Clinical Guidance

Multiple Sclerosis in Pregnancy

Document Detail	
Document Type	Clinical Guidance
Document name	Multiple Sclerosis in Pregnancy
Sites covered	Epsom & St Helier's, St Georges, Kingston, Croydon, Royal Surrey, East Surrey, Ashford & St Peters
Document location	SWL & SH Clinical Guidance Database
Version	1
Effective from	25.09.2024
Review date	25.09.2027
Owner	Madeleine Trowsdale Stannard (ST5 Obstetrics & Gynaecology Registrar)
Author(s)	Madeleine Trowsdale Stannard (ST5 Obstetrics & Gynaecology Registrar) Carlotta Modestini (Consultant Obstetrician & Maternal Medicine Specialist) Siara Teelucksingh (Consultant Obstetric Physician) Amanda Ali (Consultant Obstetrician & Maternal Medicine Specialist)
Approved by: Date:	Clinical Reference Group 21.10.2024

Related documents	Dobson R, Dassan P, Roberts M*, et al* UK consensus on pregnancy in multiple sclerosis: 'Association of British Neurologists' guidelines *Practical Neurology* 2019;**19:**106-114. Iyer P, Wiles K, Ismail A, et al. Developing evidence-based guidelines for the safety of symptomatic drugs in multiple sclerosis during pregnancy and breastfeeding: A systematic review and Delphi consensus. *Multiple Sclerosis Journal*. 2023;29(3):395-406.
Keywords	Multiple Sclerosis

Change History		
Date	Change details, since approval	Approved by

Contents

1.0 **Introduction**

Multiple Sclerosis (MS) is a condition which commonly affects women of reproductive age and is therefore commonly seen in pregnancy. This guideline aims to provide clinicians caring for women with MS in pregnancy with a standardized guide to aid counselling, investigation, and management from the preconception period, during pregnancy and postpartum.

2.0 **Scope**

This guideline is aimed at obstetricians, GP's and midwives caring for women with Multiple Sclerosis in pregnancy. This guideline does not cover diagnosis of Multiple Sclerosis.
For diagnosis of Multiple Sclerosis please refer to the NICE Guidance 'Multiple sclerosis in adults: management' (NG220 published in June 2022).

3.0 **Guidance**

3.1 Pre-pregnancy counselling (PPC):

PPC should be advised for all women with childbearing potential and MS at, or soon after diagnosis. This should be repeated annually, especially for women who are on or considering treatment with Disease Modifying Drugs (DMDs).

The key points which should be discussed are:

- MS does not affect fertility
- Pregnancy does not worsen MS related disability in the short or long-term
- DMDs should not be routinely deferred in women of reproductive age (see below for details regarding medications)
- Those who discontinue DMDs in pregnancy may experience a relapse of symptoms in pregnancy
- When DMDs are restarted it usually takes around 3/12 to achieve full effect of the drug
- Some may experience a reduction of symptoms in pregnancy, but there remains a chance of relapse. The risk of a relapse is highest in the postpartum period

3.2 Antenatal management:

- Refer to the maternal medicine team for review
- Prescribe vitamin D supplementation – 2000-4000IU per day
- Encourage patient to join MS pregnancy register, signpost to pregnancy information resources, and provide drugs information leaflet
- Prescribe high dose folic acid (5mg daily) for patients taking carbamazepine/pregabalin/gabapentin
- Patients should be counselled regarding use of DMDs (see below for details regarding medications) – joint decisions between patient, obstetric, maternal medicine and neurology teams should be made
- Assess MS symptoms and control
- If sensory bladder symptom or incomplete bladder emptying - consider MSU each visit.
- Ensure patients neurology team are aware of pregnancy and establish link if neurologist is at different trust
- Consider anesthetic referral if known new spinal lesions

- There is no indication for growth scans based on a diagnosis of MS, though this may be considered for those taking DMDs
- When investigating new symptoms, MRI is safe, although gadolinium contrast should be avoided
- IV methylprednisolone can be used for relapse in pregnancy
- If unresponsive to steroids, plasma exchange can be considered

3.3 Intrapartum care:

- There is no indication for induction of labour. Mode of delivery should be as per obstetric indications
- Women with sensation loss below T11 may be unaware of the onset of symptoms so should be counselled regarding symptoms such as increase in pain, spasticity, flushing and gastrointestinal symptoms
- Consider physical disability when positioning patient
- There is no contraindication to regional or general anaesthesia
- For troubling spasticity in labour: use epidural or diazepam
- IV hydrocortisone should be given in labour for those taking steroids in pregnancy

3.4 Postpartum care:

- Breastfeeding should be encouraged as it improves bonding and may reduce postnatal depression. There is no evidence that it reduces the chance of a postpartum flare
- Vitamin D should be continued
- IV methylprednisolone can be used for relapse in the postpartum period

3.5 Medications

- Early treatment with DMDs may reduce long-term disability. It is therefore important not to unnecessarily withhold treatment.
- In general, aim for the lowest dose required to maintain symptom control, and the fewest medications overall when multiple medications are used. Risk and benefit should be weighed up and discussed with the patient and their team.

