eTable 2. Recommendations for the Use of Symptomatic Treatments Commonly Prescribed for MS During Pregnancy and/or Breastfeeding

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
Depression and anxiety	Duloxetine[1]	Caution during pregnancy[2]	Data indicate that use in the month before delivery may be associated with an increased risk of postpartum hemorrhage[1] Neonates exposed late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding[1] The risk of relapse when discontinuing duloxetine should be considered[1]	May be used when breastfeeding[1,2]	There are reports of sedation, poor feeding, and poor weight gain in infants exposed to duloxetine through breast milk[1] The developmental and health benefits of breastfeeding should be considered alongside the mother's clinical need for duloxetine[1]

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
Depression	Sertraline[3]	May be used during pregnancy[4]	Studies in the first trimester highlight no change in the major birth defect risk vs background rates[3] Exposure in the third trimester may increase the risk of persistent pulmonary hypertension and symptoms of poor adaptation in the neonate[3]	May be used when breastfeeding[4]	Data demonstrate low levels of sertraline and its metabolites in human milk[3]
Fatigue	Amantadine[5]	No during pregnancy[5]	Amantadine-related complications during pregnancy have been reported[5]	No during breastfeeding[5]	Amantadine is present in breast milk and adverse drug reactions have been reported in breastfed infants[5]

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
Fatigue	Modafinil[6]	Only if potential benefit justifies potential risk to fetus[6,7]	There are no adequate and well-controlled studies of modafinil in pregnant women[6] Intrauterine growth restriction and SA have been reported in associated with modafinil[6]	Caution during breastfeeding[6]	It is not known whether modafinil is present in breast milk[6,8] No adverse events are known from the limited information available on women who breastfed their infant while receiving modafinil[6,8]
Mobility issues	Dalfampridine[9]	No during pregnancy[9,10]	Adequate data on the developmental risk associated with dalfampridine during pregnancy are not available[9] Based on animal data, may cause fetal harm[9]	No during breastfeeding[10]	There are no data available on the presence of dalfampridine in breast milk or potential effects on breastfed infants[9]

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
Mobility issues	Fampridine[11]	No during pregnancy[11]	Limited information[11] Animal studies have demonstrated reproductive toxicity[11]	No during breastfeeding[11]	Limited information. It is not known whether fampridine is excreted in breast milk[11]
Muscle stiffness	Baclofen[12]	No during pregnancy[13]	Adequate data on the developmental risk associated with baclofen during pregnancy are not available[12] Withdrawal symptoms can occur in neonates whose mothers have been treated with oral baclofen throughout pregnancy[12]	May be used when breastfeeding[12,13]	Small amounts of baclofen have been detected in breast milk[12] Withdrawal symptoms can occur in breastfed infants following maternal discontinuation or cessation of breastfeeding[12]
Muscle stiffness	Cyclobenzaprine[14]	Only if clearly needed[15]	No drug-associated risk of major birth defects, miscarriage, or adverse	Caution when breastfeeding[14,15]	No data are available on cyclobenzaprine in milk, effects on

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
			maternal or fetal outcomes identified from case reports[14]		breastfed infants, or effects on milk production[14]
Muscle stiffness	Tizanidine[16]	Benefit should outweigh risk[16,17]	Based on animal data, may cause fetal harm[16]	Caution when breastfeeding[16]	It is not known whether tizanidine is excreted in human milk[16]
Muscle stiffness/spasms	Intramuscular Botox[18]	Benefit should outweigh risk to the unborn fetus[18]	In animal studies, there were adverse effects on fetal growth (decreased fetal weight and skeletal ossification) at clinically relevant doses, which were associated with maternal toxicity[18]	Caution when breastfeeding[18]	No data exist on the use of botulin A during breastfeeding, but excretion into breast milk is considered unlikely[18,19]
Pyelonephritis	Parenteral antibiotic therapy[20]	May be used during pregnancy[20]	Use should be guided by urine culture and sensitivity reports as soon as available[7]	May be used when breastfeeding (recommendations for individual antibiotics should be followed)[21]	Intravenous antibiotics are unlikely to be passed on to babies in sufficient amounts to cause issues via milk[21]

