UKMi Q&A 73.5

# Drug treatment of inadequate lactation

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals



Date prepared: October 2014

## Background

Lactation is the physiological completion of the reproductive cycle. It 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).

An intact hypothalamic-pituitary axis regulating prolactin and oxytocin levels is essential for the initiation and maintenance of lactation. Successful lactation requires both milk synthesis and milk release into the alveoli and lactiferous ducts. When milk is not removed, the increased pressure lessens capillary blood flow and inhibits the lactation process. Lack of suckling reduces prolactin release from the pituitary gland. Sensory nerve endings, located mainly in the areola and nipple, are stimulated by suckling. Stimulation of afferent neural reflex pathways via the spinal cord and hypothalamus produce secretion of prolactin and oxytocin (3). The release and production of prolactin is dependent on the inhibition of prolactin inhibitor factor, which is produced by the hypothalamus and dopamine-releasing neurones (3,4).

As lactation progresses, the prolactin response to suckling diminishes and milk removal becomes the driving force behind milk production (5). This is now known to be due to the presence in secreted milk of a whey protein that is able to inhibit the synthesis of milk constituents (6,7). The definitive indicator of an adequate milk supply is infant weight gain in the early neonatal period (8).

The evidence (9) suggests that when babies are breastfeeding well:

- Maximum weight loss occurs by 72 hours: “Day 3”.
- Maximum loss of bodyweight is 6-8%.
- Birth weight is regained by 5-7 days of life.

## Causes of inadequate lactation

Since lactation is such a complex process, it is unsurprising that there are a number of causes of insufficient milk supply. A review discussed risk factors for failed lactogenesis (10). While insufficient milk supply is a commonly perceived problem by mothers it actually occurs rarely (8). The most common causes of prolactin deficiency include postpartum pituitary necrosis (Sheehan syndrome) and other causes of anterior pituitary dysfunction, medications (such as dopamine, ergot preparations and pyridoxine) and nicotine. A single case report noted a significant loss of milk supply 4 days after the mother received an injection of 80 – 120 mg triamcinolone into vertebral joints. Milk production was restored after use of domperidone and frequent expression (11). It has been postulated that failed lactation and perinatal depression are linked via a shared neuroendocrine mechanism (12). A systematic review concluded that in prospective studies, obese mothers are more likely to have delayed lactogenesis and reduced lactation (13).

An apparently low milk supply is one of the most common reasons for discontinuing breastfeeding (14).

## Answer

### Use of drugs to initiate or augment milk supply

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 (15). There are only a few randomised, placebo-controlled, blinded studies on the use of galactagogues and these studies are

small (1). A recent Cochrane review noted that two studies with a total of 59 mothers suggested modest improvements in short-term expressed breast milk (EBM) volumes when domperidone was used after insufficient EBM occurs following preterm delivery (16). Neither study showed significant improvements in long term outcomes. The timing of introduction of medication remains controversial. Currently, no studies support prophylactic use of a galactagogue.

**Indications for the use of galactagogues are** (1):

- Increase of an inadequate milk supply due to maternal or infant illness or prematurity
- Separation of mother and infant.
- After a period of milk expression by hand or with a pump when a decline in milk production may occur after several weeks.
- Adoptive nursing
- Relactation (re-establishing milk supply after weaning)

## Specific galactagogues

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 (15).

### Domperidone (POM)

Domperidone is a dopamine antagonist. Unlike metoclopramide, it passes poorly into the brain and has few central nervous system (CNS) side effects (8), has a higher molecular weight and binds more strongly to plasma proteins (17,18). It produces significant increases in prolactin levels and has proved useful in enhancing lactation (17,19,20) including use in mothers of preterm infants (21,22,23) and critically ill neonates (24) and for augmentation of lactation after caesarean delivery at full term (25). Domperidone is generally well tolerated by treated mothers and fewer cases of dystonia have been reported than after metoclopramide (26). To date, no adverse effects in breastfed infants have been reported (27).

A small crossover study in 6 women with inadequate lactation for their preterm infants compared the effect of domperidone 10mg three times daily with doses of 20mg three times daily. Only 4 of the 6 women responded and there was no significant difference in milk production between the two regimens but side effects were more common in the higher dose group (22). A second study in 15 mothers of preterm infants compared the effects of domperidone 10 or 20 mg three times daily for 4 weeks, twice daily for a further week and once daily for a final week. Both regimens gave a statistically significant increase in daily milk volumes over the first 4 weeks. The between group difference was not statistically significant over this period but was considered to be clinically significant. There was no difference between the groups during weeks 5 and 6 (28). The Academy of Breastfeeding Medicine has observed that there is no clear advantage for dose tapering at the end of treatment (1). Further studies are needed to define the optimal regimen and length of treatment.

