



British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update

C.H. Smith ,¹ Z.Z.N. Yiu ,² T. Bale,³ A.D. Burden,⁴ L.C. Coates ,^{5,6} W. Edwards,⁷ E. MacMahon,⁸ S.K. Mahil ,¹ A. McGuire,⁹ R. Murphy,^{10,11,12} C. Nelson-Piercy,¹³ C.M. Owen,¹⁴ R. Parslew,¹⁵ O.A. Uthman,¹⁶ R.T. Woolf ,¹ L. Manounah ,¹⁷ M.C. Ezejimofor ,¹⁷ L.S. Exton ,¹⁷ and M.F. Mohd Mustapa ,¹⁷ on behalf of the British Association of Dermatologists' Clinical Standards Unit

Correspondence

Catherine H. Smith.
Email: catherine.smith@kcl.ac.uk;
guidelines@bad.org.uk

Accepted for publication

14 March 2020

The author affiliations can be found in the Appendix.

T.B., A.D.B., L.C.C., W.E., E.M., S.K.M., A.M., R.M., C.N.-P., C.M.O., R.P., O.A.U. and R.T.W. contributed equally to this project and are listed alphabetically.

Funding sources

The work of C.H.S. and S.K.M. was funded and supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London. S.K.M. is funded by a Medical Research Council (MRC) Clinical Academic Research Partnership award (MR/T02383X/1). L.C.C. is an NIHR Clinician Scientist and Senior Clinical Research Fellow funded by a NIHR Clinician Scientist award. The research was supported by the NIHR Oxford Biomedical Research Centre. The views expressed in this guidance are those of the authors and not necessarily those of the National Health Service, the NIHR or the Department of Health.

Conflicts of interest

Details of declarations of interests (cumulative, throughout the project) can be found in File S2: Appendix L and are consistent with the NICE Accreditation policy.

This is an updated guideline prepared for the Clinical Standards Unit of the British Association of Dermatologists (BAD), which includes the Therapy & Guidelines subcommittee. Members of the Clinical Standards Unit who have contributed: N.J. Levell (Chair, Therapy & Guidelines subcommittee), B. McDonald (BAD Assistant Honorary Secretary), S.L. Chua, A. Bardhan, P. Laws, L. Manounah (BAD Guideline Research Fellow), M.C. Ezejimofor (BAD Guideline Research Fellow), L.S. Exton (BAD Guideline Research Fellow) and M.F. Mohd Mustapa (BAD Clinical Standards Manager).

These guidelines were first produced in 2005 by the British Association of Dermatologists; they have been reviewed and updated in 2009, 2017 and 2020.

DOI 10.1111/bjd.19039



NICE has renewed accreditation of the process used by the British Association of Dermatologists to produce clinical guidelines. The renewed accreditation is valid until 31 May 2021 and applies to guidance produced using the processes described in the updated guidance for writing a British Association of Dermatologists clinical guideline – the adoption of the GRADE methodology 2016. The original accreditation term began on 12 May 2010. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

Purpose and scope of the guideline

The overall aim of the guideline is to provide up-to-date, evidence-based recommendations on the use of biologic therapies targeting tumour necrosis factor (TNF) (adalimumab, etanercept, certolizumab pegol, infliximab), interleukin (IL)-12/23p40 (ustekinumab), IL-17A (ixekizumab, secukinumab), IL-17RA (brodalumab) and IL-23p19 (guselkumab, risankizumab, tildrakizumab) in adults, children and young people for the treatment of psoriasis; consideration is given to the specific needs of people with psoriasis and psoriatic arthritis. This rapid update is part of an annual evidence review to factor in the latest evidence for biological drugs evaluated in the 2017 publication of the guideline,¹ and newer biological drugs that have been licensed for psoriasis in the UK or are expected to be licensed in the near future.

This set of guidelines has been developed using the recommended methodology of the British Association of Dermatologists (BAD)² with reference to the Appraisal of Guidelines Research and Evaluation (AGREE II) instrument (www.agree-trust.org),³ and the Grading of Recommendations Assessment, Development and Evaluation (GRADE).⁴ Additional online Supporting Material includes our Implementation Toolkit (File S1), Appendices (File S2), and Audit standards and methodology (File S3). Further information on the guideline development process can be found in Appendix I (File S2; see Supporting Information). The multidisciplinary guideline development group (GDG) comprised medical specialists (consultants in dermatology, paediatric dermatology, rheumatology, virology and obstetric medicine), a clinical nurse specialist, dermatology trainees, a pharmacist specialist, a patient representative and a research team providing technical and methodological support [a full list of GDG members can be found in Appendix K (File S2; see Supporting Information)].

The recommendations were developed for implementation in the National Health Service (NHS) in the UK. The guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline assumes that prescribers cross-reference a drug's summary of product characteristics (SPC) to inform clinical decision making for individual patients. Where relevant, this guidance applies to biosimilars (similar biological medical products), subject to recommendations given within the BAD position statement and the European Medicines Agency guidelines.^{5,6} This guidance does not cover agents licensed outside the UK or

use of biologic therapies for indications other than psoriasis, or use when psoriatic arthritis is the main indication.

Immunomodulators Registry, BADBIR, in the UK and Republic of Ireland; www.badbir.org).

