East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Evidence review for Surrey & North West Sussex Area Prescribing Committee (APC)

Medicine details[1]	
Name, brand name	Domperidone
Manufacturer	Zentiva (Motilium®) 10mg tablets, also available as a generic. Suppositories available as an unlicensed import.
Proposed indication	Licensed indication: 1. Nausea and Vomiting Off label use: 1. Nausea and vomiting in pregnancy 2. Gastric reflux in neonates and children 3. Gastro-oesophageal reflux disease in adults 4. Dyspepsia in adults 5. Gastroparesis in adults 6. Stimulation of lactation 7. Pre-treatment for patients to be commenced on apomorphine for Parkinson's disease 8. Nausea and vomiting in patients with Parkinson's disease.
Requested by	Update request by SNWS APC: Currently, the SNWS APC has a GREEN traffic light status for domperidone for the licensed indication of nausea and vomiting, RED for use in gastric reflux in neonates and children but no formal traffic light status for other off-label uses. Following the MHRA alert in 2014, the purpose of this review is to: 1. Review the existing traffic light status 2. Assign traffic light status to the other uses of domperidone.

SUMMARY

Clinical Effectiveness

In 2014 the MHRA issued a safety alert concerning the cardiac side effects of domperidone and the licenced use of domperidone was restricted to nausea and vomiting. It was found that the drug was associated with a small increased risk of potentially life-threatening cardiac side-effects.[2]

The other uses of domperidone are therefore considered to be off-label.

<u>Licensed indication:</u>

<u>Nausea & Vomiting</u>

Domperidone is licensed for nausea & vomiting[1]. The MHRA recommended that domperidone can continue to be used as a treatment option in nausea and vomiting at the lowest effective dose with a maximum treatment duration of one week and a maximum dose of 30mg/day.

It was contraindicated in people with conditions where cardiac conduction is, or could be, impaired, with underlying cardiac diseases such as congestive heart failure, receiving other

medications known to prolong QT interval or potent CYP3A4 inhibitors or with severe hepatic impairment.

Unlicensed indications:

1. Nausea and vomiting in pregnancy

In pregnancy, domperidone is not a recommended first line choice of anti-emetic for nausea & vomiting due to general safety concerns with its use and because safer options to treat nausea and vomiting are available.[3] The RCOG suggests that domperidone is used second-line if first line agents such as the antihistamines cannot be used.[4]

Treatment duration is restricted to a maximum of one week in all patients[2] which limits its usefulness for nausea and vomiting in pregnancy.

2. Gastric Reflux in neonates and children

NICE undertook an evidence review for the development of their guidelines for gastro-oesophageal reflux disease in children and young people.[5] They concluded that if metoclopramide or domperidone were used then caution should be taken and therefore initiation of treatment should only be offered by healthcare professionals who can make individual assessments on the cardiac risk and potential benefit on a case by case basis. This recommendation remained in the October 2019 update to the guidelines.

3. Gastro-oesophageal reflux disease (GORD) in adults
4. Dyspepsia in adults

The evidence review by the Trent Medicines Information Service (2014) summarised potential options for the off-label use of domperidone in GORD and dyspepsia. It suggested reviews for all patients receiving long-term domperidone should be undertaken with a view to undertaking a trial withdrawal in conjunction with optimising other treatment options for GORD and dyspepsia.[6]

5. Gastroparesis in adults

NICE guidelines for Type 2 diabetes in adults: Management (2015)[7] and NICE guidelines for Type 1 diabetes in adults: Management (2015)[8] state that there is no strong evidence that any available anti-emetic therapy is effective in nausea and vomiting caused by gastroparesis in these patients.

However the strongest evidence is for domperidone but the safety profile must be considered and NICE recommends its use only in exceptional circumstances.

The recommendations on the NHS website in regard to gastroparesis[9] are that domperidone, erythromycin and anti-emetics may improve symptoms but 'the evidence that these medicines relieve the symptoms of gastroparesis is relatively limited and they can cause side effects'.

It states that domperidone should only be taken at the lowest effective dose for the shortest possible time because of the small risk of potentially serious heart-related side effects.