Concentrations of domperidone in milk vary according to the maternal dose. Following a dose of 10mg three times daily, reported average milk concentrations ranged from 0.28 micrograms/L (22) to 2.6 micrograms/L (8). Because of extensive first pass and gut-wall metabolism, oral bioavailability is only 13-17% (18). The total amount of drug ingested by the infant via milk is very small (about 180 nanograms/kg/day) (29). The mean relative infant dose was 0.01% after a 30mg daily dose and 0.009% at 60mg (22).

The effect of withdrawal of domperidone on subsequent milk production was studied in 25 women given domperidone 20mg four times daily. After a stepwise dose reduction over 2-4 weeks, there was no increased use of formula milk in 23 of the 25 women and normal infant growth was seen in all cases (30). This suggests that once sufficient milk production is established, it is maintained without the use of domperidone.

In one study in 46 mothers who delivered infants of less than 31 weeks gestation, domperidone or placebo was given for lactation failure. The effect of domperidone on macronutrient composition of breast milk was also studied (23). By day 14, breast milk volumes increased by 267% in the treatment group compared to 18.5% in the placebo group. Although mean breast milk protein declined by 9.6% in the domperidone group, changes in energy, fat, carbohydrate, sodium and phosphate content did not differ significantly between the groups. Increases in calcium (61.8% vs. -4.4%) were noted in the treatment group compared with the placebo group. No adverse effects were reported in the mothers or their infants. The authors concluded that domperidone was effective in increasing milk volume of mothers of preterm infants without substantially altering nutrient content. The full significance of the increase of calcium concentration is unclear and requires further study.

The U.S. FDA issued a warning in June 2004 about the use of domperidone in inadequate lactation due to concerns over cardiac problems following intravenous use (31). Domperidone can prolong the QT interval. As discussed above, amounts of the drug in milk are very low and lactation experts did not consider the warnings relevant to its use in inadequate lactation (32).

In October 2011, the Pharmacovigilance Working Party of the European Medicines Agency (EMA) issued a summary assessment (33) of the risk of cardiac disorders based on a Dutch study (34) published in the previous year. This suggested that the current use of domperidone, especially at high doses, was associated with an increased risk of serious ventricular arrhythmia (SVA) and sudden cardiac death (SCD). A second case control study (35) involving over 80,000 individuals evaluated the risk of SVA and SCD in users of oral domperidone versus users of proton pump inhibitors or non-users of these medications. The adjusted odds ratio for SVA/SCD for domperidone compared with non-use was 1.59. This increased risk remained after adjustment for multiple co-variates. The EMA advice was that domperidone should be used at the lowest effective dose as it may be linked to an increased risk of SVA/SCD particularly in patients over 60 years or with daily doses exceeding 30mg (33).

Following a review of domperidone-containing medicines used to relieve symptoms of nausea and vomiting, fullness, abdominal discomfort and heartburn (36) the European Medicines Agency (EMA) issued new guidance in April 2014 (37) in which it advised that “domperidone should be used at the lowest effective dose for the shortest possible duration. The maximum treatment duration should not usually exceed one week”. It was further recommended that the oral dose should not exceed 30 mg daily. This recommendation was endorsed by the MHRA (38). The review and its subsequent recommendations apply only to its licensed indications – use as a galactogogue is off-label, which is not specifically mentioned in the review.

The applicability of the EMA’s recommendations on domperidone to breastfeeding mothers has been challenged on the grounds that domperidone is an effective option for inadequate lactation when other management strategies have failed, it is used in a cohort of younger women, and there is no direct evidence for any cardiac-related adverse effects in lactating mothers (39,40). However, until the evidence relating to the safety of its off-label use as a galactogogue is clarified, it is advisable to follow the recommendations of the regulatory authorities, which does give some flexibility of use. Also, domperidone should not be used where the mother or infant has a cardiac disorder or are receiving treatment with drugs known to affect the QT interval, e.g. ketoconazole or erythromycin

The conclusion of an in-depth review prior to the new EMA/MHRA guidance was that 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 (41). This is still considered to be a valid conclusion as long as the possible cardiac effects, although not seen with this indication, are taken into account.

