert text here]*

Adverse events	Action
Gastrointestinal: Dry mouth Diarrhoea	Stop if pateint unable to tolerate side-effects and inform specialist.
Cardiac disorders Ventricular arrhythmias Sudden cardiac death QTc prolongation	Stop immediately if symptoms suggestive of cardiac arrhythmias and refer to specialist for review.
Skin and subcutaneous tissue disorders (uncommon): Rash	If skin disorder considered to be due to domperidone stop treatment and inform specialist.
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.	Stop treatment and inform specialist.