6. Stimulation of lactation

An evidence review of the treatment of inadequate lactation by the UK Medicines Information service (UKMI) in 2016 noted that there are no licensed treatment options in the UK.[10] It concluded that drugs to manage inadequate lactation should only be used where there is objective evidence to support diagnosis and where non-drug methods have failed.

It suggested that as long as the possible cardiac effects are taken into account, domperidone is considered to be the agent of choice for inadequate lactation because of its superior side effect profile, efficacy, and minimal passage into breast milk. The maximum daily dose should not exceed 30mg and treatment duration should not exceed one week.

However, NICE CKS on Breastfeeding problems (Last revised in May 2017) available at: https://cks.nice.org.uk/breastfeeding-problems#!scenario states that:

'If these measures do not improve a true low milk supply and maternal prolactin deficiency is a possible cause, consider referral to an endocrinologist for advice on prescribing a galactogogue drug (such as domperidone, off-label indication) to help improve milk supply.

The recommendation on considering the use of a galactogogue if self-management measures do not help is based on the fact that short-term use of domperidone (a dopamine antagonist, off-label indication) may improve milk supply, as it increases maternal prolactin secretion [Academy of Breastfeeding Medicine, 2011; National Infant Feeding Network, 2014b]. CKS recommends specialist referral before this is started, however, as there is very limited evidence on its effectiveness, and there is no direct correlation between maternal prolactin levels and rates of milk production [Academy of Breastfeeding Medicine, 2011; Amir, 2014; UKMi, 2015].'

7. Pre-treatment for patients to be commenced on apomorphine for Parkinson's Disease

NICE Guidelines for Parkinson's Disease in Adults (2017) does not cover the use of domperidone.[11]

The MHRA safety update 'Apomorphine with domperidone: minimising cardiac side effects' (April 2016) recommends that when using domperidone with apomorphine, to consider the benefits vs risk, check the patients QT interval before and during treatment and use the lowest effective dose.[12]

The APO go® SPC states that domperidone will usually need to be started at least two days before the apomorphine commences.[13]

The shared care document for apomorphine on the PAD includes information on specialist assessment of suitability for domperidone treatment.

8. Nausea and vomiting in patients with Parkinson's Disease

NICE CKS on Parkinson's disease (Last revised in February 2018) guidance available at: https://cks.nice.org.uk/parkinsons-disease#!scenario:1 states that for nausea and vomiting:

'Initially, if nausea or vomiting is mild and related to starting or increasing the dose of levodopa or a dopamine agonist:

- Reassure the person that nausea often settles over time as tolerance to adverse effects occurs.
- Advise the person to take their medication with food.

If nausea or vomiting persists, is severe, or is unrelated to levodopa or dopamine agonist drug treatment:

- Do *not* use metoclopramide or prochlorperazine anti-emetics — can cause or exacerbate parkinsonism.
- Consider prescribing low-dose domperidone, reducing or stopping it when the nausea or vomiting settles.

- Be aware that domperidone has been associated with an increased risk of ventricular tachyarrhythmias and sudden cardiac death.
- Advise the person to seek urgent medical attention if symptoms such as syncope or palpitations occur during treatment with domperidone.
- If domperidone is taken with high doses of apomorphine there is an increased risk of QT prolongation — only consider prescribing concomitantly after assessment of cardiac risk factors and ECG monitoring.
- See the electronic Medicines Compendium (eMC), or the British National Formulary (BNF) for full information on the contraindications and cautions when prescribing domperidone.

- If domperidone is ineffective or not tolerated, seek specialist advice, as one or more of the following options may be recommended:

  - An increase in the proportion of decarboxylase inhibitor to levodopa (for people taking co-careldopa specifically).
  - A slower titration of the anti-parkinsonian drug.
  - A switch to an alternative anti-parkinsonian drug.
  - A switch to an alternative anti-emetic drug.'

Safety

In December 2014 the MHRA issued a drug safety update on the risks of cardiac side effects with domperidone[2] following a European Medicines Authority (EMA) safety review[14] on this topic. The EMA noted increased reports of cardiac side effects particularly in patients over 60 years, taking oral doses of more than 30mg/day or taking interacting medication.

