# Oseltamivir or zanamivir – can they be used in breastfeeding mothers for the treatment or prophylaxis of influenza?

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


Date prepared: 30th July 2020

## Summary


- Both oseltamivir and zanamivir are considered acceptable for use in breastfeeding mothers.
- The benefits of breastfeeding are considered to outweigh any, albeit unidentified, risks. Use of either drug is not a reason to discontinue, or put limitations on breastfeeding.
- Oseltamivir and its active metabolite, oseltamivir carboxylate, are excreted into human breast milk in very small amounts. Limited data suggest that clinical sequelae from maternal use would not be expected in a breastfed infant.
- There are no data on zanamivir use during lactation but based on limited oral bioavailability the systemic exposure of a breastfed infant from maternal treatment, via any route, is expected to be insignificant.
- If the mother is receiving oseltamivir or zanamivir and the breastfed infant also needs direct treatment or prophylaxis, the recommended dose of oseltamivir or zanamivir for infants should be given to the infant.
- The UK Drugs in Lactation Advisory Service (UKDILAS) advises that, as a precaution, infants should be monitored for vomiting or diarrhoea.
- This guidance applies to infants born full term and healthy. If an infant is unwell, premature, or the mother is taking multiple medicines, then an individual risk assessment will need to be made.


## Background

Oseltamivir (Tamiflu®) and zanamivir (Relenza® and Dectova®) are neuraminidase inhibitors licensed for prophylaxis and treatment of influenza. Treatment in adults should be started within 48 hours of onset of symptoms (or later at clinical discretion). Oseltamivir is administered orally whilst zanamivir is administered by inhalation or, for complicated and potentially life-threatening influenza, administered intravenously. For uncomplicated influenza a treatment course lasts five days for both drugs. Post-exposure prophylaxis is generally given for 10 days (1).

The use of oseltamivir and zanamivir for the prophylaxis and treatment of influenza is covered by guidance from the National Institute for Health and Clinical Excellence (NICE) (2,3) and Public Health England (PHE) (1). Breastfeeding mothers may require treatment or prophylaxis of influenza with these agents and therefore, advising on suitability is essential.

## Answer

The only specific national guidance on the use of antivirals in breastfeeding mothers is contained in the NICE Clinical Knowledge Summary (4) and Department of Health (DH) guidance (now archived) (5). The DH guidance states that 'women who are breastfeeding and have symptoms of influenza should be treated with an antiviral medicine. The preferred medicine is Tamiflu, as for other adults. However, if a woman's baby is born and breastfeeding is started while the woman is taking Relenza, she should complete the course of Relenza; it is not necessary to switch to Tamiflu. If it is decided that a woman who is breastfeeding requires prophylaxis because of family or other contact with a novel pandemic virus strain, the preferred antiviral medicine is Tamiflu'.

## Oseltamivir

*Oseltamivir and its active metabolite, oseltamivir carboxylate, are excreted into human breast milk in very small amounts. Limited data suggest that clinical sequelae from maternal use would not be expected in a breastfed infant. Although not expected, as a precaution monitor the infant for vomiting or diarrhoea (6).*

Oseltamivir phosphate is a prodrug that is readily absorbed after oral administration and converted hepatically into its active metabolite, oseltamivir carboxylate. Only 5% of a dose is found as oseltamivir phosphate in the systemic circulation (7). Oseltamivir carboxylate, if given orally, has very limited bioavailability (8). The manufacturer advises that 'administration of oseltamivir may be considered where there are clear potential benefits to lactating mothers' (7).

In a case report, the mother of a 9-month-old infant was treated with oseltamivir, 75 mg twice daily. She provided 11 milk samples over the 5-day treatment period, during which the infant was not breastfed. Oseltamivir carboxylate was undetectable in the first milk sample, and reached a steady state concentration of 37–39 micrograms/L after 3 days. Concentrations of oseltamivir were significantly lower than those of the carboxylate. The authors calculated that a fully breastfed infant would ingest a maximum of 12 micrograms/kg daily (9).

In a second report, seven postpartum women who were bottle feeding their infants donated milk samples at intervals from zero to 24 hours after a single 75 mg oral dose of oseltamivir phosphate (10). Both oseltamivir phosphate and oseltamivir carboxylate, were detected in milk samples with mean peak milk levels of 26.9 microgram/L (at mean 3.4 hours after the dose) and 41.9 microgram/L (at mean 18.9 hours after the dose) respectively. Assuming a normal milk intake of 150 mL/kg daily, a fully breastfed infant would receive approximately 0.9 microgram/kg oseltamivir and 3.6 microgram/kg oseltamivir carboxylate daily. It should be noted however, that these levels are from administration of half the normal treatment daily dose.

The studies above do have some limitations (single dose, non-steady state conditions, in one case half normal daily maternal dose and breastfeeding was not established) however, the calculated amount ingested by an infant would be considerably less than the normal infant dose given directly for influenza treatment (4-6 mg/kg daily (7)). From the levels that have been reported in the literature and due to the limited oral bioavailability of oseltamivir carboxylate, clinical effects of maternal treatment with oseltamivir on a breastfed infant would not be expected (11). Due to the availability of data, oseltamivir is preferred in breastfeeding mothers however, zanamivir can be considered if necessary for the maternal condition. If the mother is receiving oseltamivir and the breastfed infant also needs treatment or prophylaxis, the recommended dose of oseltamivir or zanamivir for infants should be given to the infant.