**Metoclopramide** (POM)

Like domperidone, metoclopramide increases prolactin levels via blockade of dopamine receptors. Reports of its successful use as a galactagogue have appeared since the 1980s and it is the agent for which most data have been published (42-49). Metoclopramide has been used in mothers of preterm infants (43,45 47) and in the intended mother of a surrogate pregnancy (48).

The increase in serum prolactin and milk production appears to be dose-related with daily doses of 30 and 45mg proving effective and 15mg daily ineffective (42). Although metoclopramide does increase

milk supply, the effect is very dose-dependent and some mothers do not respond. Side effects such as gastric cramping and diarrhoea may limit compliance. If no effect is seen within 7 days, it is unlikely that longer therapy will be effective. After discontinuation of medication, the milk supply may diminish rapidly and a slow tapering of the dose over several weeks (e.g. by 10mg per week) is recommended in those women who respond. Metoclopramide is not suitable for women with a prior history of depression, and use for more than four weeks is not recommended as this may increase the risk of depression (8).

Estimated intake of the drug via milk varies from 1 to 24 micrograms/kg/day. These levels are very low compared to those used to treat reflux in paediatric patients, 100-500 micrograms/kg/day (8).
In one study, the plasma prolactin concentration in 4 of 7 neonates sampled during administration of metoclopramide to the mother were higher than the highest plasma prolactin level in infants of the same age with untreated mothers (46).

A recent study was the first to compare the effects of metoclopramide and domperidone on breast milk output of mothers (49). A double-blind, randomised controlled trial in 80 mothers expressing breast milk for their infants (mean gestational age 28 weeks) based in a neonatal intensive care unit, compared the effects of domperidone or metoclopramide 10mg three times daily for 10 days. After adjusting for the amount of milk produced prior to medication, the mean amount of milk produced on medication was 31ml/24 hours greater for domperidone than the mean for those taking metoclopramide. There were small differences in milk output between the two groups and in the incidence of side effects, but these were non-significant.

In August 2013, the EMEA Committee on Medicinal Products for Human Use (CHMP) recommended changes to the use of metoclopramide-containing medicines in the European Union in order to minimise the risk of neurological and other adverse reactions (50). Metoclopramide should only be prescribed for short term use (up to 5 days). The maximum dose in 24 hours is 0.5 mg per kg body weight and the usual dose for adults is 10 mg up to three times daily.

### Sulpiride(POM)

Sulpiride is a selective dopamine antagonist. Limited data suggest successful use as a galactagogue (51,52). A small study in 7 non-lactating women found that prolactin response to sulpiride is not dose related and reached a maximum at 3-10mg (53). The use of higher doses, 50mg sulpiride two or three times a day, have been reported in studies to improve inadequate lactation (51,54). No adverse effects on breastfed infants were noted in these studies. Reported concentrations in breast milk range from 0.26-1.97 mg/L (55). The estimated average maximum infant intake of sulpiride via breast milk following a maternal dose of 50 mg twice daily has been calculated as 146 micrograms/kg/day (27).

### Herbal medications

Various herbal remedies, including milk thistle and fenugreek, have been suggested to improve poor milk supply. However, there is insufficient evidence of safety or efficacy to recommend such use (56,57). There may be concerns over the relative potency and quality control of herbal products (8).

### Other

In one small study, 19 puerperal women with inadequate lactation (less than 50% normal milk yield) were randomised to receive thyrotrophin-releasing hormone (TRH) 1mg (n=10) or placebo (n=9) four times daily by nasal spray for 10 days, starting on day 6 postpartum. Milk yield increased significantly in the active treatment group whilst there was no significant change in the controls. A further rise in prolactin and milk yield was seen in seven of the TRH treated group given a second 10-day course at their own request. No significant changes in levels of TRH, thyroxine or tri-iodothyronine were seen in either group (58).

Small studies have been conducted on the effects of oxytocin (59,60) and somatropin (61,62) on human milk production but there is insufficient experience to recommend their use as galactagogues

A single session of acupuncture had variable effect in 90% of 30 women with postpartum inadequate lactation. Improved lactation was more marked after 3-5 sessions, especially in primiparae, within 10 days of delivery. Acupuncture was less effective the longer the duration of inadequate lactation (63).

Similar positive outcomes were seen in a study of two courses of acupuncture in 96 mothers (64). Acupuncture was also effective at maintaining breastfeeding until infants were age three months in a study of 90 mother-infant pairs (65).

