5 mg twice daily, respectively (335,336), with the lowest concentration 14 hours after oral intake. The tofacitinib concentration was higher in human milk than in plasma at 2 single time points at 5.5 and 8 hours after oral tofacitinib intake (336). Based on the highest milk concentration, both cases revealed that the infant would receive (RID), at worst, 3.4% of the mother's weight-adjusted dosage (335,336). This percentage is higher than found in other drugs used to treat IBD, but lower than the internationally accepted arbitrary safety cutoff value of 10% (310,320,335–339). Considering these findings, along with a mean tofacitinib half-life of 3.2 hours, the labeling recommendation to refrain from breastfeeding for at least 18 hours after oral intake of the immediate-release product and 36 hours after the sustained-release product makes breastfeeding not feasible in a mother regularly taking this medication (278). Of note, in 3 infants exposed to tofacitinib during pregnancy and breastfeeding, normal infant development was noted at the age of 3.5, 12, and 14 months of age, respectively (335,340). Moreover, at 12 weeks of age, a comprehensive immunologic assessment was conducted on a fully breastfed infant exposed to tofacitinib, with normal results (341).

With respect to upadacitinib and filgotinib, it is currently unknown whether these drugs or their metabolites are excreted in human milk. Both European and United States labeling recommend avoidance of breastfeeding (279,280,307).

In summary, due to limited or no human safety data including unknown effects on the immune system of the suckling infant, breastfeeding should be avoided on S1P-receptor modulator or a JAKi therapy at this time. Careful monitoring of the infant is recommended if the patient chooses to breastfeed despite the current recommendation against it.

Antibiotics

Short-term use of most antibiotics during lactation is generally considered low risk. Metronidazole and ciprofloxacin are the most frequently prescribed antibiotics for patients with IBD. Metronidazole and its metabolite are excreted into breast milk with a median absolute infant dose of 1.59 mg/kg/d equivalent to 10.61% of the 'therapeutic infant dose.' (342) Passmore and colleagues calculated that a breastfed newborn consuming 500 mL of milk daily from a mother taking 400 mg of oral metronidazole 3 times daily would receive less than 10% of the recommended metronidazole dose for newborns (343). Infants exposed to metronidazole through breast milk have shown instances of diarrhea and increased growth of *Candida* species in oral and perianal swabs (307). After a single 2-gram dose of metronidazole in breastfeeding women, peak drug concentration in breast milk occurs 2–4 hours post-administration, gradually decreasing over 12–24 hours (344). Given relatively high exposure to metronidazole and its metabolite through breast milk, and its unknown effects on the microbiome and immune system of the infants, we generally advise against breastfeeding for mothers taking metronidazole. However, if a short course of oral metronidazole (eg, 1 week) is necessary, we recommend closely monitoring the infant for possible effects on gastrointestinal flora, such as diarrhea or candidiasis.

Ciprofloxacin, a fluoroquinolone, has minimal concentrations in breast milk. Although milk calcium could potentially reduce absorption of small fluoroquinolone amounts in milk, there is insufficient data to confirm or refute this hypothesis (307). In a study of 3 nursing women receiving 750 mg ciprofloxacin twice daily, the peak concentration in breastmilk of 3.79 mg/L occurred 2 hours after maternal intake, equivalent to an estimated low maximum infant exposure of 0.57 mg/kg/d. Of note, the ciprofloxacin concentration in milk at 12 and 24 hours after intake reached a very low concentration of 0.20 mg/L and 0.02 mg/L, respectively (345). Very few side effects have been reported in newborns of mothers treated with ciprofloxacin during lactation (307). In summary, ciprofloxacin is of low risk in nursing mothers. Monitoring of the infant for potential effects on the gastrointestinal flora such as diarrhea or candidiasis is advisable. Other commonly used antibiotics in IBD, including amoxicillin and vancomycin, are also considered low risk in nursing mothers (307).

Medication for endoscopy while breastfeeding

As highlighted in the 2012 guideline for endoscopy in pregnant and lactating women by the American Society for Gastrointestinal Endoscopy (ASGE), the sensitivity to and risks of sedation in a lactating woman are comparable to those for any adult (116).

Midazolam is excreted in low doses in breast milk (307). A mother undergoing surgery received a single intravenous dose of 6 mg of midazolam for anesthesia induction. The concentration of midazolam in her breastmilk was 25 μg/L at 30 minutes post-dose, 12 μg/L at 1 hour post-dose, and 7 μg/L at 2 hours post-dose. After 4 hours, the drug was undetectable (<5 μg/L) (307,346). In another study, 5 women who were 6–15 weeks postpartum, were given a single 2-mg intravenous dose of midazolam before undergoing general anesthesia with propofol and fentanyl. Multiple milk samples were collected from each woman between 5 and 24 hours after the injection. It was estimated that the infants would receive an average of 0.016 μg/kg of midazolam in the 24 hours following a single dose, which corresponds to 0.06% of the RID. Hydroxy-midazolam levels were not measured (307,347). This amount of midazolam in breast milk is unlikely to affect a healthy, full-term infant. The 2012 ASGE guideline recommends withholding nursing of the infant for 4 hours following administration of midazolam, given the paucity of data. With a newborn or preterm infant, a cautious approach would be to wait a period of 6–8 hours before resuming nursing (307). After conscious sedation, breastfeeding can be resumed as soon as the mother has recovered sufficiently to nurse (307).

Fentanyl is excreted in low doses in breast milk (307). Five women, who were 6–15 weeks postpartum, received a single intravenous dose of 100 μg of fentanyl before undergoing general anesthesia. Multiple milk samples were collected from each woman between 5 and 24 hours after the injection. It was estimated that infants would receive an average of 0.005 μg/kg of fentanyl in the 24 hours following a single dose, which is approximately 0.38% of the RID (347). This small amount of fentanyl in breast milk is unlikely to affect a healthy, full-term infant. Therefore, no waiting period or discarding of milk is required before resuming breastfeeding after fentanyl is used for endoscopy. After conscious sedation, breastfeeding can be resumed as soon as the mother has recovered sufficiently to nurse (307).

Propofol is excreted in very low doses in breast milk (307). Five women, who were 6–15 weeks postpartum, received a single intravenous dose of 2.5 mg/kg of propofol before undergoing general anesthesia. Multiple milk samples were collected from each woman between 5 and 24 hours after the injection. It was estimated that infants would receive an average of 0.0052 mg/kg of propofol in the 24 hours following a single dose, which