## Zanamivir

*There are no data on zanamivir use during lactation but based on limited oral bioavailability the systemic exposure of a breastfed infant from maternal treatment, via any route, is expected to be insignificant. Although not expected, as a precaution monitor the infant for vomiting or diarrhoea (6).*

Maternal systemic absorption after inhalation of zanamivir is low, approximately 4–17% (12); intravenous administration will result in higher maternal serum concentrations. The serum half-life of zanamivir following administration by inhalation ranges from 2.6 to 5.05 hours (12) and in adults with normal renal function, the half-life following intravenous administration is approximately 2-3 hours (13).

There are no data on the excretion of zanamivir into human breast milk via any route, and the manufacturer advises that the use of zanamivir in breast-feeding mothers should be considered only if the possible benefit to the mother is thought to outweigh possible risk to the child (12, 13).

Zanamivir has extremely limited oral bioavailability (approximately 1–5% (12)) therefore; any drug that is present in milk will be minimally absorbed from the infant's gastrointestinal tract. Its relatively short half- life will reduce the risk of accumulation in a breastfed infant. There is no experience with the use of zanamivir directly in infants younger than 6 months, however the injectable formulation is licensed for treatment in older infants (12). Based on its pharmacokinetic properties the exposure of any breastfed infant, when administered to the mother via any route, would be expected to be insignificant (6,11) If the mother is receiving zanamivir and the breastfed infant also needs treatment or prophylaxis, the recommended dose of oseltamivir or zanamivir for infants should be given to the infant.

## Limitations

Evidence relating to the secretion of oseltamivir in breast milk is limited. It is based on small population, uncontrolled and single-dose studies. There is no evidence relating to the secretion of zanamivir in breast milk and the recommendations are based on pharmacokinetic principles only.

The above information applies to maternal monotherapy and a full-term, fit and healthy infant only. Should the infant be premature, unwell, or the mother taking multiple medication, an individual risk assessment is required. Please contact the UK Drugs in Lactation Advisory Service for advice on 0116 258 6491**/**0121 424 7298 or ukdilas.enquiries@nhs.net.

## References


1. Public Health England. PHE guidance on use of antiviral agents for the treatment and prophylaxis of influenza. Version 10.0. Public Health England September 2019. Accessed 30/07/2020 at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/833572/PHE_guidance_antivirals_influenza_201920.pdf
2. NICE Technology Appraisal Guidance TA158. Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza. September 2008. Accessed 30/07/2020 at http://www.nice.org.uk/guidance/TA158 .
3. NICE Technology Appraisal Guidance TA168. Amantadine, oseltamivir and zanamivir for the treatment of influenza. February 2009. Accessed on 30/07/2020 at http://www.nice.org.uk/guidance/TA168
4. NICE Clinical Knowledge Summary. Prescribing Information, Influenza – Seasonal. Last revised April 2019. Accessed on 30/07/20 at https://cks.nice.org.uk/influenza-seasonal#!prescribingInfo
5. Department of Health. Pandemic Influenza: Recommendations on the use of antiviral medicines for pregnant women, women who are breastfeeding and children under the age of one year. Updated September 2009. Accessed 30/07/2020 at http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_100361
6. Hale TW. Medication and Mother's Milk. Texas: Hale publishing 2014. Available from http://medsmilk.com/menu.html. Accessed on-line 30/07/20.
7. Summary of Product Characteristics. Tamiflu 6 mg/ml powder for oral suspension. Roche Products Ltd. Last revised 08/04/2020 . Available at https://www.medicines.org.uk/emc/ . Accessed 30/07/2020
8. Li W, Excarpe PA, Eisenberg EJ et al. Identification of GS 4104 as an orally bioavailable prodrug of the influenza virus neuraminidase inhibitor GS 4071. Antimicrob Agents Chemother 1998;42:647-653
9. Wentges-van Holthe N, van Eijkeren M, van der Laan JW. Oseltamivir and breastfeeding. Int J Infect Dis 2008;12:451
10. Greer LG, Leff RD, Rogers VL et al. Pharmacokinetics of oseltamivir in breast milk and maternal plasma. Am J Obstet Gynecol 2011;204:524.e1-4
11. Tanaka T, Nakajima K, Murashima A et al. Safety of neuraminidase inhibitors against novel influenza A (H1N1) in pregnant and breastfeeding women. CMAJ 2009;181:55-58.
12. Summary of Product Characteristics. Relenza 5mg/dose inhalation powder . Glaxo Smith Kline UK. Last revised -18/11/2019. Available at https://www.medicines.org.uk/emc/. Accessed 30/07/2020
13. Summary of Product Characteristics. Dectova 10 mg/mL solution for infusion. Glaxo Smith Kline UK. Last revised -01/09/2019. Available at https://www.medicines.org.uk/emc/. Accessed 30/07/2020

## Quality Assurance

### Prepared by
Nicola Dickson, Specialist Pharmacist
Trent Medicines Information Centre and the UK Drugs in Lactation Advisory Service

### Date Prepared
30 July 2020

### Checked by
Vanessa Chapman**,** Director
Trent Medicines Information Service, and the UK Drugs in Lactation Advisory Service

### Date of check
7 August 2020

### Contact
ukdilas.enquiries@nhs.net

### Search strategy
- UKDILAS standard Embase search strategy
- UKDILAS standard Medline search strategy
- UK Drugs in Lactation Information & Advisory Service (UKDILAS) database
- Manufacturer information via eMC (Roche Products Ltd and Glaxo Smith Kline).
- US National Library of Medicine Drugs & Lactation (Lactmed) database. Accessed via http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT
- Medications & Mother's Milk Online. Accessed via http://www.medsmilk.com/
- Relevant national guidance

UKDILAS
UK Drugs in Lactation Advisory Service

**www.sps.nhs.uk/ukdilas**