

Best practice management of women of child-bearing age with inflammatory rheumatic diseases

Guidelines

summarising clinical guidelines for primary care

Guidelines identified a need for clinical guidance in this area and approached UCB Pharma Ltd for an educational grant to support the development of a working party guideline. This working party guideline was developed by *Guidelines*, and the Chairs and members of the group were chosen by and convened by *Guidelines*. The content is independent of and not influenced by UCB Pharma Ltd, who checked the final document for technical accuracy and to ensure compliance with regulations.

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Best practice management of women of child-bearing age with inflammatory rheumatic diseases

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Introduction and rationale for this guidance

Estimates of the prevalence of inflammatory rheumatic diseases in women of child-bearing age range from 7 per 100,000 for systemic sclerosis to 130 per 100,000 for psoriatic arthritis.¹ Rheumatoid arthritis, axial spondyloarthritis, and systemic lupus erythematosus (SLE) fall within this range. The prevalence of Sjögren syndrome and primary systemic vasculitis is likely to be low as they usually occur in those aged over 40 years who are towards the upper limit of child-bearing age.¹ This working party guideline covers the management of these inflammatory rheumatic diseases in women of child-bearing age and is intended for all healthcare professionals who interact with these patients. Treatment of chronic pain syndromes such as fibromyalgia are outside the scope of this guidance and patients with these conditions who are pregnant or considering pregnancy will require appropriate specialist advice.

Improved treatments for inflammatory diseases mean that many women with these conditions will have better control of their disease and quality of life than they have in the past.^{1,2} This disease suppression has meant that women with severe disease who would previously not have considered having a child are now more likely to consider pregnancy as an option and need appropriate advice.^{1,2} Data on the effect of pregnancy on rheumatic diseases are conflicting and while some studies have suggested improvements in disease activity, others have reported the opposite.¹ A recent systematic review and meta-analysis found that rheumatoid arthritis disease activity improved in 60% of patients during pregnancy; however, it also found that 46.7% of patients experienced disease flares postpartum.³ In addition, active rheumatic disease is associated with a number of adverse pregnancy outcomes (Box 1).^{1,4} Therefore, disease-modifying anti-rheumatic drugs (DMARDs) compatible with pregnancy are required to control disease activity before and during pregnancy to ensure a positive pregnancy outcome.^{1,2}

In 2016, the British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology published a two-part guideline on prescribing drugs in patients with rheumatic diseases before and during pregnancy and breastfeeding.^{5,6}

Box 1: Adverse pregnancy outcomes due to uncontrolled inflammatory rheumatic diseases^{1,4}

- › Fetal growth restriction and small for gestational age
- › Fetal loss
- › Gestational hypertension and pre-eclampsia
- › Preterm delivery
- › Complications of labour, such as increased risk of caesarean section
- › Neonatal lupus and congenital complete heart block
- › Venous thromboembolic disease.

Additional evidence-based guidelines from the European League Against Rheumatism (EULAR),⁷⁻⁹ the BSR,¹⁰ and the American College of Rheumatology (ACR)¹¹ offer advice on the management of SLE and/or anti-phospholipid syndrome (APS) in women who are of child-bearing age and discuss drugs that can be prescribed during pregnancy. Although a number of drugs have been recommended in national and international guidelines,⁵⁻¹¹ many of them are not licenced for use in pregnancy and breastfeeding (due in part to the exclusion of pregnant women from the clinical trials used to support the licensing application), which can lead to healthcare professionals withdrawing treatment from pregnant women unnecessarily.¹² Discontinuation of treatment early during pregnancy can increase the risk of disease activity and flares during pregnancy, something that has been seen when biologics were discontinued in patients with rheumatoid and axial spondyloarthritis.¹³

Evidence-based guidelines that discuss the principle of disease control in pregnancy to improve outcomes are available for gastroenterologists to use in women with inflammatory bowel disease¹⁴ and similar guidance is available to dermatologists for women with psoriasis.¹⁵ These guidelines have reviewed drugs relevant to women with inflammatory rheumatic diseases and provide healthcare professionals with additional information to share with patients and colleagues about the use of biologics in women who are considering starting a family that should help to improve pregnancy outcomes.

Women are naturally concerned about the risks of medication, any changes that need to be made to their medications and the possible adverse effects of these on their pregnancy but are frequently unaware of the risks of active inflammation. The message that needs to be conveyed to the potential mother is that the best option for a woman with inflammatory rheumatic disease who is pregnant or planning a pregnancy is to continue the treatment that controls her disease if it is compatible with conception and pregnancy, or if not appropriate she should switch to an alternative. She is more likely to follow recommendations given to her by healthcare professionals if she understands these treatments have been prescribed with her health, and the health of her baby, in mind.

