RHEUMATOLOGY

Rheumatology 2019;58:220–226
doi:10.1093/rheumatology/key207
Advance Access publication 21 August 2018

Guidelines

British Society for Rheumatology

The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis—Executive summary

Christopher R. Holroyd[1], Rakhi Seth[1], Marwan Bukhari[2], Anshuman Malaviya[3], Claire Holmes[1], Elizabeth Curtis[4], Christopher Chan[1], Mohammed A. Yusuf[3], Anna Litwic[4,5], Susan Smolen[3], Joanne Topliffe[3], Sarah Bennett[1], Jennifer Humphreys[6], Muriel Green[7] and Jo Ledingham[8] for the British Society for Rheumatology Standards, Guidelines and Audit Working Group

Key words: rheumatoid arthritis, psoriatic arthritis, psoriatic arthritis, ankylosing spondylitis, biologic, Anti-TNF, safety

This is the executive summary of The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis, doi: 10.1093/rheumatology/key208

GUIDELINES

Scope and purpose

Need for guideline

The use of biologic therapies has transformed the management of inflammatory arthritis, with disease remission becoming an increasingly achievable goal. Although efficacious, biologic therapies are not without potential risk; hence it is important that clinicians are aware of these risks and ensure that appropriate precautions are taken to minimize them. Precautions include adequate screening prior to initiation, vigilant monitoring, especially in higher risk individuals, and an understanding of the implications of certain co-morbidities.

This guideline supersedes the previous BSR/BHPR anti-TNF [1], rituximab (RTX) [2] and tocilizumab (TCZ) [3] guidelines and has been developed in line with the BSR Guidelines Protocol. It covers safety recommendations for all biologic therapies approved by the National Institute for Health and Care Excellence (NICE) up to June 2016, for use in all inflammatory arthritides [RA, PsA and axial SpA (SpA) including AS].

Objectives of guideline

To provide evidence-based recommendations, which do not imply a legal obligation, for the safe prescription of biologic therapies approved by NICE for the management of inflammatory arthritis.

Biologics covered by this guideline are as follows: anti-TNF inhibitors: infliximab (IFX); etanercept (ETN); adalimumab (ADA); certolizumab pegol; golimumab; anti-CD20: rituximab (RTX); CTLA4-Ig: abatacept (ABA); anti-IL-6 receptor: tocilizumab (TCZ); and anti-IL-12/IL-23: ustekinumab.

NICE accredited
www.nice.org.uk/accreditation

NICE has accredited the process used by the BSR to produce its guidance on the safety of biologic DMARDs in inflammatory arthritis. Accreditation is valid for 5 years from 10 June 2013. More information on accreditation can be viewed at www.nice.org.uk/accreditation. For full details on our accreditation visit: www.nice.org.uk/accreditation.

[1]Rheumatology Department, University Hospital Southampton NHS Foundation Trust, Southampton, [2]Rheumatology Department, University Hospitals of Morecombe Bay NHS Foundation Trust, Lancaster, [3]Rheumatology Department, Mid Essex Hospital NHS Trust, Chelmsford, [4]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, [5]Rheumatology Department, Salisbury District Hospital, Salisbury, [6]Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, [7]National Rheumatoid Arthritis Society and [8]Rheumatology Department, Queen Alexandra Hospital, Portsmouth, UK

Submitted 7 February 2018; revised version accepted 7 June 2018

Correspondence to: Christopher Holroyd, Rheumatology Department, University Hospital Southampton, Tremona Road, Southampton, Hampshire, SO16 6YD, UK. E-mail: Christopher.holroyd@uhs.nhs.uk

Target audience

Secondary care health professionals directly involved in the management of patients with inflammatory arthritis.

Areas not covered

This guideline does not cover the following topics: the use of biologic therapy for conditions other than RA, axial SpA (including AS) and PsA; safety in individuals aged <18 years; safety in the context of pregnancy and breastfeeding, as this has recently been covered in the BSR/BHPR prescribing drugs in pregnancy guidelines [4]; biologics approved by NICE after June 2016 (such as secukinumab and sarilumab) or Janus-kinase inhibitors; and biosimilar preparations of branded biologics; until further clinical data are available, the safety recommendations we propose for originator biologics can be applied to their biosimilar counterparts.