The MHRA recommended new contraindications, a maximum daily doses, a maximum treatment duration of one week and the need to measure doses accurately in children. It concluded that for indications other than nausea and vomiting the benefits did not outweigh the risks and that patients on long term treatment should be reviewed.

In 2004 the Federal Drugs Agency warned that breastfeeding mothers should not use unlicensed domperidone to increase breast milk production due to reports of cardiac side effects.[15]

Domperidone is excreted in human milk and breast-fed infants receive less than 0.1% of the maternal weight-adjusted dose. Occurrence of adverse effects, in particular cardiac effects cannot be excluded after exposure via breast milk.[1]

In pregnancy: One prospective cohort study enrolled 120 first-trimester pregnant women treated with domperidone (10 to 30mg/day) and 212 controls. Exposure was between 2 and 20 weeks gestation (median 5 weeks), with half the patients discontinuing after 5 weeks gestation. Three babies in each group were born with malformations but none in the domperidone group were considered treatment-related, due to the type of malformation and timing/duration of maternal exposure to domperidone. Routine ECG monitoring was not done so asymptomatic electrocardiogram alterations in sensitive patients taking 30mg/day would not have been noted. While this study shows that domperidone did not have major teratogenic effects, the findings need to be confirmed in larger studies, including assessment of maternal and foetal cardiac function.[16]

Patient factors

Transfer of prescribing of domperidone for off-label indications to non-specialists (e.g. General Practitioners) could cause difficulties as the prescriber would need to take clinical responsibility despite the MHRA safety warning which states that for indications other than nausea and vomiting the benefits were not considered to outweigh the cardiac risk.

If primary care practitioners are not prepared to prescribe, this has implications on patients

including difficulties in obtaining supplies which may result in additional hospital visits.

There are additional costs for the CCG in terms of hospital appointments.

Primary care prescribers should be aware that their patient is receiving domperidone and ensure that this is recorded in the patient's notes in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will also ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.

Cost implications

NHS price for generic preparations (Oct 2019):[17] 30x10mg tablets = £0.96
200ml 1mg/ml sugar-free oral suspension = £24.85

Current annual spend (Sep 18 – Aug 19):

	Tablets items	Tablets cost	Liquid items	Liquid cost	Suppository items	Suppository cost
Crawley CCG	861	£1,455	74	£2,957		
East Surrey CCG	899	£1,821	167	£9,201		
Guildford & Waverley CCG	839	£1,416	88	£7,335		
Horsham & Mid Sussex CCG	1079	£2,318	222	£10,817	2	£115
North West Surrey CCG	1250	£2,370	150	£4,728		
Surrey Downs CCG	1066	£2,227	165	£7,534		
Surrey Heath CCG	420	£926	65	£3,325		
TOTAL	**6414**	**£12,537**	**931**	**£45.902**	**2**	**£115**

Total annual spend: £58,555

Relevant guidance / reviews

The following references and their recommendations have been used and quoted in the clinical effectiveness section above:

- Medicines and Healthcare Products Regulatory Agency. Domperidone: risks of cardiac side effects. December 2014.
- UK Medicines Information Service. Medicines Q&A How can nausea and vomiting be treated during pregnancy? September 2014 Revised August 2019.
- Royal College of Obstetricians and Gynaecologists (RCOG). The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum (Green-top Guideline No. 69). 2016.
- National Institute for Health and Care Excellence. NICE guideline NG1. Gastro-oesophageal reflux disease in children and young people: diagnosis and management. January 2015. Updated October 2019.
- Trent Medicines Information Service. Rapid communication. Domperidone: new restrictions in use. 2014.
- National Institute for Health and Care Excellence. NICE guideline NG28. Type 2 Diabetes in Adults: Management. December 2015. Updated August 2019.
- National Institute for Health and Care Excellence. NICE guideline NG17. Type 1 Diabetes in Adults: Diagnosis and Management. August 2015. Updated July 2016
- NHS website: Gastroparesis. Available at: https://www.nhs.uk/conditions/gastroparesis/
- UK Medicines Information Service. Medicines Q&A 73.5 Drug Treatment of Inadequate Lactation. January 2015 Updated March 2016.
- National Institute for Health and Care Excellence. NICE guideline NG71. Parkinson's Disease in Adults: July 2017.
- Medicines and Healthcare Products Regulatory Agency. Apomorphine with

Domperidone: minimising the risks of cardiac side effects. April 2016.