Summary of recommendations

These evidence- and consensus-based (good practice point, GPP) recommendations should be considered in the context of the individual needs of the patient, with cross-reference to the relevant drug's SPC and the Implementation Toolkit (File S1: Tables S1–S5; see Supporting Information). The strength of recommendation is expressed by the wording and symbols featured in Table 1. The supporting information for the guideline details the systematic review of the newly identified evidence underpinning the updated or new recommendations (File S2; Appendices A–M see Supporting Information); Appendix D, 'linking evidence to recommendations' (LETR), describes the factors that were taken into consideration for each of these recommendations, which should be read in conjunction with the full version of the 2017 guidelines.¹ A pathway algorithm based on the recommendations to guide choice of biologic therapy in adults with psoriasis is shown in Figure 1.

Using biologic therapy

R1 (↑↑) Initiation and supervision of biologic therapy for people with psoriasis should be undertaken by specialist physicians experienced in the diagnosis and treatment of psoriasis. Routine monitoring may be delegated to other healthcare professionals, for example clinical nurse specialists. Manage psoriatic arthritis and/or multimorbidity in consultation with the relevant healthcare professionals.

R2 (↑↑) Agree and formalize arrangements for drug administration, monitoring and follow-up between health carers and the person receiving treatment.

R3 (↑↑) Offer people with psoriasis who are starting biologic therapy the opportunity to participate in long-term safety registries (the British Association of Dermatologists Biologics and

Criteria for biologic therapy

R4 (↑↑) Offer biologic therapy to people with psoriasis requiring systemic therapy if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated [see National Institute for Health and Care Excellence (NICE) guidelines CG153]⁷ and the psoriasis has a large impact on physical, psychological or social functioning [for example, Dermatology Life Quality Index (DLQI) or Children's DLQI > 10 or clinically relevant depressive or anxiety symptoms] and one or more of the following disease severity criteria apply:

- the psoriasis is extensive [defined as body surface area (BSA) > 10% or Psoriasis Area and Severity Index (PASI) ≥ 10]
- the psoriasis is severe at localized sites and associated with significant functional impairment and/or high levels of distress (for example nail disease or involvement of high-impact and difficult-to-treat sites such as the face, scalp, palms, soles, flexures and genitals).

R5 (↑) Consider biologic therapy earlier in the treatment pathway (e.g. if methotrexate has failed, is not tolerated or is contraindicated) in people with psoriasis who fulfil the disease severity criteria and who also have active psoriatic arthritis (see the NICE musculoskeletal conditions overview)⁸ or who have psoriasis that is persistent, i.e. that relapses rapidly (defined as > 50% baseline disease severity within 3 months of completion of any treatment) off a therapy that cannot be continued in the long term (e.g. narrowband ultraviolet B and ciclosporin).

Prescribing biologic therapy

R6 (↑↑) Be aware of the benefits of, contraindications to and adverse effects associated with biologic therapies and reference the drug-specific SPCs (www.medicines.org.uk/emc).

R7 (↑↑) Provide high-quality, evidence-based information to people being prescribed biologic therapies. Explain the risks

Table 1 Strength of recommendation ratings

Strength	Wording	Symbols	Definition
Strong recommendation for the use of an intervention	'Offer' (or similar, e.g. 'provide', 'advise', 'screen')	↑↑	Benefits of the intervention outweigh the risks; most patients would choose the intervention while only a small proportion would not; for clinicians, most of their patients would receive the intervention; for policymakers, it would be a useful performance indicator
Weak recommendation for the use of an intervention	'Consider'	↑	Risks and benefits of the intervention are finely balanced; many patients would choose the intervention but many would not; clinicians would need to consider the pros and cons for the patient in the context of the evidence; for policymakers, it would be a poor performance indicator where variability in practice is expected
No recommendation		⊖	Insufficient evidence to support any recommendation
Strong recommendation against the use of an intervention	'Do not offer'	↓↓	Risks of the intervention outweigh the benefits; most patients would not choose the intervention while only a small proportion would; for clinicians, most of their patients would not receive the intervention

and benefits to people undergoing this treatment (and their families or carers where appropriate), using absolute risks and natural frequencies when possible (see File S1: Table S2: Decision Aid; see Supporting Information). Explain the treatment regimen and importance of treatment adherence. Allow them adequate time to consider the information. See also R14.

R8 (↑↑) Support and advice should be offered to people with psoriasis (and their families or carers where appropriate) by healthcare professionals who are trained and competent in the use of biologic therapies.

Reviewing biologic therapy

R9 (↑↑) Assess initial response to biologic therapy in people with psoriasis at time points appropriate for the drug in question, and then on a regular basis during therapy (e.g. every 6 months); see the Summary of licensed indications and posology in File S1: Table S1 in the Supporting Information.

R10 (↑↑) Review the response to biologic therapy by taking into account:

- psoriasis disease severity compared with baseline (e.g. PASI baseline to endpoint score)⁹
- the agreed treatment goal
- control of psoriatic arthritis disease activity and/or inflammatory bowel disease (in consultation with a rheumatologist and/or gastroenterologist)
- the impact of psoriasis on the person's physical, psychological and social functioning
- the benefits vs. the risks of continued treatment
- the views of the person undergoing treatment (and their family or carers, where appropriate)
- adherence to the treatment.

R11 (↑↑) Assess whether the minimal response criteria have been met, as defined by:

- a 50% or greater reduction in baseline disease severity (e.g. PASI 50 response, or percentage BSA where PASI is not applicable) and
- clinically relevant improvement in physical, psychological or social functioning (e.g. ≥ 4 -point improvement in DLQI or resolution of low mood).