A multidisciplinary group was convened by *Guidelines* from across the UK to create a working party guideline with clear and straightforward guidance on the holistic management of women of child-bearing age with inflammatory rheumatic diseases. The aims of the guideline are to:

- highlight existing guidance on drugs suitable for pre-conception, pregnancy, and breastfeeding
- remind healthcare professionals of the many touch points where reproductive health should be discussed
- aid discussions with patients around the perceived risk of DMARDs to pregnancy versus the risk of disease activity
- empower healthcare professionals to prescribe drugs/authorise prescriptions that will ensure disease control and positive pregnancy outcomes.

Holistic management of women of child-bearing potential with inflammatory rheumatic disease

Healthcare professionals managing women of child-bearing age need to be comfortable discussing reproductive health and disease management with women of child-bearing age before, during, and after pregnancy, to:

- make women aware of their options, the impact of their pregnancy on their disease and vice versa, and the possible complications of pregnancy with rheumatic diseases
- prescribe contraception for those taking medicines that are contraindicated in pregnancy
- consider the timing of pregnancy with respect to disease activity
- prescribe therapies appropriate for pregnancy and breastfeeding before a woman conceives
- discuss the need for adherence to ensure a positive pregnancy outcome
- plan postpartum appointments to assess disease activity.

Pregnancy is often not discussed with healthcare providers, or if discussed, women often find their concerns are not adequately addressed, and/or they are given conflicting advice.² Indeed, a multinational survey of patients with systemic inflammatory diseases found that 49% of UK patients reported receiving inconsistent advice around reproductive health.² Regular open discussions and good communication between healthcare professionals will ensure women of child-bearing age are aware of the options available to them.

As part of pre-pregnancy counselling it is necessary to obtain information on the disease history, its manifestations and activity to date, and if there has been any systemic involvement. This history should help with the risk stratification of pregnancy to determine the appropriate level of care required during pregnancy. Patients should aim to conceive during a period when their disease is inactive. If the patient has active disease in the 3–6 months prior to conception or at the time of conception, there is an increased risk of flare during pregnancy and adverse pregnancy outcomes.^{1,7}

While few drugs are licensed for use in pregnancy, there are drugs that are not contraindicated and therefore can be prescribed if the benefits outweigh the risks to the patient.^{1,2,5–11} When a patient is considering pregnancy (or is already pregnant) discussions should cover the risk to them and their baby from uncontrolled inflammation if their treatment is stopped as well as the patient's disease, obstetric history, and postpartum considerations. **If a woman is better able to control her rheumatic disease through the use of treatments that reduce active inflammation and are compatible with pregnancy, the outcomes for mother and baby will be greatly improved.** This message must be clearly communicated to patients to improve their understanding of the importance of planning their pregnancy with healthcare professionals and adherence to their medication.^{1,2}

Reproductive health and prescribing considerations before, during, and after pregnancy

At the time of publication, no drugs mentioned in this best practice guideline have a UK marketing authorisation for use during pregnancy and breastfeeding for the indications discussed. Prescribers should refer to the individual summaries of product characteristics for further information and recommendations regarding the use of pharmacological therapies. For off-licence use of medicines, the prescriber should follow relevant professional guidance,^{5–11} taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's *Good practice in prescribing and managing medicines and devices* for further information.¹⁶

- Active inflammation from any source, be it the joints, the skin, or the bowel, is a predictor of adverse pregnancy outcomes regardless of the type of inflammatory disease.^{1,7,8}
- Good disease control can promote good pregnancy outcomes,¹ but this message is not consistently communicated to women by those involved in their care²
- All healthcare professionals involved in the care of women with inflammatory rheumatic diseases should be prepared to question patients about their contraceptive needs and make the appropriate referral for advice from specialist services or a colleague with this as a specialist interest

- As part of any discussion on treatment choice in women of reproductive age, questions should be asked about whether the patient is considering pregnancy, and if so, whether it is in the near or distant future, as that could preclude the use of some drugs
- All healthcare professionals seeing women of reproductive age and issuing, or re-issuing, prescriptions should have some understanding of which treatments can be used in pregnancy and those that are contraindicated
 - drugs that are contraindicated for conception or during pregnancy should only be prescribed after appropriate contraceptive advice has been given.