## Summary

- A health professional should always be involved in the decision to use a galactagogue.
- Drugs to manage inadequate lactation should only be used where there is objective evidence to support diagnosis and where non-drug methods have failed.
- There are no drugs licensed in the UK to improve lactation.
- 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.
- Domperidone should not be used for inadequate lactation where the mother or infant has a cardiac disorder or are receiving treatment with drugs known to affect the QT interval e.g. ketoconazole or erythromycin, in which case metoclopramide is preferred.
- A maternal daily dose of 30mg domperidone should not be exceeded. The maximum treatment duration should not usually exceed one week.
- Further studies are needed to determine the optimum regimen and duration of treatment.
- There are insufficient data to support the use of herbal remedies.

## Limitations

Published reports of drug use in lactation are generally limited to small numbers of subjects or to single case reports. Quantitative reports are often limited to single time point estimations. Many of the studies were performed before the introduction of modern lactation management. Few studies have provided encouragement and instruction to mothers. There are often inconsistencies in inclusion criteria that could minimise possible differences between drug and placebo groups (22).

## References


1. 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 http://www.bfmed.org/Resources/Protocols.aspx - accessed 02/10/2014
2. Buhimschi CS. Endocrinology of lactation. Obstet Gynecol Clin North Am 2004;31:963-979
3. Lawrence RA, Lawrence RM. Breastfeeding. A guide for the medical profession 7th Ed. Elsevier Mosby, 2010 pp68- 71 and 71-75.
4. Gabay MP. Galactagogues: Medications that induce lactation. J Hum Lact 2002;18:274-9
5. Applebaum RM. The modern management of successful breastfeeding. Pediatr Clin North Am 1970;17:203-225.
6. Prentice A, Addey CV, Wilde CJ. Evidence for local feed-back control of human milk secretion. Biochem Soc Trans 1989;17:122
7. Wilde CJ, Addey CVP, Boddy LM et al. Autocrine regulation of milk secretion by a protein in milk. Biochem J 1995;305:51-58
8. Hale TW, Berens PD. Clinical therapy in breastfeeding patients,3rd Ed Amarillo. Pharmasoft Publishing 2010 p 257
9. Fraser DM, Cooper MA, editors. Myles Textbook for Midwives, 11th Ed. Edinburgh: Churchill Livingstone 2003, p760
10. Hurst M. Recognizing and treating delayed or failed lactogenesis II. J Midwifery Womens Health 2007;52:588-591
11. McGuire E. Sudden loss of milk supply following high-dose triamcinolone (Kenacort ®) injection. Breastfeed Rev 2012;20:32-34
12. Stuebe AM, Grewen K, Pedersen CA et al. Failed lactation and perinatal depression: Common problems with shared neuroendocrine mechanisms? J Womens Health 2012;21:264-272
13. Lepe M, Bacardi Gascon M, Castaneda-Gonzalez LM et al. Effect of maternal obesity on lactation:systematic review. Nutricion Hospitalaria 2011;26:1266-1269