Key recommendations from the guideline

Specific questions were developed with regards to biologic safety including: What baseline screening is required? What monitoring is required? What effect do certain co-morbidities have on prescribing and choice of therapy? When should therapy be interrupted? Further details are given in the full guideline [5].

Rigour of development

This guideline has been developed in line with BSR's guideline protocol. A comprehensive literature search was undertaken using MEDLINE, Cochrane, PubMed and EMBASE databases with specific search terms. The reference lists of retrieved articles were manually searched for additional papers and these were included if appropriate. All searches were performed up to the end of June 2016. Abstracts from BSR, EULAR and ACR annual conferences up to and including EULAR 2016 were also included.

Grading the evidence

The GRADE method was used to assess the quality of evidence and the strength of recommendation [6]. Accompanying each recommendation in this guideline, in brackets, is the strength of recommendation, quality of evidence and strength of agreement.

Strength of recommendation

Using GRADE, recommendations were categorized as either strong (denoted by 1) or weak (denoted by 2), according to the balance between benefits, risks, burden and cost.

Quality of evidence

Using the GRADE approach, the quality of evidence was determined as either high (A), moderate (B) or low/very low (C) reflecting the confidence in the estimates of benefits or harm.

Strength of agreement

Based on the strength of recommendation and level of evidence, a strength of agreement (SOA) was calculated for each recommendation, by poling all members of the guideline working group. The results were expressed as an SOA score (0–10, where 0 denoted complete disagreement and 10 denoted complete agreement). This is presented alongside each recommendation as a percentage. Recommendations were only included where the mean SOA was $\geqslant 7$ and $\geqslant 75\%$ of respondents scored $\geqslant 7$.

The guideline

Generic recommendations

(i) The decision to initiate a biologic should be made in conjunction with the patient/carer and initiated by an expert in the management of rheumatic disease (grade 1C, SOA 99%).
(ii) Patients should be provided with education about their treatment to promote self-management (grade 1B, SOA 99%).
(iii) Patients should be assessed for co-morbidities as these may influence biologic choice, including evaluation for respiratory disease and screening for infection (grade 1C, SOA 99%).
(iv) Patients should have direct access to their specialist centre [e.g. via an advice line (Helpline)] for advice within one working day (grade 1C, SOA 98%).
(v) Clinicians should be encouraged to recruit patients to the appropriate biologic therapy registry, with patient consent (grade 1C, SOA 98%).

For patients prior to treatment with a biologic

Pre-treatment investigations

(i) Baseline assessment for all should include (grade 1C SOA 98%): laboratory evaluation of full blood count (FBC), creatinine/calculated glomerular filtration rate (GFR), alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST), albumin, tuberculin skin test (TST) or IFN-γ release assay (IGRA) or both as appropriate, hepatitis B and C serology and a chest radiograph.
(ii) Patients receiving RTX: baseline immunoglobulins (IgA, IgG and IgM) are recommended prior to initiation (grade 1A, SOA 98%).
(iii) Patients receiving TCZ: a baseline lipid profile is recommended prior to initiation. If abnormal, lipid lowering treatment should be initiated as per local guidance (grade 2A, SOA 99%).

Pre-treatment management of and screening for co-morbidity

Infection

In general:

(i) Biologics should not be initiated in the presence of serious active infections (defined as requiring intravenous antibiotics or hospitalization; not including tuberculosis) (grade 1B, SOA 98%).
(ii) Use biologics with caution in patients at high infection risk after discussing risks and benefits (grade 1B, SOA 99%).

(iii) Consider using ETN or ABA as a first line biologic therapy in patients at high risk of infection (grade 2B, SOA 94%).

Mycobacterium tuberculosis: screening for TB before starting a biologic

(i) All patients require screening for tuberculosis (TB) before starting a biologic (grade 1B, SOA 98%).
(ii) Screening for TB should include checking for previous TB exposure and treatment, perform a clinical examination, chest X-ray (CXR) and either a TST or IGRA or both, as appropriate (grade 2C, SOA 98%).
(iii) For patients on immunosuppressive therapy with a normal CXR, a TST is *not* helpful, as immunosuppression hinders interpretation (grade 2C, SOA 98%).
(iv) Patients with an abnormal CXR, previous history of TB or TB treatment should be referred to a specialist with an interest in TB prior to commencing a biologic (grade 2C, SOA 99%).
(v) Immunocompromised patients screened for latent TB with an IGRA alone or together with a TST and found to have a positive result in either test should be considered for treatment prior to starting biologic therapy (grade 2C, SOA 96%).