Contraception advice and unplanned pregnancy

- Contraceptive management is important for women with inflammatory rheumatic diseases due to the potential risks of an unplanned pregnancy during active disease on the mother and the baby and the risks to the baby associated with prescribed teratogenic drugs^{7,11}
 - certain DMARDs should not be given unless appropriate contraception is being used due to the potential risk of congenital abnormalities in the baby (Box 2)
 - small-molecule drugs such as apremilast, baricitinib, and tofacitinib are not recommended during pregnancy and breastfeeding due to the lack of pregnancy data and the potential ability of small molecules to cross the placenta¹¹
- Use of contraception must be discussed with the patient if pregnancy is contraindicated, and should be raised with patients not currently in a relationship and with those that have no plans to have a child as their situation may change
- Contraceptive services may be discussed with, and provided by, a variety of healthcare professionals so good communication between them and with the patient is essential
- Choice of contraceptive should depend on clinical factors (for example, diagnosis and activity of SLE, thrombotic risk including the presence of antiphospholipid antibodies (aPL) and proteinuria, osteoporosis risk, drug-drug interactions), the woman's needs, and the risk of unplanned pregnancy if contraception fails¹¹
- Options for contraception include:
 - highly effective long-acting reversible contraceptives such as intrauterine devices and progestogen-only implants (<1% 1-year failure rate)¹¹
 - other effective options include (1-year failure rates given in brackets):¹¹
 - daily progestogen-only pill (5–8%)
 - progestogen-only injectables (3%)
 - combined hormonal contraception (contraindicated in patients with aPL) (5–8%)
 - the vaginal ring (5–8%)
 - in patients that have completed their families, referral for sterilisation may be considered

Box 2: Treatments requiring appropriate contraception advice

When prescribing or re-issuing the following drugs commonly prescribed in inflammatory rheumatic disease, it is imperative that the patient receives appropriate contraceptive advice due to a varying level of risk of these drugs to the unborn child:^{5,11}

- mycophenolate mofetil
- methotrexate
- leflunomide
- cyclophosphamide
- non-TNFi biologics^[A]
- apremilast
- baricitinib
- tofacitinib.

[A] Non-TNFi biologic medications have limited documentation on use in pregnancy and should only be considered in consultation with specialist advice if no other pregnancy compatible drug is available. Further details can be found in Table 1.

TNFi=tumour necrosis factor alpha inhibitors

- In cases of unplanned pregnancy, urgent professional advice from the local rheumatology specialist and/or obstetric physician and/or fetal medicine specialist with relevant experience must be sought to determine the risk to the unborn child from any contraindicated drugs.

Pre-pregnancy counselling and safety advice

- All women and their care providers should have access to pre-pregnancy advice
- Depending on the level of disease, some patients could be counselled at a local level while others should seek advice from a specialist centre
- For patients with severe disease and poor obstetric history, a referral could be made for specialist care that should dovetail with national recommendations about maternal medicine centres
- There are multiple opportunities for pre-pregnancy counselling (and also for contraceptive management):
 - at diagnosis
 - opportunistically at hospital clinics and GP surgeries
 - at the time of treatment initiation and changes
 - when issuing repeat prescriptions for contraception
 - during annual review
 - when initiated by the patient
- Healthcare professionals should ascertain if the patient has intentions regarding pregnancy, either now or in the future
 - this question should be repeated at subsequent consultations and if prompted by the patient as the patient's circumstances may have changed since they were previously asked about pregnancy
 - this conversation could be instigated by nurse specialists

who are monitoring the patient or other healthcare professionals involved in the patient's care

- All medication should be reviewed at least annually, as per NICE guidance;¹⁷ depending on local circumstances, this may be undertaken by different healthcare professionals
- The best use of medicines in pregnancy (BUMPS) website,¹⁸ which provides patient information, should be consulted before any new treatment is initiated to ensure appropriate advice about contraception is given if pregnancy is contraindicated (see Box 2)
- As improving disease control can help with fertility as well as reduce the risk of miscarriage,^{1,7} patients may need to be cautioned over the possibility that their ability to conceive may improve should their disease remit
- Any pre-pregnancy counselling session should start with an explanation that if the woman's disease is controlled, it could improve fertility and reduce the risk of miscarriage, pre-eclampsia, a small baby, and preterm delivery
 - this discussion engages the woman in her care as it will direct her focus onto the successful outcome of the pregnancy and, while she may not want to take drugs during the pregnancy, she is more likely to be adherent with medication and less likely to discontinue if she understands that she needs to be healthy for the health of her baby
- Reassurance can be given regarding the very low risk of inheriting inflammatory rheumatic disease from a parent as these are polygenic diseases with a variety of environmental influences and genes implicated in the pathology
 - for example, for rheumatoid arthritis and SLE even in identical twins concordance is low, with the risk of both being affected around 12% and 11%, respectively¹⁹
- While folic acid is recommended in any pregnancy, high doses should be given to women taking sulfasalazine as well as women who are diabetic, obese, and/or have history of a neural tube defect in themselves or in a previous pregnancy, and for those that conceive on methotrexate; it should be obtained on prescription as 5 mg daily.⁵