R12 (↑) Consider changing to an alternative therapy, including another biologic therapy, if any of the following applies:

- the psoriasis does not achieve the minimum response criteria (primary failure – see R11)
- the psoriasis initially responds but subsequently loses this response (secondary failure)
- the current biologic therapy cannot be tolerated or becomes contraindicated.

Choice of biologic therapy: general considerations

R13 (↑↑) Before initiating or making changes to biologic therapy, take into account both psoriasis and psoriatic arthritis and manage treatment in consultation with a rheumatologist or

paediatric rheumatologist. Be aware that the presence of and phenotype of psoriatic arthritis (e.g. peripheral vs. axial disease) may influence access to, choice of and dose of biologic therapy. Actively screen for psoriatic arthritis (in people without this diagnosis), using a validated tool, e.g. Psoriasis Epidemiology Screening Tool (PEST), and be aware that the PEST may not detect axial arthritis/inflammatory back pain.

R14 (↑↑) Tailor the choice of agent to the needs of the person. Take into account the following factors (see File S1: Table S2: Decision Aid in the Supporting Information):

Psoriasis factors:

- the goal of therapy [for example, Physician's Global Assessment of clear or nearly clear]
- disease phenotype and pattern of activity
- disease severity and impact
- the presence of psoriatic arthritis (in consultation with an adult or paediatric rheumatologist)
- the outcomes of previous treatments for psoriasis.

Other individual factors:

- person's age
- past or current comorbid conditions (e.g. inflammatory bowel disease, heart failure)
- conception plans
- body weight
- the person's views and any stated preference on administration route or frequency
- likelihood of adherence to treatment.

Drug costs:

- including administration costs, dosage, price per dose and commercial arrangements.

Choice of biologic therapy in adults

R15 (↑↑) Offer any of the currently licensed biologic therapies as first-line therapy (and with reference to R18 and R19) to adults with psoriasis who fulfil the criteria for biologic therapy (see R4 and R5), using the Decision Aid (see File S1: Table S2 in the Supporting Information) to inform treatment choice.

R16 (↑↑) Offer any of the currently licensed biologic therapies (and with reference to R18 and R19) when psoriasis has not responded to a first biologic therapy. Use the Decision Aid (see File S1: Table S2 in the Supporting Information) and take into account all factors detailed in R14 to select the most appropriate agent.

R17 (↑↑) Offer a TNF antagonist (and with reference to R18 and R19) or an IL-17 antagonist* as a first-line therapy to adults with psoriasis and who also have psoriatic arthritis, using the Decision Aid (see File S1: Table S2 in the Supporting Information) to inform treatment choice.^{10–13} *Please note that brodalumab is not licensed for psoriatic arthritis.

R18 (↑) Consider etanercept for use in people where a TNF antagonist is indicated and other available biological agents have failed or cannot be used, or where a short half-life is important.