14. Sjolin S, Hofvander Y, Hillervik C. Factors related to early termination of breastfeeding: a retrospective study in Sweden. Acta Paediatr Scand1977;66:505-511
15. Anderson PO, Valdes V. A critical review of pharmaceutical galactagogues. Breastfeed Med 2007;2:229-242
16. Donovan TJ and Buchanan K. Medications for increasing milk supply in mothers expressing breastmilk for their preterm hospitalised infants. Cochrane Database of Systematic Reviews 2012, Issue 3. Art. No.: CD005544. DOI: 10.1002/14651858.CD005544.pub2. Accessed 02/10/2014
17. Hofmeyr GJ, van Iddekinge B. Domperidone and lactation. Lancet 1983;1:647
18. Barone JA. Domperidone, a peripherally acting dopamine 2 receptor antagonist. Ann Pharmacother 1999;33:429-40
19. Hofmeyr GJ, van Iddekinge B, Blott JA. Domperidone: secretion in breast milk and effect on puerperal prolactin levels. Br J Obstet Gynaecol 1985;92:141-144
20. Petraglia F, De Leo V, Sardelli S et al. Domperidone in defective and insufficient lactation. Eur J Obstet Gynecol Reprod Biol 1985;19:281-287
21. da Silva OP, Knoppert DC, Angelini MM et al. Effect of domperidone on milk production in mothers of premature newborns: a randomized, double-blind, placebo-controlled trial. CMAJ 2001;164:17-21
22. Wan EW, Davey K, Page-Sharp M et al. Dose-effect study of domperidone as a galactagogue in preterm mothers with insufficient milk supply, and its transfer into milk. Br J Clin Pharmacol 2008;66:283-289
23. Campbell-Yeo ML, Allen AC, Joseph KS et al. Effect of domperidone on the composition of preterm human breast milk. Pediatrics 2010;125:e107-114
24. Wagner CL, Murphy PK, Haase B et al. Domperidone in the treatment of critically ill neonates. Breastfeed Med 2011;6 Suppl 1:S21 (abstract 47)
25. Jantarasaengaram S, Sreewapa P. Effects of domperidone on augmentation of lactation following caesarean delivery at full term. Int J Gynaecol Obstet 2012;116:240–43
26. Bryant CA. Nursing the adopted infant. J Am Board Fam Med 2006;19:374-379
27. US National Library of Medicine Drugs and Lactation Database ( Lactmed) . http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT . Accessed online 14/10/2014
28. Knoppert DC, Page A, Warren J et al. The effect of two different domperidone doses on maternal milk production. J Human Lactation 2013;29:38-44
29. da Silva OP, Knoppert D C. Domperidone for lactating women. CMAJ 2004;171:725-726
30. Livingstone V, Stanchera BL, Stringer J. The effect of withdrawing domperidone on formula supplementation. Breastfeed Med 2007;2:278. Abstract 3
31. FDA warns against women using unapproved drug, domperidone, to increase milk production FDA Talk Paper, T04-17, 7 June 2004 (http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm173886.htm accessed 14/10/2014)
32. Hale TW. 2012 Medications and Mother's Milk 15th Ed. Amarillo. Hale Publishing p *359*
33. Pharmacovigilance Working Party, European Medicines Agency. Summary Assessment Report. Domperidone – risk of cardiac disorders. October 2011 http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Domperidone_31/Procedure_started/WC500139769.pdf . accessed 14/10/2014
34. Van Noord C, Dielman JP, van Herpen G et al. Domperidone and ventricular arrhythmia or sudden cardiac death. A population-based case-control study in the Netherlands. Drug Saf 2010;33:1003-1014
35. Johannes CB, Varas-Lorenzo C, McQuay LJ et al. Risk of serious ventricular arrhythmia and sudden cardiac death in a cohort of users of domperidone: a nested case-control study. Pharmacoepidemiol Drug Saf 2010;19:881-888
36. European Medicines Agency. Review of domperidone started. http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Domperidone_31/Procedure_started/WC500139769.pdf Accessed 0 2/10/2014.
37. EMA. CMDh confirms recommendations on restricting use of domperidone-containing medicines. EMA/236452/2014. 25 April 2014. http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2014/04/WC500165651.pdf – accessed 04/10/2014.
38. MHRA. Domperidone: risks of cardiac side effects - indication restricted to nausea and vomiting, new contraindications, and reduced dose and duration of use. Drug Safety Update 2014;7(10):A1
39. Grzeskowiak LE, Amir LH. Pharmacological management of low milk supply with domperidone: separating fact from fiction. Med J Aust 2014;201:257-8.
40. Grzeskowiak L. Use of domperidone to increase breast milk supply: are women really dying to breastfeed. J Hum Lact 2014;30:498-9.
41. Zuppa AA, Sindico P, Orchi C et al. Safety and efficacy of galactagogues: Substances that induce, maintain and increase breast milk production. J Pharm Pharm Sci 2010;13:162-174
42. Kauppila A, Kivinen S, Ylikorkala O. A dose response relation between improved lactation and metoclopramide. Lancet 1981;1:1175-77
43. Ehrenkranz RA, Ackerman BA. Metoclopramide effect on faltering milk production by mothers of premature infants. Pediatrics 1986;78:614-620
44. Budd SC, Erdman SH, Long DM et al. Improved lactation with metoclopramide. Clin Pediatr 1993;32:53-57