Topics for discussion during pre-pregnancy counselling

- The following topics should be discussed with the patient during pre-pregnancy counselling:
 - the importance of controlling disease activity
 - the importance of pre-pregnancy folic acid
 - drugs that are compatible with pregnancy and/or breastfeeding, those that are not, and if any changes are needed to drug therapy
 - disease-specific questions
 - auto-antibody profile (see Box 3)
 - patient characteristics including risk of pulmonary embolism (PE) and venous thromboembolism (VTE)—if

necessary, women can be given low molecular weight heparin during pregnancy to reduce their risk²¹

- women with underlying renal dysfunction or proteinuria have an increased risk of pre-eclampsia²²
- previous history of pre-eclampsia, hypertensive disease during pregnancy, or chronic hypertension
 - monitor and manage hypertension as per NICE guidance²²
 - review prescribed drugs in those with chronic hypertension
- ability and support to help care for the baby after the birth especially if the new mother experiences a postpartum flare or there is an exacerbation of back or other joint pain due to the pregnancy
- smoking status
- activity/exercise
- age-related pregnancy risks (for example, chromosomal abnormalities)
- importance of keeping body mass index (BMI) within a healthy range before pregnancy
- nutrition
- obstetric history
- immunisation status
- method of delivery
 - rarely is vaginal birth contraindicated and caesarean section indicated for maternal rheumatic disease (as opposed to obstetric reasons).

Prescribing considerations during pregnancy

- Most women with inflammatory rheumatic disease should continue treatments compatible with pregnancy to maintain control of their inflammatory disease during pregnancy
- Table 1 provides a summary of standard and biologic DMARDs and corticosteroids that can be used in pre-pregnancy, during pregnancy, and postpartum when breastfeeding^{5,8,11,14}
 - see reference 6 for details on prescribing other drugs used in rheumatology practice during pregnancy and breastfeeding
- For patients taking drugs that require monitoring, such as azathioprine, this monitoring should be continued throughout the pregnancy
- A number of tumour necrosis factor alpha inhibitor (TNFi) biologics can be used during pregnancy if clinically needed; continuation and duration of treatment should be decided by a specialist and with agreement from the maternal medicine team after a risk-benefit analysis and discussing the options with the patient^{5,8,11}
 - the decision whether to stop or interrupt biologic therapy in the second or third trimester should be based on the individual patient and consideration of the patient's underlying disease, other options for therapy available to that patient, and the characteristics of the specific biologic that they have been prescribed^{1,11}

Box 3: Risk factors for neonatal lupus and thrombosis**Neonatal lupus**

Anti-Ro/anti-SSA and anti-La/SSB autoantibodies can be present in patients with SLE and Sjögren's syndrome, and can occasionally be found in women with other rheumatic diseases. Women with these conditions should ideally be screened before pregnancy for the presence of these antibodies as they are associated with an increased risk of neonatal lupus. Congenital complete heart block occurs in 1–2% of babies born to mothers with these antibodies.^{1,11} Babies with potential heart block due to the anti-Ro and/or anti-La status of the mother should be identified in utero using fetal heart rate monitoring from 16 weeks gestation.¹¹ If a heart block is identified, the baby needs to be assessed by a fetal cardiologist for signs of other cardiac abnormalities and delivery can be planned via elective caesarean section due to the risk of fetal bradycardia resulting from complete heart block masking signs of fetal distress during delivery. Women with these antibodies who have experienced neonatal lupus in previous pregnancies and are treated with hydroxychloroquine before and during pregnancy may have a reduced risk of complete heart block in a subsequent pregnancy.^{11,20} Complete heart block usually requires treatment with a pacemaker, either soon after birth or during childhood, and ongoing monitoring of the child is required.