Likely place in therapy relative to current treatments

Domperidone use was previously well established and it was used extensively in practice.

The MHRA alert in 2014 states:[2]

'A European review assessed the benefits and risks of domperidone following continued reports of cardiac side effects.

The review confirmed a small increased risk of serious cardiac side effects. A higher risk was observed particularly in people older than 60 years, people taking daily oral domperidone doses of more than 30 mg, and those taking QT-prolonging medicines or CYP3A4 inhibitors at the same time as domperidone.

For indications other than nausea and vomiting, the benefits were not considered to outweigh the cardiac risk. Based on the results of this review, the treatment advice for domperidone has been updated.

The overall safety profile of domperidone, and in particular its cardiac risk and potential interactions with other medications, should be taken into account if there is a clinical need to use it at doses or durations greater than those authorised (e.g., to control side effects of Parkinson's disease treatment in some patients).

Advice for healthcare professionals:

Indication

- Domperidone is now restricted to use in the relief of nausea and vomiting
- It should be used at the lowest effective dose for the shortest possible time

Contraindications

- Domperidone is now contraindicated in people:
    - with conditions where cardiac conduction is, or could be, impaired
    - with underlying cardiac diseases such as congestive heart failure
    - receiving other medications known to prolong QT interval or potent CYP3A4 inhibitors
    - with severe hepatic impairment
- Patients with these conditions should have their treatment reviewed at their next routine appointment and be switched to an alternative treatment if required

Posology

Oral formulations

- For adults and adolescents over 12 years of age and weighing 35 kg or more, the recommended maximum dose in 24 hours is 30 milligrams (dose interval: 10 milligrams up to three times a day)
- In children under 12 years of age and weighing less than 35 kg, the recommended maximum dose in 24 hours is 0.75 mg/kg body weight (dose interval: 0.25 mg/kg body weight up to three times a day)

Suppository formulation

- Suppositories should only be used in adults and adolescents weighing 35 kg or more, the recommended maximum daily dose in 24 hours is 60 milligrams (dose interval: 30

milligrams twice a day)

Duration of treatment

- The maximum treatment duration should not usually exceed one week
- Patients currently receiving long-term treatment with domperidone should be reassessed at a routine appointment to advise on treatment continuation, dose change, or cessation

Administration of liquid formulations

- 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.'

Following this, the use of domperidone is restricted. Recommendations for the off-label use are included in the section above on clinical efficacy together with the sources of the recommendation.

Recommendation to APC

Recommended changes to traffic light status:

Indication	Current status on PAD	Proposed status
Licensed indication:		
1. Nausea and vomiting	GREEN	GREEN
Unlicensed indications:		
1. Nausea and vomiting in pregnancy	None	RED
2. Gastric reflux in neonates and children	RED	RED
3. Gastro-oesophageal reflux disease in adults	None	BLUE – Specialist input WITHOUT formal shared care
4. Dyspepsia in adults	None	BLUE – Specialist input WITHOUT formal shared care
5. Gastroparesis in adults	None	BLUE – Specialist input WITHOUT formal shared care
6. Stimulation of lactation:		
From clinical services such as Breast Feeding Clinics	None – local decision from G&W MOG	RED
Patients presenting in General Practice	None	BLUE – Specialist input WITHOUT formal shared care
7. Pre-treatment for patients to be commenced on apomorphine for Parkinson's Disease	None	RED
8. Nausea and vomiting in patients with Parkinson's Disease	None	GREEN

Medicine details

Name and brand name

Domperidone (Brand Motilium®)

Licensed indication, formulation and usual dosage

10mg tablets
1mg/ml sugar free suspension
Suppositories available as an unlicensed import.

Licensed indication: relief of the symptoms of nausea and vomiting.