45. Hansen WF, McAndrew S, Harries K et al. Metoclopramide effect on breastfeeding the pre-term infant: a randomized trial. Obstet Gynecol 2005;105:383-89
46. Kauppila A, Arvela P, Koivisto M et al. Metoclopramide and breastfeeding: transfer into milk and the newborn. Eur J Clin Pharmacol 1983;25:819-823
47. Dastgerdi E , Shirazi M, Mohammadzadeh A et al. Effect of metoclopramide on increased milk production in mothers of preterm infants. Iranian J Obstet Gynecol Infertil 2012;14:32-36
48. Bierlivet FP, Maguiness SD, Hoy DM et al. Induction of lactation in the intended mother of a surrogate pregnancy. Case report. Hum Reprod 2001;16:581-83
49. Ingram J, Taylor H, Churchill C et al. Metoclopramide or domperidone for increasing maternal breast milk output: a randomised controlled trial. Arch Dis Child Fetal Neonatal Ed 2012;97:F241–5
50. European Medicines Agency recommends changes to the use of metoclopramide. Changes aim mainly to reduce the risk of neurological side effects. EMA/13239/2014. 20 December 2013. http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Metoclopramide_31/WC500146610.pdf Accessed 10/10/2014
51. Ylikorkala O, Kauppila A, Kivinen S et al. Sulpiride improves inadequate lactation. Br Med J (Clin Res Ed) 1982;265:249-51
52. Ylikorkala O, Kauppila A, Kivinen S et al. Treatment of inadequate lactation with oral sulpiride and buccal oxytocin. Obstet Gynecol 1984;63:57-6
53. McMurdo ME, Howie PW, Lewis M, et al. Prolactin response to low dose sulpiride. Br J Clin Pharmacol 1987;24:133-7Barguno JM, del Pozo E, Cruz M ,Figueras J. Failure of maintained hyperprolactinemia to improve lactational performance in late puerperium. J Clin Endocrinol Metab 1988;66:876-879
54. Aono T, Shioji T, Aki T et al. Augmentation of puerperal lactation by oral administration of sulpiride. J Clin Endocrinol Metab 1979;48:478-482
55. Milk thistle monograph. Natural Medicines Comprehensive Database http://www.naturaldatabase.com accessed online 26/10/2014
56. Fenugreek monograph. Natural Medicines Comprehensive Database. http://www.naturaldatabase.com accessed online 26/10/2014
57. Peters F, Schulze-Tollert J, Schuth W. Thyrotrophin-releasing hormone – a lactation-promoting agent? Br J Obstet Gynaecol 1991;98:880-885
58. Ruis H, Rolland R, Doesburg W et al. Oxytocin enhances onset of lactation among mothers delivering prematurely. Br Med J (Clin Res Ed) 1981;283:340-342
59. Fewtrell MS, Loh KL, Blake A et al. Randomised, double blind trial of oxytocin nasal spray in mothers expressing breast milk for preterm infants. Arch Dis Child Fetal Neonatal Ed 2006;91:169-174
60. Gunn AJ, Gunn TR, Rabone DL et al. Growth hormone increases breast milk volumes in mothers of preterm infants. Pediatrics 1996;98:279-82
61. Milsom SR, Breir BH, Gallaher BW et al. Growth hormone stimulates galactopoiesis in healthy lactating women. Acta Endocrinol 1992;127:337-343
62. Yan Z, Hui G. The therapeutic effects of acupuncture in 30 cases of postpartum hypogalactia. J Tradit Chin Med 2006;26:29-30
63. Lixin W, Hongcai W, Ying H et al. Clinical observation on the effects of electroacupuncture at Shaoze (SI 1) in 46 cases of postpartum insufficient lactation. J Tradit Chin Med 2008;28:168-172
64. Neri I, Allais G, Vaccaro V et al. Acupuncture treatment as breastfeeding support: Preliminary data. J Altern Complement Med 2011;17:133-7

## Quality Assurance

**Prepared by**
Peter Golightly
West Midlands Medicines Information Service

Based on earlier work by Elena Grant, West Midlands Medicines Information Service

**Date prepared**
October 2014 (version 5)

**Checked by**
Sarah Fenner
West Midlands Medicines Information Service

**Date of check**
December 2014

**Search strategy**

- Medline search per NHS Evidence http://www.library.nhs.uk/hdas [LACTATION DISORDERS OR LACTATION (limit to humans and publication year 2010 – Current)] AND DOMPERIDONE OR METOCLOPRAMIDE OR SULPIRIDE OR PLANTS,MEDICINAL
- Embase search per NHS Evidence http://www.library.nhs.uk/hdas [LACTATION DISORDERS OR LACTATION (limit to humans and publication year 2010 – Current)] AND DOMPERIDONE OR METOCLOPRAMIDE OR SULPIRIDE OR PLANTS,MEDICINAL
- Cochrane Library http://www.thecochranelibrary.com/view/0/index.html
- General Internet search per Google – lactation disorders/inadequate lactation
- Natural Medicines Comprehensive Database accessed 10/10/2014 http://naturaldatabase.therapeuticresearch.com/home.aspx?cs=&s=ND
- In house resources (past enquiries database)
- UKDILAS database
- Academy of Breastfeeding Medicine website http://www.bfmed.org/