Anti-phospholipid syndrome

There are three different types of aPL including lupus anticoagulant, anti-cardiolipin, and anti- β 2 glycoprotein 1, which can increase the risk of adverse pregnancy outcomes and maternal thrombosis. The level of risk depends on the number and type of antibody present and increases with: triple positivity in all three tests, lupus anticoagulant positivity, and persistent high antibody titre on repeated measurements.^{1,9} A repeat test is needed to demonstrate persistence as the level and type of these circulating antibodies can change due to the influence of various factors including viral infections. In all cases the patient should be followed according to the 2019 guidance from EULAR.⁹

Thrombosis

Women of child-bearing age who have active inflammatory disease are at increased risk of developing thrombosis during pregnancy. Women at high risk should be offered pre-pregnancy counselling and a management plan developed that provides thromboprophylaxis, usually with low molecular weight heparin, based on the woman's individual risk.¹ Appropriate treatment guidance such as the green top guideline from the RCOG should be followed as this identifies risk based on patient-specific factors such as previous recurrent VTE, family history of VTE, age, obesity, current systemic infection, and many other factors, including disease activity and severe proteinuria.²¹ Heparin treatment should be continued post-partum to minimise the thrombotic risk.²¹

aPL=anti-phospholipid antibodies; EULAR=European League Against Rheumatism; RCOG=Royal College of Obstetricians and Gynaecologists; SLE=systemic lupus erythematosus; SSA=Sjögren syndrome-related antigen A; SSB=Sjögren syndrome-related antigen B; VTE=venous thromboembolism

- the summaries of product characteristics for certolizumab and adalimumab state that they can be used during pregnancy if clinically/clearly needed,^{24,25} but only certolizumab does not cross the placenta at significant levels as it does not have an Fc component necessary for transport into the fetal circulation¹¹
- infants may have an increased risk of infection if certain biologic therapies that can cross the placenta were administered during the second or third trimester of pregnancy and persist in the neonatal and infant's circulation; live vaccines, should not be administered until 6 months of age to infants that have been exposed to these drugs during pregnancy (see Box 4)¹
- there are many biosimilars available and no differences are expected in safety and efficacy when compared with the reference medicine²⁶
- With continued use of high dose steroids (>20 mg prednisolone) there is a risk of complications such as steroid-induced diabetes, hypertension, osteoporosis, preterm rupture of the membranes and preterm delivery, and infection, therefore doses should be titrated to the minimum tolerable dose (ideally <10 mg prednisolone) with optimal dosing of non-steroid immunosuppressants^{1,11,27,28}
- if a woman is on steroid maintenance therapy, regular screening for hypertension and gestational diabetes is needed and optimal vitamin D levels are advised
- All patients should be monitored for adverse pregnancy outcomes in addition to disease flare regardless of whether their disease is stable or active
 - monitoring should be individualised, stratified according to risk, and whether there is organ involvement
- Women with underlying renal dysfunction or proteinuria >30 mg/mmol have an increased risk of pre-eclampsia and should be offered low dose aspirin during pregnancy and hypertension managed as per NICE guidance²²
- Routine obstetric monitoring should be consultant-led, however, if the woman has good disease control and has been in remission on stable therapies for a considerable time, care can be given by a midwife in consultation with a consultant in case of queries
 - for patients with active or previously severe disease and those requiring changes in therapy, a referral to secondary care can be made after supplying the information listed in Table 2 (see page 9)