Usual dosage: over 12 years and >35kg: 10mg up to three times a day (maximum 30mg/day). Use the lowest effective dose for the shortest duration, usually the maximum treatment duration should not exceed a week.[1]

The SPC for the suspension does not indicate doses for patients under 12 or <35kg. However doses are suggested in the BNF for Children.[18]

Summary of mechanism of action, and relevant pharmacokinetics

Domperidone is a dopamine antagonist which does not readily cross the blood brain barrier. Its antiemetic action is probably due to gastrokinetic effects and dopamine antagonism in the chemoreceptor trigger zone. It stimulates prolactin release from the pituitary gland.[1]

Oral domperidone is rapidly adsorbed but undergoes rapid and extensive first pass metabolism and extensive hepatic metabolism. It has a single dose half-life of 7-9 hours.[1]

It is recommended to take oral domperidone tablets before meals. If taken after meals, absorption of the drug is somewhat delayed.[1]

Important drug interactions

1. Drugs increasing QT interval[1]
2. CYP3A4 inhibitors[1]

Monitoring requirements

Patients should be told to promptly report any cardiac symptoms whilst taking domperidone.[1]

Prescribing considerations

Colour classification guidelines

Prescribing should be mindful of the SPC and the MHRA alert.

In particular, the duration of treatment, where the MHRA recommendations are:

- The maximum treatment duration should not usually exceed one week
- Patients currently receiving long-term treatment with domperidone should be reassessed at a routine appointment to advise on treatment continuation, dose change, or cessation

The SNWS APC is asked to review:

1. The proposed traffic light status and make final recommendations
   If BLUE status - Specialist input WITHOUT formal shared care is recommended then:
   a. whether a GP information leaflet is necessary
   b. Recommended minimum duration of supply if >1 month
2. Whether there is a need for existing patients on long-term treatment with domperidone to be reassessed.

Recommended changes to traffic light status:

Indication	Current status on PAD	Proposed status	Reference/s
Licensed indication:			
1. Nausea and vomiting	GREEN	GREEN	Domperidone SPC.[1] Medicines and Healthcare Products Regulatory Agency. Domperidone: risks of cardiac side effects. December 2014.[2]
Unlicensed indications:			
1. Nausea and vomiting in pregnancy	None	RED	In pregnancy, domperidone is not a recommended first line choice of anti-emetic for nausea & vomiting due to general safety concerns with its use and because safer options to treat nausea and vomiting are available.[3] The RCOG suggests that domperidone is used second-line if first line agents such as the antihistamines cannot be used.[4] Treatment duration is restricted to a maximum of one week in all patients[2] which limits its usefulness for nausea and vomiting in pregnancy.
2. Gastric reflux in neonates and children	RED	RED	NICE undertook an evidence review for the development of their guidelines for gastro-oesophageal reflux disease in children and young people.[5] They concluded that if metoclopramide or domperidone were used then caution should be taken and therefore initiation of treatment should only be offered by healthcare professionals who can make individual assessments on the cardiac risk and potential benefit on a case by case basis. This recommendation remained in the October 2019 update to the guidelines.[5]
3. Gastro-oesophageal reflux disease in adults	None	BLUE – Specialist input WITHOUT formal shared care	The evidence review by the Trent Medicines Information Service (2014) summarised potential options for the off-label use of domperidone in GORD and dyspepsia. It suggested reviews for all patients receiving long-term domperidone should be undertaken with a view to undertaking a trial withdrawal in conjunction with optimising other treatment options for GORD and dyspepsia.[6]
4. Dyspepsia in adults	None	BLUE – Specialist input WITHOUT formal shared care	The evidence review by the Trent Medicines Information Service (2014) summarised potential options for the off-label use of domperidone in GORD and dyspepsia. It suggested reviews for all patients receiving long-term domperidone should be undertaken with a view to undertaking a trial withdrawal in conjunction with optimising other treatment options for GORD and dyspepsia.[6]