Latent and reactivated TB

(i) Patients should be treated with prophylactic anti-TB treatment prior to commencing a biologic (grade 1B, SOA 99%); therapy may be commenced after completing at least 1 month of anti-TB treatment and patients should be monitored every 3 months (grade 2C, SOA 91%).
(ii) Patients who have had previous inadequate treatment for active TB should be investigated for active TB. In these individuals even when active disease has been excluded, the annual risk of TB (reactivation) is much higher than the general population rate, so the risk–benefit analysis favours chemoprophylaxis (grade 1C, SOA 98%).
(iii) As TB reactivation risk is higher with anti-TNF mAb drugs (notably ADA and IFX) than for ETN, consider ETN in preference for those who require anti-TNF therapy and are at high risk of TB reactivation (grade 1B, SOA 99%).

Active TB

(i) Patients with evidence of active TB should be treated before starting a biologic (grade 1C, SOA 99%); therapy may be commenced after completing at least 3 months of anti-TB treatment, and there is evidence that the patient is improving with evidence of culture negativity (grade 2C, SOA 91%).

HBV and HCV

(i) Patients should be screened for HBV and HCV infection (grade 1C, SOA 98%).
(ii) In patients who are HBV positive, a risk–benefit assessment should be undertaken, as biologics may be safe if appropriate anti-viral treatment is given, working closely with a hepatologist (grade 1C, SOA 99%).
(iii) Studies to date suggest that though biologic therapy does not appear to have a detrimental effect on HCV infection, it should continue to be used only with caution in such patients, following a risk–benefit decision made with a hepatologist (grade 1C, SOA 96%).

HIV

(i) Risk factors for HIV infection should be documented prior to commencing a biologic and, if present, an HIV test should be performed (grade 2C, SOA 97%).
(ii) If considering the use of biologic therapy in HIV positive patients, this should be discussed with an HIV specialist. It should be borne in mind that a reasonable benefit–risk ratio for HIV patients exists with anti-TNF therapy if HIV infection is controlled ($CD4^+$ count >200 cells/mm^3 and viral load undetectable) and anti-TNF is given in combination with highly active anti-retroviral therapy (grade 2C, SOA 99%).

Malignancy

(i) Biologic therapies should not be commenced in patients with clinical signs of, or under investigation for, malignancy (basal cell carcinoma excluded) (grade 1C, SOA 96%).
(ii) Patients should be advised that there is no conclusive evidence for an increased risk of solid tumours or lymphoproliferative disease linked with biologic therapy, but that on-going vigilance is required (grade 1A, SOA 99%).
(iii) There is conflicting evidence regarding the risk of skin cancers with anti-TNF therapy; patients should be advised of the need for preventative skin care, skin surveillance and prompt reporting of new persistent skin lesions (grade 1B, SOA 96%).
(iv) Anti-TNF therapy is relatively contraindicated in patients who have had prior treatment with >150 psoralen and ultraviolet A (PUVA) and/or >350 ultraviolet B (UVB) phototherapy. Such patients should be discussed with a dermatologist prior to commencing anti-TNF therapy (grade 2C, SOA 96%).
(v) Caution should be exercised in the use of biologics in patients with previous malignancy (grade 1C, SOA 97%). The timing of commencement of biologic therapy post-malignancy is not fixed and will depend on type and stage of malignancy, risk of metastasis and patient views. RTX may be considered as a first-line biologic option in RA patients with previous malignancy (grade 2C, SOA 90%).
(vi) The effect of biologics on pre-malignant conditions remains unclear. Caution should be exercised in the use of biologics in such patients. RTX may be

considered as a first-line biologic option is these patients (grade 2C, SOA 97%).

Cardiac problems

(i) Although recent data are reassuring, biologics should be used with caution in patients with class III or IV cardiac failure, working closely with a cardiologist (grade 2C, SOA 96%).
(ii) Biologic therapy may be used in patients with previous myocardial infarction or cardiovascular events (grade 2B, SOA 99%).