3.5a Medications for MS itself:

Role in pregnancy	Drug treatment
Licensed in pregnancy	**IFN-B (Avonex, Betaferon, Extavia, Plegridy, Rebif, Copaxone)** **Copaxone is the only drug with license in pregnancy** ✓ Safe to continue until conception ✓ No evidence of harm to fetus • Risk vs benefit discussion regarding continuing/discontinuing • If stopped, it will take 3/12 to reach full effect after restarting • Encourage restarting in postpartum period – benefit outweighs risk
Consider use in pregnancy based on risk vs benefit	**Natalizumab** ✓ No evidence of congenital malformations ✓ Exposure in late pregnancy may result in minor haematological abnormalities ✓ Consider continuing in pregnancy with last dose ~34/40 ✓ High risk of relapse if discontinued ✓ Those eligible usually have severe disease, hence continuing medication in these patients may be even more important ✓ Low absorption in breastfeeding
Not recommended in pregnancy	**Teriflunomide** ! Teratogenic in animal studies ! Washout period of 2yrs recommended before conception (accelerated elimination period may be used) ! In unplanned pregnancies, accelerated elimination period and referral for fetal medicine scan is recommended ! Breastfeeding is contraindicated
	Dimethyl fumarate ! Limited data in pregnancy ! Breastfeeding is contraindicated
	Fingolimod ! Limited data in pregnancy ! Washout period of 2/12 ! In unplanned pregnancy, stop immediately ! Breastfeeding is contraindicated
	Ocrelizumab ! Likely harmful ! Washout period of 1yr ! In unplanned pregnancy, stop immediately ! Breastfeeding is contraindicated
	Cladribine ! Teratogenic ! Washout period of 6/12 ! Breastfeeding is contraindicated
	Alemtuzumab ! Washout period of 4/12 ! Breastfeeding is contraindicated ! High risk of autoimmune disease for 4 years after taking

3.5b Medications for MS associated symptoms: (Rommer PS 2019 Oct)

- The commonest reported symptoms of MS in pregnancy are fatigue and spasticity. Other symptoms include depression, pain, urinary tract infections and bladder symptoms

- **Fatigue**
  - Fatigue and difficulty sleeping are common symptoms in women with MS.
  - Screen for anaemia and optimise haemoglobin
  - For women who take medications for sleeping:
    - *Amantadine*: not recommended in pregnancy or breastfeeding (limited evidence)
    - *Modafinil*: not recommended in pregnancy or breastfeeding (limited evidence and evidence of possible congenital malformation if used in first trimester) – if used in the third trimester, monitor neonate for withdrawal
    - *Zopiclone*: consider use – monitor neonates for drowsiness, and then withdrawal if discontinued
- **Spasticity**
  - Refer to a neuro-physiotherapist
  - Where medication is necessary:
    - *Clonazepam/Diazepam:* both are safe in pregnancy and breastfeeding. Can be used for short periods – avoid abrupt withdrawal
    - *Baclofen*: may be used with caution (possible increased risk of congenital malformation)
    - *Fampridine*: avoid as limited evidence exists
    - *Sativex*: avoid as evidence of cannabis (similar drug) suggests harm
  - If clonazepam, diazepam, or baclofen are used, monitor the neonate for signs of withdrawal

- **Depression** should be managed as in all pregnant women.
  - Postpartum depression is more common in women with MS so women should be considered for enhanced postnatal support. The mainstay of medication is with SSRIs

- **Pain** should be treated promptly with:
  - Paracetamol and dihydrocodeine as first line medications.
  - Ibuprofen can be used except for in the first trimester and after 32 weeks.
  - When considering neuropathic analgesic agents: for all medications the risk of withdrawal or switch in medications should be weighed up against the risk of taking the medication.
    - *Amitriptyline/Nortriptyline:* limited evidence demonstrates safety in pregnancy and breastfeeding. This is the first choice neuropathic agent if needed.
    - *Carbamazepine*: low doses may be used to control pain in MS. Most evidence is extrapolated from use in epilepsy where much higher doses are used, hence risks of malformation and neurodevelopmental delay may be lower when lower doses are used in MS. Carbamazepine may be used if benefit outweighs risk. High dose folic acid should be prescribed in conjunction.
    - *Duloxetine*: there is not enough evidence to recommend use in pregnancy, although evidence suggests safety when breastfeeding.
    - *Gabapentin/pregabalin*: limited evidence exists. Gabapentin is preferable to pregabalin as one study suggested potential increase in malformation with pregabalin. High dose folic acid should be prescribed in conjunction.
    - *Tramadol*: limited evidence exists. Can be considered if other agents are ineffective.
  - Where lignocaine patches are available and used prior to pregnancy, people should be counselled regarding a complete lack of clinical safety data; however animal studies do not indicate a teratogenic potential.
  - Neonates exposed to opiates or neuropathic agents should be monitored for withdrawal.
  - Additional measures sures as physiotherapy, TENs machines, ice and heat packs.