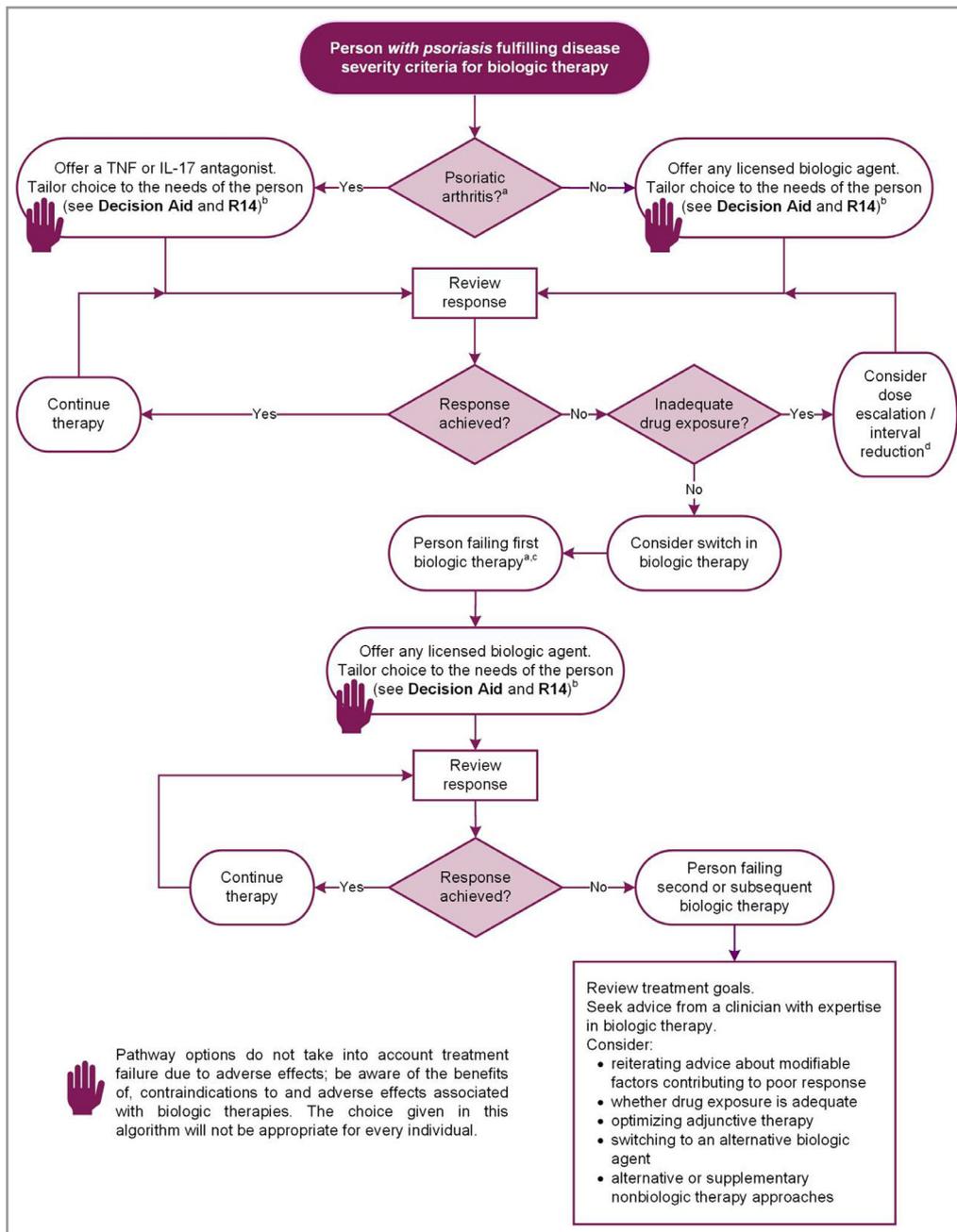


Figure 1 Pathway algorithm to guide choice of biologic therapy in adults with psoriasis. This guidance applies to biosimilars, subject to recommendations given within the British Association of Dermatologists position statement and European Medicines Agency guidelines.⁶

^aTake into account both psoriasis and psoriatic arthritis before initiating or making changes to biologic therapy, and manage treatment in consultation with a rheumatologist; be aware that the presence of and phenotype of psoriatic arthritis (for example, peripheral vs. axial disease) may influence access to, choice of and dose of biologic therapy. ^bTake into account psoriasis factors (the goal of therapy, e.g. Physician's Global Assessment clear or nearly clear, disease phenotype and pattern of activity, disease severity and impact, presence of psoriatic arthritis, outcomes of previous treatment for psoriasis); other individual factors (age, past or current comorbid conditions, conception plans, body weight, the person's views and any stated preference on administration route or frequency, adherence); and drug costs (including administration costs, dosage, price per dose and commercial arrangements). ^cConsider changing to an alternative biologic therapy if any of the following applies: the psoriasis does not achieve the minimum response criteria (primary failure: see R11) or the psoriasis initially responds but subsequently loses this response (secondary failure). ^dConsider escalating the dose of/reducing the interval for biologic therapy in adults (R20) when an inadequate primary response may be due to insufficient drug exposure (e.g. in people who are obese and/or whose psoriasis relapses during the treatment cycle and/or if the drug level is known to be subtherapeutic). Take into account that dose escalation/interval reduction may be associated with an increased risk of infection, and, depending on the drug, it may be off-licence and not funded. Currently, a dose-escalation/interval-reduction strategy is not applicable to brodalumab, guselkumab, risankizumab or secukinumab. IL, interleukin; TNF, tumour necrosis factor

R19 (↑↑) Reserve infliximab for use in people with very severe disease, or where other available biological agents have failed or cannot be used, or where weight-based dosing is a priority.

When to consider dose escalation/interval reduction

R20 (↑) Consider escalating the dose of or reducing the interval for biologic therapy in adults (see Table 2) and when an inadequate primary response might be due to insufficient drug exposure (e.g. in people who are obese and/or whose psoriasis relapses during the treatment cycle and/or if the drug level is known to be subtherapeutic). Take into account that this may be associated with an increased risk of infection/adverse events and, depending on the drug, off-licence (see Table 2) and may not be approved by NICE and therefore not funded.

What to do when a second or subsequent biologic therapy fails in adults

R21 (↑↑) When a person's psoriasis responds inadequately to a second or subsequent biological agent, review treatment goals, seek advice from a dermatologist with expertise in biologic therapy and consider any of the following strategies:

- reiterate advice about modifiable factors contributing to poor response such as obesity and poor adherence (intentional or nonintentional)
- consider whether drug exposure is adequate (see R20)
- optimize adjunctive therapy (e.g. switch from oral to subcutaneous methotrexate)
- switch to an alternative biological agent
- alternative or supplementary nonbiologic therapy approaches (e.g. inpatient topical therapy, phototherapy or systemic therapies).

Choice of biologic therapy in children and young people

R22 (↑↑) Offer adalimumab (age ≥ 4 years), etanercept (≥ 6 years) or ustekinumab (≥ 12 years) to children and young people who fulfil the criteria for biologic therapy (see also R4 and R5).

R23 (↑↑) When a child's or young person's psoriasis responds inadequately to a first or subsequent biological agent seek

advice from a dermatologist with expertise in biologic therapy in this age group and consider any of the following strategies:

- reiterate advice about modifiable factors contributing to poor response (e.g. obesity and poor adherence)
- optimize adjunctive therapy (e.g. switch from oral to subcutaneous methotrexate)
- switch to an alternative biological agent
- alternative or supplementary nonbiologic therapy approaches (e.g. inpatient topical therapy or systemic therapies).

Transitioning to or between biologic therapies

R24 (↑↑) When choosing the transitioning strategy from one drug therapy to another and whether a therapy washout (or no washout) should be used, take into consideration:

- the pharmacology of the drugs that are being stopped and started (see File S1: Table S1: Summary of licensed indications and posology, in the Supporting Information)
- the person's clinical circumstances (see R14)
- the person's views on the risks and benefits of transitioning option(s).