5. Gastroparesis in adults	None	BLUE – Specialist input WITHOUT formal shared care	NICE guidelines for Type 2 diabetes in adults: Management (2015)[7] and NICE guidelines for Type 1 diabetes in adults: Management (2015)[8] state that there is no strong evidence that any available anti-emetic therapy is effective in nausea and vomiting caused by gastroparesis in these patients. However the strongest evidence is for domperidone but the safety profile must be considered and NICE recommends its use only in exceptional circumstances.
6. Stimulation of lactation:			
From clinical services such as Breast Feeding Clinics	None – local decision from G&W MOG	RED	In September 2016, the G&W MOG made a local decision and agreed that GPs should NOT be asked to prescribe domperidone for lactation stimulation from services such as the Breast Feeding Clinics at the RSCH. The RSCH DTC had previously agreed that if domperidone is required for its unlicensed use as a galactagogue, arrangements should be made to prescribe and supply from the RSCH. (Note - a maternal dose of 30mg/day for a max of 1 week should not be exceeded).
Patients presenting in General Practice	None	BLUE – Specialist input WITHOUT formal shared care	NICE CKS Breastfeeding problems https://cks.nice.org.uk/breastfeeding-problems#!scenario Low milk supply: If these measures do not improve a true low milk supply and maternal prolactin deficiency is a possible cause, consider referral to an endocrinologist for advice on prescribing a galactogogue drug (such as domperidone, off-label indication) to help improve milk supply. CKS recommends specialist referral before this is started, however, as there is very limited evidence on its effectiveness, and there is no direct correlation between maternal prolactin levels and rates of milk production.
7. Pre-treatment for patients to be commenced on apomorphine for Parkinson's Disease	None	RED	The MHRA safety update 'Apomorphine with domperidone: minimising cardiac side effects' (April 2016) recommends that when using domperidone with apomorphine, to consider the benefits vs risk, check the patients QT interval before and during treatment and use the lowest effective dose.[12] The use and supply of domperidone is considered to be within the episode of care from the trust.

8. Nausea and vomiting in patients with Parkinson's Disease	None	GREEN	NICE CKS on Parkinson's disease https://cks.nice.org.uk/parkinsons-disease#!scenario:1 If nausea or vomiting persists, is severe, or is unrelated to levodopa or dopamine agonist drug treatment: • Do *not* use metoclopramide or prochlorperazine anti-emetics — can cause or exacerbate parkinsonism. • Consider prescribing low-dose domperidone, reducing or stopping it when the nausea or vomiting settles. • If domperidone is ineffective or not tolerated, seek specialist advice

Prescribing should be mindful of the SPC and the Medicines and Healthcare Products Regulatory Agency. Domperidone: risks of cardiac side effects. December 2014.

In addition, prescribers should advise patients to seek urgent medical attention if symptoms such as syncope or palpitations occur during treatment with domperidone.

Other considerations

Transfer of prescribing of domperidone for off-label indications to non-specialists (e.g. General Practitioners) could cause difficulties as the prescriber would need to take clinical responsibility despite the MHRA safety warning which states that for indications other than nausea and vomiting the benefits were not considered to outweigh the cardiac risk.

The maximum recommended treatment length is one week.

Potential patient group (if appropriate to include)

Brief description of disease

Domperidone is used to alleviate nausea and vomiting in a variety of conditions.

It stimulates prolactin release from the pituitary gland and hence is used in stimulation of lactation in nursing mothers.

Potential patient numbers per 100,000

Fluctuates.

Outcomes required

Summary of current treatment pathway

Currently, the SNWS APC have a GREEN traffic light status for domperidone for the licensed indication of nausea and vomiting, RED for use in gastric reflux in neonates and children use but no formal traffic light status for the other off-label uses.

Evidence review

See summary section.

Equity / Stakeholder views (if relevant)

Decisions of local Trusts DTCs and neighbouring APCs

GWCCG local decision September: 2016
The G&W MOG agreed that GPs should NOT be asked to prescribe domperidone for lactation stimulation from services such as the Breast Feeding Clinics at the RSCH.
The RSCH DTC had previously agreed that if domperidone is required for its unlicensed use as a galactagogue, arrangements should be made to prescribe and supply from the RSCH.