Respiratory disease

(i) Pre-existing interstitial lung disease (ILD) is not a specific contraindication to biologic therapy; however, caution is advised in patients with poor respiratory reserve (in whom a significant drop in lung function would be potentially life threatening); in this situation it is advised to work closely with a respiratory physician with a specialist interest in ILD (grade 2C, SOA 99%).
(ii) RTX or ABA may be considered a first-line biologic in patients with ILD (grade 2C, SOA 84%).

Uveitis

(i) ADA and IFX can be considered for the treatment of uveitis, in preference to ETN, which appears to be associated with lower rates of treatment success and has been associated with the development of uveitis. The relative risks of the available agents should be taken into account when selecting which treatment to use (grade 1C, SOA 96%).

Demyelinating disease

(i) Anti-TNF therapy should not be given when there is a personal history of multiple sclerosis or other demyelinating diseases. Consider using a non-anti-TNF biologic in this situation (grade 2B, SOA 97%).

Diverticular disease

(i) Exercise caution with TCZ in patients with diverticular disease, particularly when using concurrent NSAIDs and/or steroids (grade 2C, SOA 98%).

Vaccinations

(Also refer to vaccination recommendations while on biologic therapy.)

(i) HBV immunization should be considered for at risk patients (grade 2C, SOA 94%).
(ii) Patients >50 years should undergo vaccination against herpes zoster assuming there are no contraindications (e.g. treatment within the past 3 months with >40 mg prednisolone per day for >1 week, >20 mg prednisolone per day for >14 days, MTX >25 mg/week, AZA >3.0 mg/kg/day). This should be administered preferably >14 days before starting biologic therapy (grade 2C, SOA 97%).
(iii) Patients who do not have a positive history of varicella zoster (chickenpox) infection should have a varicella zoster virus antibody test. If this is negative, and there are no contraindications (as listed in 3.31), varicella zoster vaccination should be offered prior to biologic commencement (grade 2C, SOA 98%).

For patients receiving biologic therapy

Monitoring on treatment

(i) All patients should be reviewed for drug safety in a specialist department at least every 6 months. High risk patients (e.g. those at high risk of TB) should be reviewed every 3 months (grade 2C, SOA 94%).
(ii) Patients prescribed a biologic (other than TCZ) without concomitant csDMARD (or with csDMARDs that do not require blood test monitoring), should have monitoring blood tests (FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 3–6 months (grade 2C, SOA 97%).
(iii) Patients receiving csDMARD may require more regular laboratory monitoring (as per BSR/BHPR non-biologic DMARD guidelines, 2017) (grade 2B, SOA 96%).
(iv) Patients receiving RTX should have serum immunoglobulins (especially IgG and IgM) checked prior to each cycle of RTX. Clinicians and patients should be aware that the risk of infection increases as serum IgG levels fall below normal (grade 2A, SOA 99%).
(v) Patients receiving i.v. or s.c. TCZ, with or without MTX, should have laboratory monitoring every 4 weeks for neutrophils and ALT/AST (grade 2B). Blood tests should ideally be in the week before i.v. TCZ, and in the 3 days before every fourth s.c. injection. Any decision to halt treatment should be made in accordance with the guidance in the TCZ SPC (grade 2C, SOA 96%).
(vi) Patients receiving TCZ should have their serum lipids checked at 3 months, and be treated appropriately if abnormal; they may be checked again thereafter at physician's discretion (grade 2A, SOA 99%).

Co-morbidity management on treatment

(i) Patients with significant co-morbidities who are also receiving biologic therapies, should have close involvement with specialists in that field (grade 1C, SOA 99%).

Infection

In general:

(i) All biologics should be discontinued in the presence of serious infection, but can be recommenced once the infection has resolved (grade 1A, SOA 99%).

Mycobacterium tuberculosis

(i) Patients commenced on biologics should be closely monitored for TB while on treatment and for at least 6 months after stopping treatment (grade 2C, SOA 98%).
(ii) Patients on biologics who develop symptoms suggestive of TB should receive full anti-TB treatment but may continue with their biologic if clinically indicated after risk–benefit analysis and discussion with a TB expert (grade 2C, SOA 96%).