R25 (↑) When transitioning from standard systemic therapy to biologic therapy consider these:

- in stable disease, aim to allow 1 month to elapse between the last dose of any current standard systemic immunosuppressant psoriasis therapy (except methotrexate) and the planned date of biologic initiation
- start a biologic therapy with no drug washout period in people taking methotrexate, or in people on other therapies where this would lead to unstable disease
- when standard, systemic immunosuppressant therapy cannot be stopped (e.g. in people for whom a disease flare would be severe or hazardous), rationalize use of therapy and stop as soon as possible (e.g. when a minimum response has been achieved).

R26 (↑) When transitioning to a new biologic therapy (from a previous biologic therapy) consider using a 1-month washout period, or the length of the treatment cycle (whichever is longer), between the last dose of the current biologic therapy and the planned date of biologic initiation.

Table 2 Dose-escalation/interval-reduction strategy

Biological agent	Suggested dose-escalation/interval-reduction strategy
Adalimumab 40 mg every other week	Adalimumab 40 mg weekly
Certolizumab pegol 200 mg every 2 weeks	Certolizumab pegol 400 mg every 2 weeks
Etanercept 50 mg once weekly	Etanercept 50 mg twice weekly
Infliximab 5 mg kg ⁻¹ every 8 weeks	^a Infliximab 5 mg kg ⁻¹ every 6 weeks
Ixekizumab 80 mg every 4 weeks	^a Ixekizumab 80 mg every 2 weeks
Tildrakizumab 100 mg every 12 weeks	Tildrakizumab 200 mg every 12 weeks (high disease burden or ≥ 90 kg)
Ustekinumab 45 mg every 12 weeks (≤ 100 kg)	^a Ustekinumab 90 mg every 8 or 12 weeks (≤ 100 kg)
Ustekinumab 90 mg every 12 weeks (> 100 kg)	^a Ustekinumab 90 mg every 8 weeks (> 100 kg)

^aOff-licence use.

Conception and pregnancy

R27 (↑↑) Advise women of childbearing potential, who are starting biologic therapy for psoriasis, to use effective contraception and to discuss conception plans with the consultant supervising their care (see R29). There are no known interactions between biologic therapies and contraceptive methods (see drug-specific SPCs).

R28 (↑↑) For women planning conception or who are pregnant, provide information about what is known about the effects of biologic therapy (see drug-specific SPCs), including these:

- the importance of controlling severe or unstable psoriasis to maintain maternal health
- most of the available evidence relates to TNF antagonists in women with rheumatological or inflammatory bowel disease
- most pregnancies reported in women exposed to TNF antagonists at conception and/or during pregnancy have successful outcomes, with no increase in stillbirths, congenital malformations, preterm births or neonatal infections
- exposure to TNF antagonists during pregnancy may increase the risk of maternal infection
- maternal IgG, and therefore biological drugs currently licensed for psoriasis (with the exception of certolizumab pegol), is actively transferred to the developing fetus during the second and third trimesters and the impact of this on neonatal development and risk of infection has not been adequately studied
- certolizumab pegol transfer across the placenta is low or negligible
- in general, live vaccines must be avoided for the first 6 months of life in infants born to mothers taking biologic therapy beyond 16 weeks' gestation (see drug-specific SPCs)
- relevant patient information resources.¹⁴

R29 (↑↑) Discuss the risks and benefits of using biologic therapy in women who are planning conception or who are pregnant. Offer advice on a case-by-case basis by taking into account the woman's views and:

- the available evidence (see R28)
- her current disease status
- the course of psoriasis disease and the fetal outcome during any prior pregnancies
- the risk of severe or unstable psoriasis without biologic therapy
- her physical, psychological and social functioning without biologic therapy
- the options for alternative treatment strategies in the event of disease flare.

R30 (↑) If the decision to use biologic therapy when planning conception or during pregnancy has been made:

- consider using certolizumab pegol as a first-line choice when starting biologic therapy in women planning conception

- consider stopping biologic therapy in the second/third trimester to minimize fetal exposure and limit the potential risk to the neonate, taking into account individual biologics' pharmacokinetics and transfer across the placenta (File S1: Table S1: Summary of licensed indications and posology; see Supporting Information)
- consider using ciclosporin or certolizumab pegol as first-line options when it is necessary to start a systemic therapy during the second or third trimester.

R31 (GPP) Consider continuing or restarting biologic therapy in women wishing to breastfeed. Explain the benefits of breastfeeding and that the small amounts of biologic therapy present in breast milk are unlikely to be absorbed systemically by the infant.

R32 (↑↑) Ensure consultation and information sharing across specialities, including with an obstetrician who has expertise in caring for pregnant women with medical problems. Collect pregnancy outcome data for safety registries, for example BADBIR in the UK and Republic of Ireland.

R33 (↑↑) Be aware that limited evidence reports that use of TNF antagonist therapy by men around the time of conception resulted in successful outcomes in most pregnancies, with no increased risk of congenital malformations, preterm births or small for gestational age infants.

Biologic therapy and cancer risk

R34 (↑↑) Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:

- their past or current history of cancer (see R36 and R37) and/or
- any future risk of cancer.

R35 (↑↑) Provide information to people with psoriasis about the importance of participating in national cancer screening programmes.

R36 (↑↑) Exercise caution and discuss with the relevant cancer specialist when prescribing biologics in people with psoriasis and:

- a history of cancer, particularly if this has been diagnosed and treated less than 5 years previously and/or
- where the baseline risk of skin cancer is increased.