Table 1. Drug compatibility with pre-conception, pregnancy, and breastfeeding			
Drug^[A]	Pre-conception	During pregnancy	Breastfeeding
Corticosteroids			
Prednisolone (oral)	Yes	Yes	Yes
IV methylprednisolone	Reserve for flares	Reserve for flares	Reserve for flares
Antimalarials			
Hydroxychloroquine	Yes	Yes	Yes
Mepacrine ^[B]	No	No	No
DMARDs			
Azathioprine	Yes	Yes	Yes
Ciclosporin	Yes	Yes ^[C]	Yes ^[D]
Cyclophosphamide	No	No	No
Intravenous immunoglobulins	Yes	Yes	Yes
Leflunomide	No; cholestyramine washout	No	No
Methotrexate	Stop 3 months in advance	No	No
Mycophenolate mofetil	Stop 6 weeks in advance	No	No
Sulfasalazine (with 5 mg folic acid)	Yes	Yes	Yes
Tacrolimus	Yes	Yes ^[C]	Yes ^[D]
TNFi biologics			
Adalimumab	Yes	Maintain pregnancy dosing until third trimester and resume post-partum	Caution ^[D]
Certolizumab	Yes	Yes	Yes
Etanercept	Yes	Maintain pregnancy dosing until third trimester and resume post-partum	Caution ^[D]
Golimumab	Yes	Maintain pregnancy dosing until third trimester and resume post-partum	Caution ^[D]
Infliximab	Yes	Maintain pregnancy dosing, stop in second trimester and resume post-partum	Caution ^[D]
Non-TNFi biologics			
Anakinra	Yes	Limited but reassuring data on use in systemic autoinflammatory diseases in pregnancy ²³	Caution ^[D]
Rituximab	Stop 6 months pre-conception. Due to limited documentation on use in pregnancy only consider using after specialist advice if no other pregnancy compatible drug available.		Caution ^[D]
Abatacept Belimumab Secukinumab Tocilizumab Ustekinumab	Discontinue in first trimester, due to limited documentation on use in pregnancy only consider use later in pregnancy after consultation with specialist advice if no other pregnancy compatible drug is available.		Caution ^[D]
Small molecules			
Apremilast Baricitinib Tofacitinib	Stop 1 month before conception ¹	Not recommended due to lack of data; potential ability of small molecules to cross the placenta and into breast milk	
<p>[A] At the time of publication, no drugs mentioned in this guideline have a UK marketing authorisation for use during pregnancy and breastfeeding. Prescribers should refer to the individual SmPCs for further information regarding the use of pharmacological therapies. For off-licence use of medicines, prescribers should follow relevant professional guidance,^{5–11} taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's <i>Good practice in prescribing and managing medicines and devices</i> for further information.¹⁶ [B] At the time of publication, mepacrine did not have UK marketing authorisation; it has been included in this table as it is used in clinical practice. [C] Suggested monitoring of maternal blood pressure, renal function, blood glucose, and drug levels. [D] Limited data.</p> <p>DMARDs=disease-modifying anti-rheumatic drugs; SmPC=summary of product characteristics ;TNFi=tumour necrosis factor alpha inhibitors</p> <p>Adapted from references 5, 8, 11, and 14.</p>			

Box 4: Immunisation in infants born to women who are being treated for inflammatory rheumatic disease^{1,14}

- › Non-live vaccines should be given on schedule
- › Live vaccines, such as BCG and rotavirus, should be avoided in the first 6 months of life in infants who may have had *in utero* biologic exposure later than recommended in Table 1
- › Live vaccines that are given at 12 months of age, such as MMR and varicella, can be given on schedule even in breastfed infants who have mothers treated with biologics.

BCG=Bacillus Calmette-Guérin vaccine;
MMR=measles, mumps, and rubella

- › If a woman is usually on biologic therapy and treatment is to be restarted after delivery, the drug should be ordered in advance of delivery so that the biologic therapy can be administered when needed.

Prescribing considerations postpartum

- › If there is concern about disease control, biologic treatment can be resumed no earlier than 24 hours after a vaginal delivery and 48 hours after a caesarean section if there is no sign of infection¹⁴
- › Contraception needs postpartum should be discussed prior to delivery (refer to the section on contraception advice) and at postpartum assessment
- › A postpartum appointment should be scheduled in advance of the birth and planned for 6–8 weeks after delivery to evaluate disease activity, assess if any dose changes are needed, and provide contraception advice

- › After birth, breastfeeding should be encouraged where possible, as there is no theoretical reason why biological agents will be absorbed intact into the infant's system (see Table 1 for drugs that are compatible with breastfeeding)
- › Advice regarding vaccinations as stated in Box 4 should be followed to protect the infant against infectious diseases
- › Rheumatic disease activity and/or inflammation is a risk factor for thrombosis;²⁹ if the patient has had a disease flare during her pregnancy, she should be re-assessed for all thrombotic risk factors to see if she requires antithrombotic therapy postpartum.

Management algorithm

- › The algorithm in Figure 1 (see pages 10 and 11) summarises the treatment pathway for women of child-bearing potential who have inflammatory rheumatic disease.

