

UKMi Q&amp;A 96.4

## Can oral fluconazole be used with breastfeeding?

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

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### Background

Fluconazole is a triazole antifungal used orally for treating a variety of superficial fungal infections and either orally or parenterally for systemic infections including candidiasis, coccidioidomycosis and cryptococcosis (1,2). Dosages used in these conditions vary widely. In the UK, fluconazole is available over-the-counter as a single oral 150 mg dose for the treatment of vulvovaginal candidiasis (thrush). This condition is common in women and is even more common during pregnancy with a higher prevalence of both asymptomatic colonisation with *Candida albicans* and symptomatic candidiasis.

The Product Licenses for fluconazole-containing products permit breastfeeding after a single dose of 200 mg fluconazole or less, but that breastfeeding is not recommended after repeated use or after high dose fluconazole (3).

However, a review by the Canadian Motherisk program concluded that there is no need to interrupt breastfeeding when a mother is treated with fluconazole (4).

### Answer

The evidence which quantifies the excretion of fluconazole in breast milk is limited to two case reports.

In a lactating mother taking fluconazole, 200 mg orally once daily, levels in milk were determined on days 18 (0.5 hours pre-dose and 2, 4 and 10 hours post-dose) and 30 (12, 24, 36, and 48 hours post-dose) of treatment (8 and 20 days postpartum respectively) and in maternal plasma on day 18. A peak milk level of 4.1 micrograms/ml was found at 2 hours post dose. The half-life of elimination from breast milk was 26.9 hours, compared to 18.6 hours in maternal plasma with a milk:plasma ratio of 0.9 (5).

In the second case a 12-week postpartum mother was given a single oral dose of fluconazole 150 mg for vaginal candidiasis. The highest milk and plasma levels were 2.93 and 6.42 micrograms/mL respectively at 2 hours after the dose. Milk fluconazole levels were 1.76 and 0.98 micrograms/mL at 24 and 48 hours after the dose, respectively. Milk:serum ratios were 0.46 at 2 hours and 0.85 at 5 and 24 hours. The relatively low milk level at 2 hours post dose was considered to be possibly due to incomplete and early distribution of fluconazole into breast milk. The half-life in milk was about 30 hours, compared to 35 hours in plasma (6).

A review of the use of antifungals during lactation suggests that because fluconazole has excellent bioavailability, which is unaffected by gastric pH, the nursing infant is expected to absorb a significant amount of fluconazole, which is in contrast to the other azoles. In the case of single-dose fluconazole therapy for vaginal candidiasis, the mother could withhold breastfeeding for approximately 4 days after which about 90% of the fluconazole would be excreted. The authors concluded that it may be prudent to discontinue nursing in the case of an extended period of therapy or switch to another azole antifungal (7).

Fluconazole is licensed in the UK for use in neonates. Neonates excrete fluconazole slowly. The neonatal dose of fluconazole for mucosal candidiasis is 3 mg/kg every 72 hours for age 0-2 weeks, the frequency increasing to every 48 hours for age 2-4 weeks and then daily for age over 4 weeks. The doses are doubled for invasive candidal infections (2, 3). Using peak milk level data from these two case reports (5, 6) an exclusively breastfed infant whose mother was taking 200 mg daily of fluconazole would receive a maximum of approximately 0.6 mg/kg daily - based on milk consumption of 150mL/kg/day (8) - which is 60% of the lowest recommended neonatal dosage for age <2 weeks and 20% for infants aged one month and over (2, 3).

Fluconazole has been used successfully during breastfeeding to treat the symptoms of candidal infections (9-12). A survey of members of the Academy of Breastfeeding Medicine found that oral fluconazole is often prescribed for nursing mothers to treat breast candidiasis, especially with recurrent or persistent infections (13). However, it is also considered that some symptoms of breast infection,

breast and nipple pain are frequently inaccurately misdiagnosed to be due to candida infection (14,15) leading to inappropriate treatment with fluconazole, whereas staphylococcal infection is the most likely cause (14).

Fluconazole has also been successfully used in preterm neonates without reported adverse effects to treat candidal infections including: a 28 week gestation infant treated with IV fluconazole, 6mg/kg/d, for 20 days for disseminated candidiasis (16); a 3-day old premature infant treated with IV fluconazole, 5mg/kg/d, for 22 days for candidal meningitis (17); and a 36 week gestation infant treated with IV fluconazole, 6mg/kg/d for 14 days for disseminated candidiasis (18).

## Summary

- ◆ There are very limited data on the excretion of fluconazole in breast milk.
- ◆ Fluconazole, after a 200 mg oral dose, produces levels in breast milk similar to those found in maternal plasma.
- ◆ Fluconazole is recommended for use in the treatment of neonates with fungal infections at a dose starting at 3 mg/kg every 72 hours. The calculated dose of fluconazole ingested by an infant feeding at times of peak milk levels of fluconazole would be approximately 0.6 mg/kg/day, which is 60% of the neonatal dose and 20% of the dose for infants aged one month and over.
- ◆ Fluconazole is often used to treat lactation-associated candidal infections, and has been used to treat serious candidal infections in preterm and full term neonates. There is therefore clinical experience in the exposure of fluconazole to neonates and infants
- ◆ The combination of these factors, and the common use of fluconazole without reported adverse effects in breastfed infants, suggests that oral fluconazole is safe in mothers breastfeeding full term infants, and no interruption of breastfeeding is necessary, regardless of which dosing regime is used.
- ◆ Oral fluconazole use in mothers breastfeeding preterm infants should be approached with caution due to no direct evidence of safety and limited clinical experience.

## Limitations

- Evidence relating to excretion of fluconazole in breast milk is relatively poor.
- There is no evidence, and limited experience, for assessing risks of exposure of preterm infants to levels of fluconazole found in breast milk.
- Set against these limitations is a consensus of expert opinion and the common use of fluconazole without confirmed evidence of risk when used in mothers who are breastfeeding their infants.

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### Search strategy

- Embase and Medline (Standard UKDILAS Search Patterns) [\[link\]](#)
- In-house UKDILAS database
- Medications and Mothers' Milk Online (Medilact): Fluconazole
- Drugs and Lactation Database (LactMed). Toxnet Toxicology Data Network, United States National Library of Medicine. Available from <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>. Fluconazole monograph
- Manufacturers (eMC) of fluconazole products