R37 (↑↑) Discuss the risks and benefits of continuing vs. stopping biologic therapy in patients who develop or have completed recent treatment for cancer. Offer advice on a case-by-case basis by taking into account the advice from the treating oncologist, multidisciplinary team discussion and patient choice considering:

- the risk of severe or unstable psoriasis if the biologic therapy were stopped
- the physical, psychological and social functioning if the biologic therapy were stopped
- the options for alternative treatment strategies
- the impact of cancer progression/recurrence.

Biologic therapy and infections

R38 (↑↑) Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:

- risk factors for infection (e.g. comorbidities, cotherapy, lifestyle and travel)
- known infections (past or current)
- signs or symptoms suggestive of infection.

Biologic therapy and chronic viral infections – hepatitis B, hepatitis C and HIV

R39 (↑↑) Test for hepatitis B (surface antigen and core antibody), hepatitis C (IgG) and HIV (HIV-1 and HIV-2 antibodies and HIV-1 antigen) infection in people starting biologic therapy.

R40 (↑) Consider ongoing screening (e.g. annually) for hepatitis B, hepatitis C and HIV, particularly in people who are at increased risk of infection (File S1: Table S5: Groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV; see Supporting Information).¹⁵

R41 (↑↑) Retest for viral hepatitis in any person who develops unexplained transaminitis (raised alanine aminotransferase and/or aspartate aminotransferase); retest for HIV infection in any person who has symptoms or other conditions that might represent HIV seroconversion/infection.

R42 (↑↑) Consult a hepatitis specialist when treating all people with biologic therapy who have hepatitis B or C infection, whether newly diagnosed or previously known.

R43 (↑↑) Provide treatment options to people with psoriasis who are HIV seropositive on a case-by-case basis; be aware that severe psoriasis can occur in people with uncontrolled HIV infection. Involve relevant specialists and ensure HIV viral load is suppressed on antiretroviral therapy before considering biologic therapy.

R44 (GPP) Test for varicella zoster (VZ) virus antibody in people with a negative or uncertain history for chickenpox before starting biologic therapy. Consider varicella vaccination before initiating biologic therapy in those who are not varicella immune and seek expert advice. Be aware of the indications for postexposure prophylaxis in VZ-susceptible individuals taking biologics, with VZ immunoglobulin or oral aciclovir/valaciclovir.¹⁶

Use of biologic therapy and tuberculosis

R45 (↑) Consider screening for latent tuberculosis (TB) with an interferon-gamma release assay (IGRA) alone, or with an IGRA and concurrent Mantoux test; be aware of the individual's risk factors for TB when interpreting results.¹⁷

R46 (↑↑) Apply local policy on the use of a plain chest radiograph for screening for TB to rule out abnormalities at baseline including granulomas indicative of prior infection and other confounding lung diseases. If positive, assess for active

TB and/or management of latent TB in consultation with a TB specialist (see NICE tuberculosis guideline).¹⁷

R47 (GPP) In people who require treatment for latent TB [3 months of isoniazid (with pyridoxine) and rifampicin, or 6 months of isoniazid (with pyridoxine)], aim to complete 2 months of treatment before commencing biologic therapy.

R48 (GPP) Any symptoms or signs suggestive of TB, new exposure to TB or prolonged residence in a high-incidence setting should prompt further clinical assessment and investigation, including a repeat IGRA. Be aware that active TB on TNF antagonist therapy is often disseminated and extrapulmonary; symptoms may include unexplained weight loss, night sweats, nonresolving cough, haemoptysis and lymphadenopathy.

R49 (GPP) Inform people that they should seek medical advice if symptoms of TB develop during or after treatment with a biologic therapy and issue a patient alert card in line with Medicines and Healthcare products Regulatory Agency guidance.¹⁸

Biologics and vaccination

R50 (↓↓) Do not give live vaccines to people on biologic therapy or to infants (up to 6 months of age) whose mothers have received biologic therapy beyond 16 weeks' gestation. Please check individual drug SPC.

R51 (↑↑) Stop biologic therapy for 6–12 months before giving live vaccines, e.g. the varicella and shingles (herpes zoster) vaccine. Be aware that the UK Green Book (*Immunisation Against Infectious Disease*)¹⁹ has recently advised increasing the interval from 6 to 12 months; expert opinion suggests the interval required will vary depending on the pharmacokinetic/pharmacodynamic profile of each drug and should be determined on a case-by-case basis, taking into account the SPC drug specifications and expert advice. Biologic therapy can be started 4 weeks after administration of a live vaccine.

R52 (↑↑) Provide people on biologic therapy with information on safe use of vaccinations including which vaccination should be used and which to avoid (see BAD Patient Information Leaflet on immunization, www.bad.org.uk/leaflets, and the Green Book,¹⁹ with reference to the clinical risk category 'immunosuppression').

R53 (↑↑) Where possible, complete all required vaccinations prior to initiation of biologic therapy and review vaccination requirements during therapy with reference to the Green Book¹⁹ and the clinical risk category 'immunosuppression'.

Important contraindications to biologic therapies

R54 (GPP) Do not use TNF antagonists in people with demyelinating diseases and consider alternative interventions in people who have a first-degree relative with demyelinating disease.

R55 (GPP) Stop treatment and seek specialist advice if neurological symptoms suggestive of demyelinating disease develop

during TNF antagonist therapy. Symptoms include loss or reduction of vision in one eye with painful eye movements; double vision; ascending sensory disturbance and/or weakness; problems with balance, unsteadiness or clumsiness; altered sensation travelling down the back and sometimes into the limbs when bending the neck forwards (Lhermitte symptom); please see NICE guidelines CG186.²⁰

R56 (GPP) Avoid TNF antagonist therapy in people with severe cardiac failure [New York Heart Association (NYHA) class III and IV].