- **Urinary tract infections (UTI)**
  - Are more common in pregnancy and may temporarily worsen symptoms of MS, so women should be counselled to present early if they develop any symptoms of UTI.
  - Treatment of UTI should be as per usual for pregnant women.

3.6 Non-pharmacological therapy:

- Physiotherapy: specialist neuro-physiotherapy can benefit pain, depression, spasticity, fatigue and insomnia.
- CBT and psychological therapy: can benefit pain, depression, fatigue and insomnia.

4.0 References and abbreviations

References

1. NICE guideline 'Multiple sclerosis in adults: management' (NG220) https://www.nice.org.uk/guidance/ng220.
2. Clancy M, Drerup M, Sullivan AB. "Outcomes of Cognitive-Behavioral Treatment for Insomnia on Insomnia, Depression, and Fatigue for Individuals with Multiple Sclerosis: A Case Series." *Int J MS Care.*, 2015 Nov: 17(6):261–7.
3. Comi G, Radaelli M, Soelberg Sørensen P. "Evolving concepts in the treatment of relapsing multiple sclerosis. ." *Lancet*, 2017: 389:1347–56.
4. Dobson R, Dassan P, Roberts M, et al. "UK consensus on pregnancy in multiple sclerosis: 'Association of British Neurologists' guidelines." *Practical Neurology*, 2019: 19:106-114.
5. Iyer P, Wiles K, Ismail A, Nanda S, Murray K, Hughes S, Ford HL, Pearson OR, White S, Bonham N, Hoyle N, Witts J, Middleton R, Brex PA, Rog D, Dobson R. "Developing evidence-based guidelines for the safety of symptomatic drugs in multiple sclerosis during pregnancy and breastfeeding: A systematic review and Delphi consensus. ." *Mult Scler.* , 2023 Mar;: 29(3):395-406. doi: 10.1177/13524585221148094. Epub 2023 Feb 5. PMID: 36740816.
6. Learmonth YC, Motl RW. "Exercise Training for Multiple Sclerosis: A Narrative Review of History, Benefits, Safety, Guidelines, and Promotion." *Int J Environ Res Public Health* , 2021 Dec : 16;18(24). Available from: http://dx.doi.org/10.3390/ijerph18.
7. Rommer PS, Eichstädt K, Ellenberger D, Flachenecker P, Friede T, Haas J, et al. "Symptomatology and symptomatic treatment in multiple sclerosis: Results from a nationwide MS registry." *Mult Scler.*, 2019 Oct: 25(12):1641–52.

Abbreviations

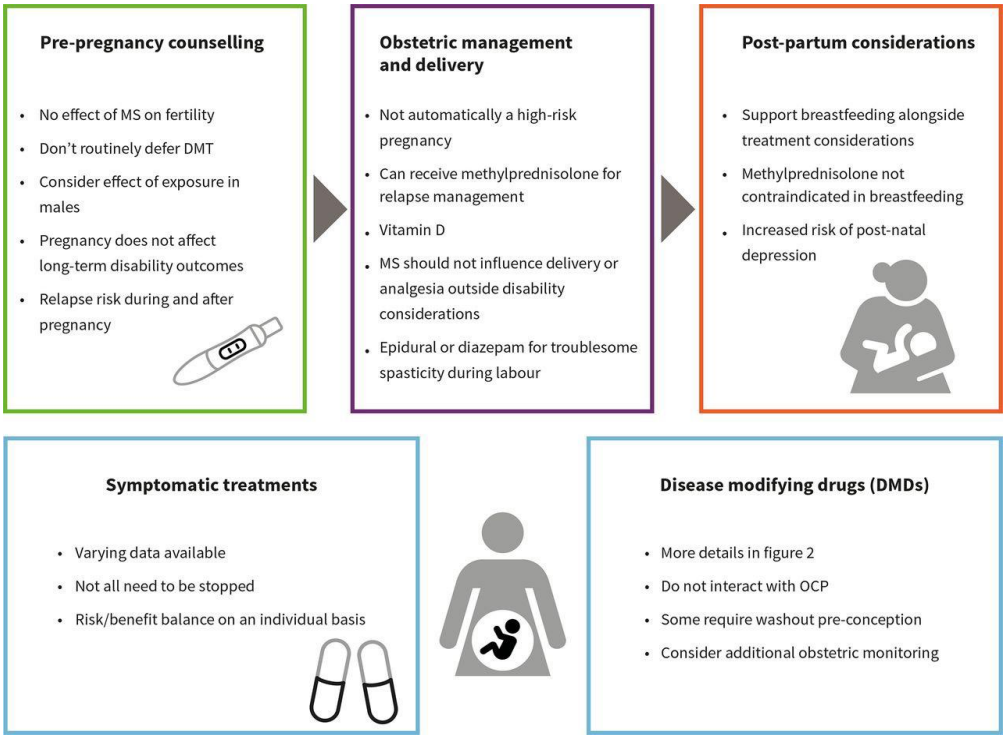
MS = Multiple Sclerosis
PPC = Pre-pregnancy counselling
DMD = Disease modifying drugs
UTI = Urinary tract infections