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
Seizures and neuropathic pain	Gabapentin[22]	Benefit should outweigh risk to the unborn fetus[23]	Adequate data on the developmental risks for gabapentin in pregnancy are not available[22] Based on animal data, may cause fetal harm[22]	May be used when breastfeeding[23]	Gabapentin passes into breast milk in small amounts, but has not been known to cause side effects in breastfed infants[23]
Seizures and neuropathic pain	Carbamazepine[24]	Benefit should outweigh risk to the unborn fetus[24,25]	Can cause fetal harm when administered to pregnant women[24]	No during breastfeeding[24]	Carbamazepine and its epoxide metabolite are transferred into breast milk and may cause serious adverse events in nursing infants[24]
Seizures	Lamotrigine[26]	Benefits should outweigh risk to the unborn fetus[27]	Data from prospective exposure registries and epidemiological studies of pregnant women have not detected an increased frequency of	May be used during breastfeeding[26]	Lamotrigine is present in breast milk[26] Patients should monitor their children for potential adverse events when

Symptom	Drug	Pregnancy		Breastfeeding	
		Use during pregnancy	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
			major congenital malformations[26] Dose adjustments may be necessary to maintain clinical response[26]		breastfeeding while receiving lamotrigine[26]
Seizures	Levetiracetam[28]	May be used during pregnancy[29]	Based on animal data, may cause fetal harm[28] Plasma levels of levetiracetam may fall during pregnancy, particularly during the third trimester; dose adjustments may be necessary to maintain clinical response[28]	May be used when breastfeeding[28,29]	Levetiracetam may be excreted in breast milk, but there are no data available on the effects of levetiracetam on breastfed infants[28]
Seizures	Oxcarbazepine[30]	Benefit should outweigh risk to the unborn[31]	Plasma concentrations of the active metabolite of oxcarbazepine may fall	Caution during breastfeeding[31]	Oxcarbazepine and its active metabolite pass into breast milk, but

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
			during pregnancy; pregnant patients should be monitored carefully[30] There is a risk of seizures in pregnant patients receiving oxcarbazepine[30] Data from limited pregnancies suggest that use is associated with congenital malformations[30]		their effects on breastfed infants and milk production are unknown[30]
Urinary frequency and incontinence	Solifenacin[32]	Benefit should outweigh risk to the unborn fetus[33]	No information in pregnant women available[32]	Caution when breastfeeding[33]	No data are available on solifenacin in milk, effects on breastfed infants, or effects on milk production[32]

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
Urinary incontinence	Oxybutynin[34]	Benefit should outweigh risk to the unborn fetus[35]	There are no adequate and well-controlled studies of oxybutynin in pregnant women[34]	Caution when breastfeeding[35]	It is not known whether oxybutynin is excreted in breast milk[34]
Urinary tract infection	Amoxicillin[36]	Only if clearly needed[36]	There are no adequate and well-controlled studies of amoxicillin in pregnant women[36]	Caution when breastfeeding[36]	Penicillins are excreted in human milk and may lead to sensitization in nursing infants[36]
Urinary tract infection	Cephalexin[37]	May be used during pregnancy[37]	There are no adequate and well-controlled studies of cephalexin in pregnant women[37]	Caution when breastfeeding[37]	Cephalexin is excreted in human milk[37]
Urinary tract infection	Oral nitrofurantoin[38]	May be used during pregnancy[38]	There are no adequate and well-controlled studies of oral nitrofurantoin in pregnant women[38]	Caution during breastfeeding[38]	Trace amounts of nitrofurantoin have been detected in breast milk There is potential for serious adverse events

		Pregnancy		Breastfeeding	
Symptom	**Drug**	**Use during pregnancy**	**Recommendation details**	**Use during breastfeeding**	**Recommendation details**
					in nursing infants <1 month of age[38]
Viral infection	Acyclovir[39]	Benefit should outweigh risk to the unborn fetus[39]	There are no adequate and well-controlled studies in pregnant women; however, a small registry study showed that there was no increased risk of birth defects with acyclovir exposure[39]	Caution when breastfeeding[39]	Acyclovir has been documented in breast milk following oral administration[39]
Viral infection	Valacyclovir[40]	Benefit should outweigh risk to the unborn fetus[41]	Decades of clinical trial data have found no association between valacyclovir or its metabolite with major birth defects in pregnant women[40]	Caution when breastfeeding[40]	There is no information on the presence of valacyclovir in breast milk, but its metabolite, acyclovir, is present in breast milk at levels that would not be expected to cause side

		Pregnancy		Breastfeeding	
Symptom	Drug	Use during pregnancy	Recommendation details	Use during breastfeeding	Recommendation details
			Accumulating evidence from large pregnancy registries that oral valacyclovir can be used during pregnancy[40]		effects in breastfed infants[40]

Abbreviations: MS = multiple sclerosis; SA = spontaneous abortion.

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