R57 (GPP) Assess people with well-compensated (NYHA class I and II) cardiac failure (see the NICE pathway)²¹ and consult with a cardiology specialist before using TNF antagonist therapy.

R58 (GPP) Stop TNF antagonist therapy in the event of new or worsening pre-existing heart failure and seek specialist advice.

R59 (GPP) Exercise caution and consult a gastroenterology specialist before using brodalumab, ixekizumab or secukinumab in people with inflammatory bowel disease.

R60 (GPP) In people undergoing elective surgery, balance the risk of postoperative infection against the risk of developing severe or unstable disease by stopping biologic therapy. Advise stopping biologic therapy 3–5 times the half-life of the drug in question (File S1: Table S1: Summary of licensed indications and posology; see Supporting Information) or the length of the treatment cycle (whichever is longer) between the last dose of therapy and the planned surgery. Inform the surgical team that the patient may be at a higher risk of infection postoperatively. Restart biologic therapy postoperatively if there is no evidence of infection and wound healing is satisfactory.

Implementation toolkit

To support implementation of the recommendations, a number of documents have been developed (see File S1: Implementation Toolkit, including the Decision Aid, in the Supporting Information). These comprise a summary of licensed indications and posology for biologic therapy (Table S1); a Decision Aid, informed by the evidence reviews, to help patients and clinicians choose the appropriate biologic therapy (Table S2); absolute effects of biological drugs at licensed doses relative to placebo (Table S3); a suggested schedule for screening and monitoring (Table S4) and a list of groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV (Table S5).

Audit standards, data items and data-collection methodology

Dermatology teams involved in prescribing biological interventions should use audit as a tool to monitor their service against national guidelines of care. The aim should be to ensure that the service is high in quality, safe and cost-effective. For further details see File S3: Audit standards in the Supporting Information.

Stakeholder involvement and peer review

The guideline and supplementary information was made available to the BAD membership, British Society for Paediatric Dermatology, British Dermatological Nursing Group, Primary Care Dermatological Society, British Society for Paediatric and Adolescent Rheumatology, British Society of Rheumatology, Royal College of Obstetrics and Gynaecology, Psoriasis and Psoriatic Arthritis Alliance, Psoriasis Association and relevant pharmaceutical companies (see File S2: Appendix M in the Supporting Information for the full list of stakeholders), comments from whom were actively considered by the GDG. The finalized version was peer reviewed by the Clinical Standards Unit of the BAD, made up of the Therapy & Guidelines subcommittee, prior to submission for publication.

Limitations of the guideline

This document has been prepared on behalf of the BAD and is based on the best data available when the document was prepared. It is recognized that under certain conditions it may be necessary to deviate from the guidelines and that the results of future studies may require some of the recommendations herein to be changed. Failure to adhere to these guidelines should not necessarily be considered negligent, nor should adherence to these recommendations constitute a defence against a claim of negligence. Limiting the review to English-language references was a pragmatic decision, but the authors recognize that this might exclude some important information published in other languages.

Plans for guideline revision

This 2020 guideline updates the previous version.¹ An annual literature review is planned for this fast-moving subject and the recommendations updated where necessary, in line with the BAD's recommended guideline development methodology.²

Acknowledgments

We are grateful to the following for their critical review, advice and assistance: patient representatives on the current and previous GDG for their input in ranking the outcomes, contributing to the discussion from patients' perspectives, and reviewing the evidence, subsequent draft guideline, algorithm and Decision Aid; BAD Therapy & Guidelines subcommittee; all individuals and stakeholders who commented on the draft during the consultation period.

References

- 1 Smith CH, Jabbar-Lopez ZK, Yiu ZZ *et al.* British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol* 2017; **177**:628–36.
- 2 Mohd Mustapa MF, Exton LS, Bell HK *et al.* Updated guidance for writing a British Association of Dermatologists clinical guideline:

- the adoption of the GRADE methodology 2016. *Br J Dermatol* 2017; **176**:44–51.
- 3 Brouwers MC, Kho ME, Browman GP *et al.* AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ* 2010; **182**:E839–42.
 - 4 GRADE Working Group. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group website. Available at: <http://www.gradeworkinggroup.org/> (accessed 26 February 2020).
 - 5 British Association of Dermatologists. Position Statement on Biosimilars 2017. September 2017. Available at: www.bad.org.uk/shared/get-file.ashx?itemtype=document&id=5709 (accessed 26 February 2020).
 - 6 European Medicines Agency. Guideline on similar biological medicinal products. CHMP/437/04 Rev 1. October 2014. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/10/WC500176768.pdf (accessed 26 February 2020).
 - 7 NICE guidelines. Psoriasis: assessment and management CG153. 2012 (updated September 2017). Available at: <https://www.nice.org.uk/guidance/CG153> (accessed 26 February 2020).
 - 8 NICE pathways. Musculoskeletal conditions overview. October 2019. Available at: <http://pathways.nice.org.uk/pathways/musculoskeletal-conditions#content=view-node%3Anodes-psoriatic-arthritis&path=view%3A/pathways/musculoskeletal-conditions/arthritis.xml> (accessed 26 February 2020).
 - 9 British Association of Dermatologists. Healthcare professionals: forms/downloads. Available at: <http://www.bad.org.uk/healthcare-professionals/forms-downloads> (accessed 26 February 2020).
 - 10 NICE technology appraisal guidance. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis TA199. 25 August 2010. Available at: <https://www.nice.org.uk/guidance/ta199> (accessed 26 February 2020).
 - 11 NICE technology appraisal guidance. Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs TA445. 24 May 2017. Available at: <https://www.nice.org.uk/guidance/ta445> (accessed 26 February 2020).
 - 12 NICE technology appraisal guidance. Ixekizumab for treating active psoriatic arthritis after inadequate response to DMARDs TA537. 8 August 2018. Available at: <https://www.nice.org.uk/guidance/ta537> (accessed 26 February 2020).
 - 13 NICE technology appraisal guidance. Golimumab for the treatment of psoriatic arthritis TA220. 27 April 2011. Available at: <https://www.nice.org.uk/guidance/ta220> (accessed 26 February 2020).
 - 14 UK Tetralogy Information Service. Best use of medicines in pregnancy (Bumps). Available at: <http://www.medicinesinpregnancy.org/bumps/Medicine-pregnancy> (accessed 26 February 2020).
 - 15 British HIV Association. BHIVA guidelines for routine investigation and monitoring of adult HIV-1-positive individuals (2016). 2019 Interim update. Available at: <https://www.bhiva.org/monitoring-guidelines> (accessed 26 February 2020).
 - 16 Public Health England. Guidance for issuing varicella-zoster immunoglobulin (VZIG). 2017. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/740541/VZIG_issuing_guidance.pdf (accessed 26 February 2020).
 - 17 NICE guidelines. Tuberculosis NG33. 2016 (updated September 2019). Available at: <https://www.nice.org.uk/guidance/ng33> (accessed 26 February 2020).
 - 18 Medicines and Healthcare products Regulatory Agency. Tumour necrosis factor alpha inhibitors. 11 December 2014. Available at: <https://www.gov.uk/drug-safety-update/tumour-necrosis-factor-alpha-inhibitors> (accessed 26 February 2020).
 - 19 Public Health England. Immunisation Against Infectious Disease. Contraindications and special considerations: the Green Book, chapter 6. 2013 (updated 26 October 2017). Available at: <https://www.gov.uk/government/publications/contraindications-and-special-considerations-the-green-book-chapter-6> (accessed 26 February 2020).
 - 20 NICE guidelines. Multiple sclerosis in adults: management. Clinical guideline CG186. 2014 (updated November 2019). Available at: www.nice.org.uk/guidance/cg186 (accessed 26 February 2020).
 - 21 NICE pathways. Diagnosing and assessing chronic heart failure. 12 February 2020. Available at: <https://pathways.nice.org.uk/pathways/chronic-heart-failure#path=view%3A/pathways/chronic-heart-failure/diagnosing-and-assessing-chronic-heart-failure.xml&content=view-node%3Anodes-history-examination-and-referral> (accessed 26 February 2020).

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

File S1 Implementation toolkit, including the Decision Aid. Tables: (S1) Summary of licensed indications and posology for biologic therapy for psoriasis. (S2) Decision Aid – biologic therapy for psoriasis (informed by the evidence reviews, to help patients and clinicians choose the appropriate biologic therapy). (S3) Absolute effects of biological drugs at licensed doses relative to placebo. (S4) Suggested schedule for screening and monitoring. (S5) Groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV.

File S2 Supplementary information. Appendices: (A) Systematic review protocols (B) Network meta-analyses and forest plots. (C) Clinical evidence summaries. (D) Linking Evidence To Recommendations (LETR). (E) GRADE evidence profiles. (F) Summary of included studies. (G) PRISMA diagrams – study selection. (H) Papers excluded from quantitative analysis. (I) Methodology. (J) Search strategy. (K) Guideline development group members. (L) Declarations of interests. (M) List of stakeholders.

File S3 Audit standards, data items and data-collection methodology.

Appendix Author affiliations

- ¹St John's Institute of Dermatology, ⁸Department of Infectious Diseases, ⁹Pharmacy Department and ¹³Women's Health Academic Centre; Guy's and St Thomas' NHS Foundation Trust, London SE1 9RT, UK
- ²Dermatology Centre Salford Royal NHS Foundation Trust, The University of Manchester, Manchester Academic Health Science Centre, NIHR Manchester Biomedical Research Centre, Manchester M13 9PT, UK
- ³British Dermatology Nursing Group representative Aneurin Bevan Health Board, Wales, UK
- ⁴Institute of Infection, Immunity and Inflammation University of Glasgow Glasgow G12 8QQ, UK
- ⁵British Society for Rheumatology, London EC4Y 8EE, UK
- ⁶Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences University of Oxford, Oxford OX3 7LD, UK
- ⁷Patient representative

10 BAD guidelines: rapid update: biologic therapy for psoriasis, Smith *et al.*

¹⁰Department of Dermatology Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield S10 2JF, UK

¹¹Department of Dermatology Sheffield Children's NHS Foundation Trust, Sheffield S10 3FL, UK

¹²University of Nottingham University Park, Nottingham NG7 2RD, UK

¹⁴Department of Dermatology East Lancashire Hospitals NHS Trust, Burnley BB10 2PQ, UK

¹⁵Department of Dermatology Liverpool University Hospitals NHS Foundation Trust, Liverpool L7 8XP, UK

¹⁶Warwick Centre for Applied Health Research and Delivery, Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry CV4 7AL, UK

¹⁷British Association of Dermatologists, London W1T 5HQ, UK