5.0 Patient information booklet & MS Register

MS pregnancy information https://ms-uk.org/pregnancy-and-ms-choices-booklet/
MS Pregnancy Register https://www.ukmsregister.org/pregnancy

Appendix 1: Summary of Pre-pregnancy, Antenatal and Postnatal recommendations

Infographic summarising topics to consider during prepregnancy counselling.

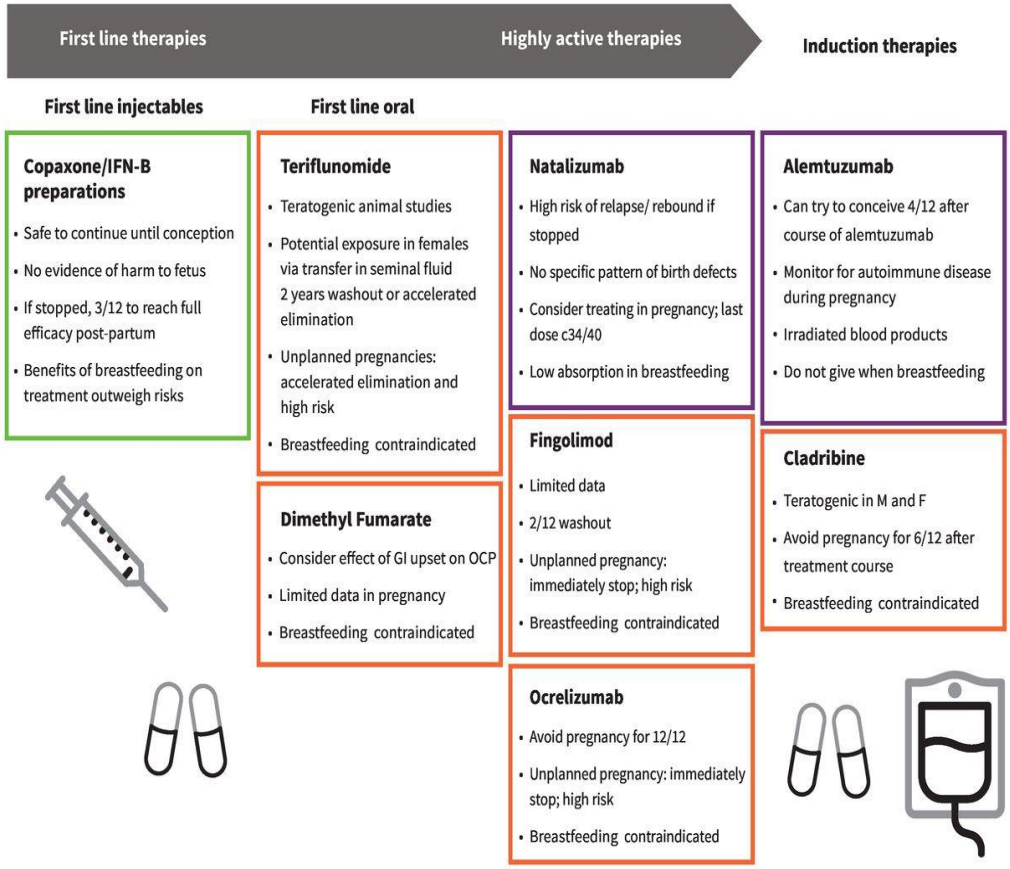


Ruth Dobson et al. Pract Neurol 2019;19:106-114

South West London & Surrey Heartlands SWL & SH MATERNAL MEDICINE NETWORK

Appendix 2: Disease modifying drugs during pregnancy and breastfeeding

Infographic summarising advice about the use of disease-modifying drugs during pregnancy and in breastfeeding.



Ruth Dobson et al. Pract Neurol 2019;19:106-114

PN