Table 2. Substance Use Disorders Treatment Pharmacokinetics

SUD treatment	*Peak effect*[a]	*Half-life*[a]	*RID (%)*
Buprenorphine (SL)	1–3 hours[237]	27–37 hours[237]	0.1–2.5[9]
Methadone	1–7.5 hours[237]	8–59 hours[237]	1.9–6.5[9]
Naltrexone	PO: 2 hours[237]	PO: 4 hours	1[9]
	IM: 2 hours (first peak), 2–3 hours (second peak)[237]	IM: 5–10 days[237]	
Acamprosate	3–8 hours[237]	20–33 hours[237]	N/A
Disulfiram	12 hours[237]	60–120 hours[237]	N/A
NRT	Transdermal: 4 hours	Transdermal: 4 hours[237]	N/A
	Gum: 0.5 hours[237]		
Varenicline	3–4 hours[237]	24 hours[237]	N/A
Bupropion	3–4 hours[237]	21 hours[237]	2.0–11[9,220]

[a]Peak and half-life values reference adult pharmacokinetic data for a potential breastfeeding individual.
IM, intramuscular; NRT, nicotine replacement therapy; PO, by mouth; RID, relative infant dose; SL, sublingual; SUD, substance use disorder.

Methadone, a full opioid agonist, is well studied in breastfeeding. Methadone concentrations in human milk are low, with a RID of 3% (Table 2). Breastfeeding should be encouraged, if desired, regardless of the methadone dose.[13,17,200] During periods of methadone titration, particularly if the dose exceeds 100 mg or is initiated postpartum, infants should be monitored for sedation and respiratory depression.[13,200–202] Long-term effects of methadone exposure through breastfeeding are poorly understood. One prospective study among 200-breastfed methadone-exposed infants found some motor delay (1.5 standard deviations) among 38% of exposed infants compared to matched controls.[203] However, given the known benefits to the parent and evidence showing breastfeeding reduces NOWS among opioid-exposed infants, we strongly recommend continuation of methadone while breastfeeding.[85,203,204]

Buprenorphine, a partial opioid agonist, has growing evidence that suggest minimal concentrations in human milk, with a RID of 0.38% (Table 2).[205] A 2016 study examining breast milk and infant plasma buprenorphine concentrations at 2, 3, 4, 14, and 30 days postdelivery among 10 buprenorphine-breastfeeding mother–infant dyads found low breast milk and infant plasma buprenorphine levels.[206] Observational data suggest there are few acute infant harms associated with buprenorphine breast milk exposure regardless of maternal dose, and breastfeeding in individuals taking buprenorphine has been found to reduce NOWS severity.[207–211] Long-term infant safety data remains lacking. In general, breastfeeding should be encouraged for women taking buprenorphine.[212] Newer monthly injectable buprenorphine formulations have not yet been studied with lactation. There are concerns about a preservative contained in the injection called N-methyl-2-pyrrolidone that may be toxic, but concentrations in breast milk are unknown.[212]

For individuals interested in providing breast milk who are stable in recovery and doing well on these medications, decisions around changing medications should be made in consultation with an addiction expert given the risks associated with changes to treatment. Like other opioids, both methadone and buprenorphine may increase prolactin, but an impact on breastfeeding has not been shown.

Naltrexone, an opioid antagonist, has limited safety data during lactation. Naltrexone is available in several formulations (oral tablet, extended-release monthly injection, and multiyear implantable device). A single case study from an individual on a stable daily oral dose of 50 mg of naltrexone assessed postpartum maternal serum and breast milk samples and infant serum samples.[213] The calculated 24-hour infant dose was low, indicating low infant exposure. Developmental assessments of the infant at 6 weeks were normal.[213] Though data are limited, given the minimal transmission of naltrexone and its metabolite into breast milk, breastfeeding is recommended.

Alcohol use disorder treatment

There are three medications commonly used to treat alcohol use disorder (AUD): acamprosate, naltrexone (discussed above under OUD treatments), and disulfiram (Table 2). For non-breastfeeding individuals, the American Psychiatric Association (APA) recommends acamprosate or naltrexone as first-line treatment for moderate-to-severe AUD, with disulfiram considered second-line therapy under close supervision.[214,215] Given there is no amount of alcohol that is considered safe during pregnancy, use of pharmacotherapy for AUD during the pregnancy can decrease the risk for Fetal Alcohol Spectrum Disorders which have significant implications for child health.[216]

There are no data available on the transfer of acamprosate into breast milk or RID. Due to its low molecular weight and lack of protein binding, it is possible that it could readily enter breast milk; however, it has low oral absorption.[9] Disulfiram is used less frequently to treat AUD and works by inhibiting aldehyde dehydrogenase (ADH), one of the enzymes responsible for the metabolism of alcohol.[9] There is no data on the transfer of disulfiram into breast milk or RID; however, it is thought that it may be transferred into milk due to its small molecular weight. It is possible that any quantity in the milk could produce long-lasting inhibition of the infant's ADH.[9] Any ingestion of alcohol while taking disulfiram causes alcohol toxicity; thus, if the breastfeeding mother were to use any alcohol at the same time as disulfiram, it could potentially cause toxicity in the infant.

There is insufficient data to make a recommendation for acamprosate or disulfiram; however, given the pharmacokinetics and demonstrated benefits of acamprosate in individuals with AUD, this is likely safer than disulfiram during breastfeeding.

Tobacco smoking cessation treatment

Individuals who continue to smoke tobacco while breastfeeding should be offered pharmacotherapy treatments to assist with cessation given the clear risks of smoking to the