Opportunistic infection

(i) Health-care professionals should have a high index of suspicion for atypical/opportunistic infections, especially if there is current or recent steroid use. Biologic therapy should be promptly stopped in suspected cases. Patients should have rapid access to specialist health care for consideration of early treatment (grade 1B, SOA 99%)
(ii) In patients exposed to primary varicella through a close household contact [and without a positive history of varicella zoster (chickenpox) infection or vaccination], post-exposure prophylaxis with varicella zoster immune globulin should be considered if the risks from infection are perceived to be significant. Shingles should be treated conventionally (grade 2C, SOA 94%).
(iii) Clinicians should be vigilant for progressive multifocal leukoencephalopathy, which has been primarily associated with RTX but has also reported with anti-TNF therapy. Treatment should be stopped if progressive multifocal leukoencephalopathy develops. Rechallenge is not recommended (grade 1C, SOA 99%).

HBV ad HBC infection

(i) Close monitoring of serum amino-transaminases and HBV DNA load is recommended in patients with occult or overt HBV infection treated with biologic therapy (grade 1C SOA 99%).
(ii) Close monitoring of serum amino-transaminases and HCV RNA during therapy should be considered in patients with HCV treated with a biologic (grade 1C, SOA 99%).
(iii) Patients with serological evidence of occult HBV infection may require concomitant anti-viral treatment if detrimental changes in monitoring tests develop (grade 1B, SOA 99%).

HIV

(i) Patients with HIV receiving anti-TNF therapy require close monitoring of viral load and CD4 count. Treatment changes should be made in light of results, with guidance from an HIV specialist (grade 2C, SOA 99%).

Malignancy

(i) Patients should be encouraged to comply with national cancer screening programmes (grade 1C, SOA 99%).
(ii) Patients should be investigated for potential malignancy if clinically suspected and biologics should be stopped if non-basal cell carcinoma (BCC) malignancy is confirmed (grade 1C, SOA 97%).
(iii) Biologic therapies may be continued in patients who develop a BCC that is fully excised, after careful discussion with the patient and a risk–benefit analysis (grade 2C, SOA 97%).

Cardiac problems

(i) If patients develop worsening cardiac failure while on anti-TNF, consideration should be given to stopping therapy if no other explanation for worsening cardiac failure is found following input from a cardiologist (grade 2 C, SOA 99%).

Respiratory disease

(i) Patients with ILD receiving biologics should be regularly reviewed by a respiratory physician with a specialist interest in ILD, and ideally in a combined rheumatology/respiratory clinic. Pulmonary function tests should be performed as clinically indicated, usually every 4–6 months (grade 2C, SOA 99%).
(ii) Consideration, in consultation with a respiratory physician with a specialist interest in ILD, should be given to stopping biologic therapy in patients with worsening or new features of ILD. RTX or ABA may be considered in patients with worsening or new ILD (grade 2C, SOA 90%).

Uveitis

(i) If patients develop uveitis while on a biologic, a trial of an alternative biologic could be considered, bearing in mind the latest reported relative risks (grade 1C, SOA 99%).
(ii) Consider switching patients with uveitis currently taking ETN to IFX or ADA (grade 2C, SOA 98%).

Demyelinating disease

(i) Anti-TNF should be withdrawn if demyelination occurs. Rechallenge with anti-TNF therapy is not recommended (grade 2B, SOA 99%).

Diverticular disease

(i) TCZ should be withdrawn if bowel perforation occurs. Reintroduction of TCZ in such patients is not recommended (grade 2C, SOA 99%).

CTD

(i) If a lupus-like syndrome or other significant autoimmune disease develops while on anti-TNF therapy, treatment should be discontinued and appropriate interventions should be initiated. In such instances, a non-anti-TNF biologic should be considered. Rechallenging with an alternative anti-TNF agent should only be undertaken with caution (grade 1C, SOA 99%).

Haematological disorders

(i) Biologic therapies may be continued in patients at increased risk of, or with, venous thromboembolism (grade 2C, SOA 99%).

Psoriasis

(i) If psoriasis develops in patients treated with anti-TNF, conventional psoriasis treatment should be started and consideration should be given to stopping anti-TNF if the skin lesions persist despite specialist dermatology input or are severe (grade 2B, SOA 99%).