Acknowledgements

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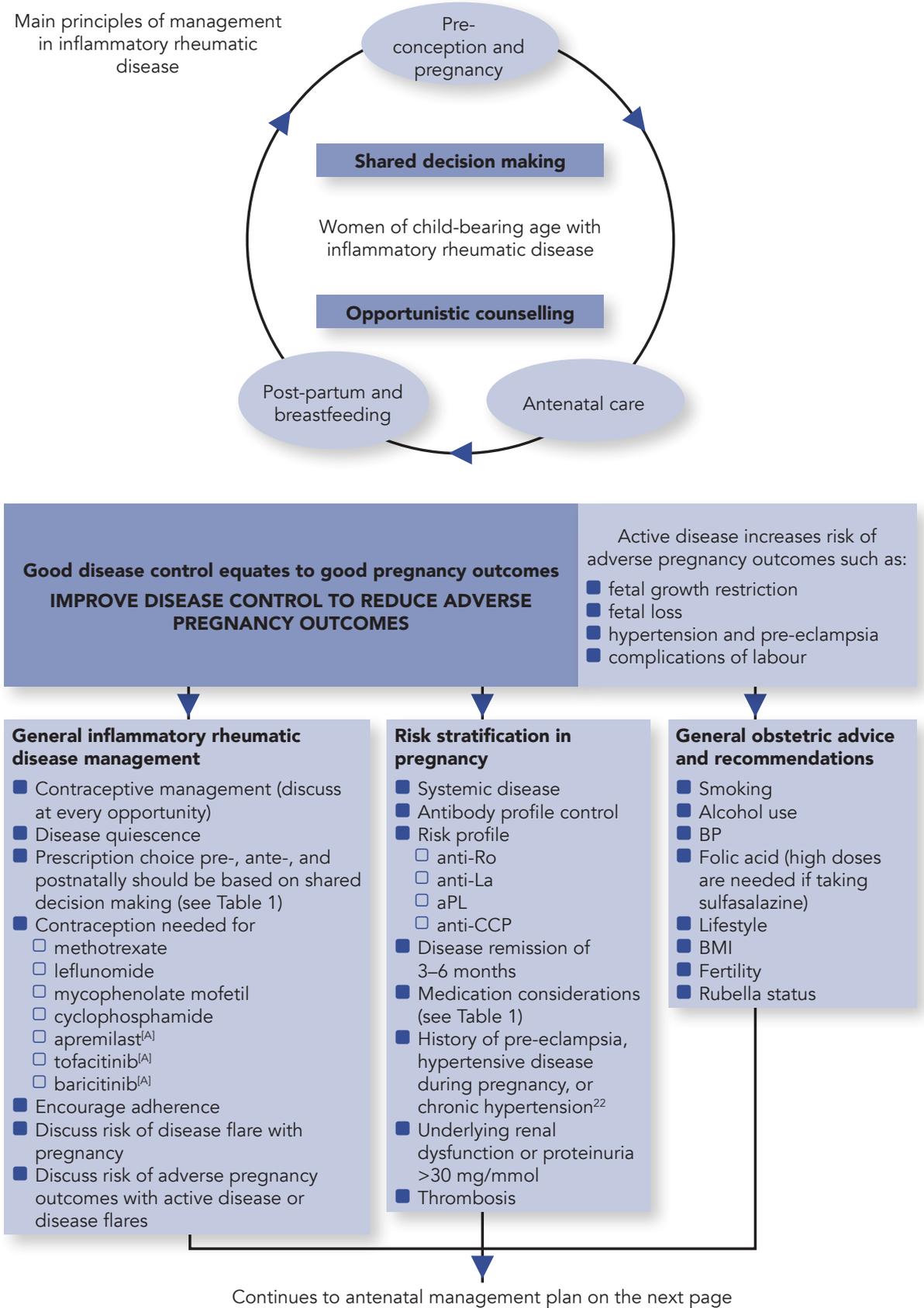
Conflicts of interest

The group members have received an honorarium to develop this best-practice guidance. Some of the group members have also received consultancy fees from other pharmaceutical companies, which may include UCB Pharma Ltd, for activities other than the development of this best-practice guidance.

Table 2: Proforma referral letter for specialist pre-pregnancy counselling and/or transfer to secondary care for pregnancy counselling in relation to rheumatic disease