Organisation	Indication	Traffic light status
CHMS CCG	Only for relief of symptoms of nausea and vomiting and at the lowest effective dose for the shortest possible duration	GREEN
	Treatment of gastric reflux in babies and children	RED
RSCH	Nausea and vomiting	GREEN
	Lactation stimulation	RED
SASH	On formulary	None
ESHUT	Hospital only when used for neonates and children	None
	Hospital only when used with apomorphine	None
ASPH	Restricted to 5 days maximum course	None

Wiltshire CCG have developed a guide to prescribing domperidone in May 2017 which is available at: https://prescribing.wiltshireccg.nhs.uk/prescribing-guidance-by-bnf-chapter/cns
Their recommendations are GREEN for licensed indication and AMBER(note 1) for following unlicensed uses:

1. Adults with gastro-oesophageal reflux disease, dyspepsia or gastroparesis
2. Adults receiving chemo-therapy for the prevention of nausea and vomiting
3. Children with gastro-oesophageal reflux disease
4. Use in nursing mothers to promote lactation
5. Pre-treatment for patients to be commenced on apomorphine for Parkinson's Disease

Note 1: AMBER on the Surrey PAD requires shared care guidelines. The exact AMBER definition for Wiltshire CCG is not known. AMBER is considered to be suitable for primary care prescribing after specialist consultation: either with or without shared care guidelines. It appears to be similar to either AMBER or BLUE – Specialist input WITHOUT formal shared care on the Surrey PAD.

Recommendations from national / regional decision making groups

See Summary section.

Stakeholder views

Comments to be attached to evidence review after consultation period.

CCG priorities

To be able to give additional guidance to prescribers for off-label use of domperidone.

Health economic considerations
Cost per year per patient
See above under cost implications
Alternative treatments cost per patient per year
See above.
Other financial considerations (if relevant)
Health economic data (if available)

References

1. Electronic Medicines Compendium. Motilium 10mg film coated tablets SPC Accessed October 2019
2. Medicines and Healthcare Products Regulatory Agency. Domperidone: risks of cardiac side effects. December 2014
3. UK Medicines Information Service. Medicines Q&A How can nausea and vomiting be treated during pregnancy? September 2014 Revised August 2019
4. Royal College of Obstetricians and Gynaecologists (RCOG). The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum (Green-top Guideline No. 69). 2016
5. National Institute for Health and Care Excellence. NICE guideline NG1. Gastro-oesophageal reflux disease in children and young people: diagnosis and management. January 2015. Updated October 2019
6. Trent Medicines Information Service. Rapid communication. Domperidone: new restrictions in use. 2014
7. National Institute for Health and Care Excellence. NICE guideline NG28. Type 2 Diabetes in Adults: Management. December 2015. Updated August 2019
8. National Institute for Health and Care Excellence. NICE guideline NG17. Type 1 Diabetes in Adults: Diagnosis and Management. August 2015. Updated July 2016
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11. National Institute for Health and Care Excellence. NICE guideline NG71. Parkinson's Disease in Adults: July 2017
12. Medicines and Healthcare Products Regulatory Agency. Apomorphine with Domperidone: minimising the risks of cardiac side effects. April 2016
13. Electronic Medicines Compendium. APO go Pen SPC. Accessed October 2019
14. European Medicines Authority. Restrictions on the use of domperidone containing medicines. September 2014
15. US Food and Drug Administration. FDA Talk Paper: FDA warns against women using unapproved drug domperidone to increase milk production. June 2004
16. Choi J-S, Han J-Y, Ahn H-K et al. Fetal and neonatal outcomes in women taking domperidone during pregnancy. J Obstet Gynaecol 2013; 33:160-162
17. NHS Business Services Authority. Drug Tariff Online. Accessed October 2019
18. British National Formulary for Children. Accessed online October 2019

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Declaration of Interest:

Deborah Bunn: Nil

Lizette Howers: Nil

Kwame Oduro: Nil

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Declaration of Interest:

Nil

Date: 13.11.19

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
1	*11.11.19*	*Deborah Bunn, Lizette Howers and Kwame Oduro*	*Draft*	*Consultation with lead pharmacists*
2	*13.11.19*	*T. Bahra*	*Final*	*Out for consultation with APC members*
3	*28.11.19*	*T. Bahra*	*Final*	*Incorporate comments from consultation*