Vaccinations

(i) The Public Health England recommendations on the use of immunizations in patients on immunosuppressive therapy should be adhered to in patients on biologics. Live attenuated vaccines, such as the herpes zoster vaccine, oral polio or rabies vaccine, should be avoided (grade 2C, SOA 99%).
(ii) Although there may be an attenuated response (particularly if MTX is co-prescribed), patients on biologics should receive influenza and pneumococcal immunizations unless there are contraindications (grade 1C, SOA 99%).
(iii) In patients who are currently receiving biologics, human papillomavirus vaccine for cervical cancer risk in young women is recommended if they have already received part of the vaccination schedule, as per national guidelines (grade 2C, SOA 99%).

Peri-operative care

(i) The potential benefit of preventing post-operative infections by stopping biologics (different surgical procedures pose different risks of infection and wound healing) should be balanced against the risk of a peri-operative flare in disease activity (grade 2B, SOA 97%).
(ii) For most biologics (exceptions: RTX and TCZ), consideration should be given to planning surgery when at least one dosing interval has elapsed for that specific drug; for higher risk procedures consider stopping 3–5 half-lives before surgery (if this is longer than one dosing interval) (grade 2B, SOA 97%).
(iii) Biologics may be recommenced after surgery when there is good wound healing (typically around 14 days), all sutures and staples are out, and there is no evidence of infection (grade 1B, SOA 99%).
(iv) For patients receiving RTX, treatment should ideally be stopped 3–6 months prior to elective surgery (grade 2B, SOA 94%).
(v) For patients receiving TCZ, i.v. TCZ should be stopped at least 4 weeks before surgery; s.c. TCZ should be stopped at least 2 weeks before surgery (grade 1C, SOA 96%).

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Disclosure statement: C.R.H. has been sponsored to attend meetings by AbbVie, Pfizer, Bristol-Myers Squibb and UCB and has received honoraria for speaking and attended advisory boards with AbbVie, Bristol-Myers Squibb, Pfizer, UCB, Janssen and Novartis. R.S. has received sponsorship to attend the national BSR conference from Pfizer and has received honoraria to speak at regional educational meetings by Abbvie and Eli Lilly. M.B. has been sponsored to attend regional, national and international meetings by UCB Celltech, Roche/Chugai, Pfizer, AbbVie, Merck, Mennarini, Janssen, Bristol-Myers Squibb, Novartis and Eli Lilly and received honoraria for speaking and attended advisory boards with Bristol-Myers Squibb, UCB Celltech, Roche/Chugai, Pfizer, AbbVie, Merck, Mennarini, Sanofi-aventis, Eli Lilly, Janssen and Novartis. A.M. has received honoraria for sponsored presentations from MSD, Bristol-Myers Squibb and Roche and received an honorarium from Pfizer for professional services. C.H. has received sponsorship to attend a national meeting by Pfizer. E.C. has received sponsorship to attend meetings by Pfizer and UCB and received honoraria for speaking for Eli Lilly. C.C. has received sponsorship to attend a national meeting by Pfizer. A.L. has received sponsorship to attend meetings and courses by AbbVie, Roche and UCB and has received honoraria for speaking by Roche/Chugai. J.T. has received honoraria from Hospira. S.B. has received sponsorship to attend a national meeting by Pfizer. All other authors have declared no conflicts of interest.

References

1 Ding T, Ledingham J, Luqmani R *et al*. BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies. Rheumatology 2010;49:2217–9.

2 Bukhari M, Abernethy R, Deighton C *et al*. BSR and BHPR guidelines on the use of rituximab in rheumatoid arthritis. Rheumatology 2011;50:2311–3.

3 Malaviya AP, Ledingham J, Bloxham J *et al*. The 2013 BSR and BHPR guideline for the use of intravenous tocilizumab in the treatment of adult patients with rheumatoid arthritis. Rheumatology 2014;53:1344–6.

4 Flint J, Panchal S, Hurrell A *et al*. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. Rheumatology 2016;55:1693–7.

5 Holroyd CR, Seth R, Bukhari M *et al*. The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis. Rheumatology 2019;58:e3–42.

6 Guyatt GH, Oxman AD, Vist GE *et al*. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924–6.