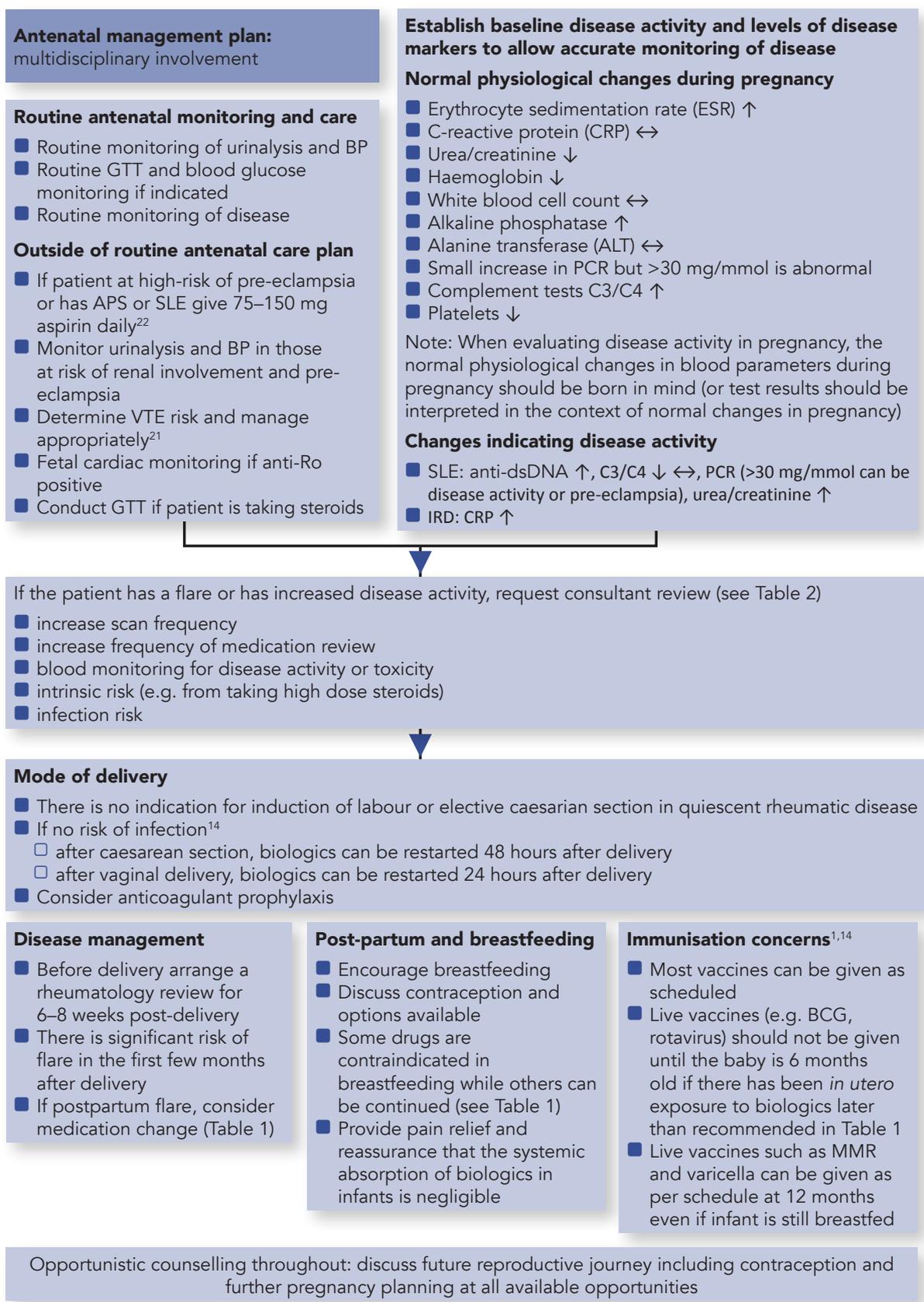
OBSTETRIC	Write details below:	RHEUMATOLOGY	Write details below:
Gravity/parity		Diagnosis	
Miscarriage history		Date of diagnosis	
Stillbirth history		Duration of disease	
Previous deliveries/ complications		Disease manifestations	
Cervical screening results		Comorbidities	
Method of contraception (if applicable)		Copy of the letter from the last specialist review	
Family history		Current treatments including dose and length of time on treatment	
Smoking status		Previous treatment for rheumatic disease and duration (if applicable)	
Alcohol consumption		Any other relevant information	
Vaccination history		Reason for referral	
Body mass index (BMI)			

Figure 1: Management algorithm for women with inflammatory rheumatic disease of child-bearing age



[A] Due to small size and potential to cross the placenta

aPL=anti-phospholipid antibodies; BMI=body mass index; BP=blood pressure; CCP=cyclic citrullinated peptide



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Guidance during the COVID-19 pandemic

- › Frequency of clinic visits, blood monitoring, and continuation of medication should be reviewed and discussed on an individual basis together with advice about social distancing, self-isolation, and shielding
- › Reduce hospital attendance by replacing non-essential face-to-face visits with telephone consultations but monitoring of patients with renal impairment, in particular, requires careful consideration
- › Minimise risk of COVID-19 exposure to non-infected patients during face-to-face attendance by providing patient education and a clean route through the hospital
- › Remind patients of the importance of maintaining disease control in pregnancy with continuation of hydroxychloroquine and/or sulfasalazine, and reassure them that these drugs do not need to be stopped during COVID-19 infection
- › In the presence of serious infection requiring therapy with antibiotics, hospitalisation, or suspicion of COVID-19, other DMARDs compatible with pregnancy should be stopped, although steroids must not be stopped.

DMARDs=disease-modifying anti-rheumatic drugs

