

**UK Drugs in Lactation Advisory Service**

**EVIDENCE SUMMARY**

**DOMPERIDONE**

<p><b>BNF category</b></p>	<p>4.6</p>
<p><b>Evidence</b></p>	<p>Lactation is a complex process involving physical and emotional factors and the interaction of multiple hormones, the most important of which is prolactin. Oxytocin is involved in the milk ejection reflex (1,2,3).</p> <p>Galactagogues (drugs that promote or increase the flow of a mother's milk) should only be used after thorough evaluation for treatable causes such as poor attachment, and when increased frequency of breastfeeding, pumping or hand expression of milk has not been successful (4).</p> <p>There are no products licensed in the UK for use as galactagogues. Such use is "off-label". There are only a limited number of randomised, placebo-controlled, blinded studies of the use of pharmaceutical galactagogues and few studies meet evidence-based criteria for review (4).</p> <p>Following a European review, due to concerns regarding cardiac adverse effects, the Medicines and Healthcare Regulatory Agency (MHRA) has issued updated advice on the use of domperidone. Domperidone should only be used in the relief of symptoms of nausea and vomiting, it should no longer be used for symptoms of abdominal discomfort such as heartburn and feelings of fullness. The maximum recommended dose for adults is 10mg up to three times a day, and the maximum treatment duration should not exceed one week.</p> <p>Domperidone is contraindicated in people:</p> <ul style="list-style-type: none"> <li>• with conditions where the cardiac conduction is, or could be, impaired,</li> <li>• with underlying cardiac diseases such as congestive heart failure,</li> <li>• receiving other medications - either known to prolong the QT interval or potent CYP3A4 inhibitors,</li> <li>• with severe hepatic impairment.</li> </ul> <p>The scope of the review does not cover use of outside the licensed indications (off-label use) the principles behind these recommendations should be considered whenever domperidone is used (5).</p> <p>The review was triggered following continued reports of cardiac side effects and a small increased risk of serious cardiac side effects was confirmed. A higher risk was observed in patients older than 60 years, adults taking daily oral doses of more than 30mg, and those taking QT-prolonging medicines or CYP3A4 inhibitors concomitantly.</p> <p>There are limited alternative treatments for stimulation of lactation; metoclopramide, which has been used, is associated with a number of neurological adverse effects. Following a recent European Medicines Agency's Committee on Medicinal Products for Human Use (CHMP) review the use of metoclopramide has also been restricted:</p> <ul style="list-style-type: none"> <li>• Metoclopramide should only be authorised for short-term use (up to 5 days).</li> <li>• It should not be used in children below 1 year of age. In children over 1 year of age it should only be used as a second-choice treatment for the prevention of delayed nausea and vomiting after chemotherapy and for the treatment of post-operative nausea and vomiting.</li> <li>• It should no longer be used in chronic conditions such as gastroparesis, dyspepsia and gastro-oesophageal reflux disease (GORD), nor as an adjunct in surgical and</li> </ul>

	<p>radiological procedures.</p> <ul style="list-style-type: none"> <li>In adults, metoclopramide remains indicated for prevention of post-operative nausea and vomiting, radiotherapy-induced nausea and vomiting and delayed (but not acute) chemotherapy-induced nausea and vomiting, and for symptomatic treatment of nausea and vomiting including that associated with acute migraine (where it may also be used to improve absorption of oral analgesics).</li> <li>For adults and children the maximum dose in 24 hours is 0.5mg per kg body weight; in adults, the usual dose of conventional formulations (all routes) is 10mg up to 3 times daily.</li> <li>Oral liquid formulations have been particularly associated with overdose in children. Oral liquids containing more than 1mg/ml will be withdrawn from the market (6).</li> </ul> <p>As there are limited alternative options for the stimulation of lactation, the use of domperidone can be considered provided there is evidence of thorough evaluation for treatable causes such as poor attachment, and when increased frequency of breastfeeding, pumping or hand expression of milk has not been successful. A maternal dose of 30mg daily for a maximum of 1 week should not be exceeded. The same contraindications recommended in the EMA review apply to its use as a galactagogue in both mother and infant (<i>see above</i>).</p>
<p><b>Conclusion/ Advice</b></p>	<p>A review has been undertaken by the EMA/MHRA <a href="#">[Link]</a> for the use of domperidone as an anti-emetic, in which restrictions on its use are recommended. Although the scope of this review does not cover use for unlicensed indications (off-label use) the principles behind these recommendations should be considered whenever domperidone is used, including as a galactagogue to enhance lactation.</p> <p><b>As there are limited alternative options for the stimulation of lactation, the use of domperidone can be considered provided there is evidence of thorough evaluation for treatable causes such as poor attachment, and when increased frequency of breastfeeding, pumping or hand expression of milk has not been successful. A maternal dose of 30mg daily for a maximum of 1 week should not be exceeded. Domperidone should not be used if the mother or infant:</b></p> <ul style="list-style-type: none"> <li><b>have conditions where the cardiac conduction is, or could be, impaired,</b></li> <li><b>have underlying cardiac diseases such as congestive heart failure,</b></li> <li><b>are receiving other medications known to prolong QT interval or potent CYP3A4 inhibitors,</b></li> <li><b>have severe hepatic impairment.</b></li> </ul>
<p><b>References</b></p>	<ol style="list-style-type: none"> <li>ABM Clinical Protocol 9: Use of galactagogues in initiating or augmenting the rate of maternal milk secretion. (First Revision January 2011). The Academy of Breastfeeding Medicine <a href="http://www.bfmed.org/Resources/Protocols.aspx">http://www.bfmed.org/Resources/Protocols.aspx</a></li> <li>Buhimschi CS. Endocrinology of lactation. <i>Obstet Gynecol Clin North Am</i> 2004;31:963-979</li> <li>Lawrence RA, Lawrence RM. <i>Breastfeeding. A guide for the medical profession</i> 7<sup>th</sup> Ed. Elsevier Mosby, 2010 pp68- 71 and 71-75.</li> <li>Anderson PO, Valdes V. A critical review of pharmaceutical galactagogues. <i>Breastfeed Med</i> 2007;2:229-242</li> <li>CMDh confirms recommendations on restricting use of domperidone-containing medicines. <a href="http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/04/news_detail_002083.js p&amp;mid=WC0b01ac058004d5c1">http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/04/news_detail_002083.js p&amp;mid=WC0b01ac058004d5c1</a> accessed 01/05/2014)</li> <li>European Medicines Agency confirms changes to the use of metoclopramide October 2013 (<a href="http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Metoclopramide-containing_medicines/human_referral_000349.jsp&amp;mid=WC0b01ac05805c516f">http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Metoclopramide-containing_medicines/human_referral_000349.jsp&amp;mid=WC0b01ac05805c516f</a> accessed 01/5/2014)</li> </ol>

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