British Association of Dermatologists guidelines for biologic therapy for psoriasis
2017


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The multi-disciplinary guideline development group (GDG) comprised medical specialists (consultants in dermatology, paediatric dermatology, rheumatology, virology and obstetric medicine), a clinical nurse specialist, dermatology trainees, two patient representatives and a research team providing technical and methodological support.

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Reviewed and updated in 2009, 2017

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Key words: biologic therapy, psoriasis, guideline, systematic review, meta-analysis, network meta-analysis, GRADE

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 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 evidence-based recommendations on the use of biologic therapies (adalimumab, etanercept, infliximab, ixekizumab, secukinumab and ustekinumab) 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. Biologic therapies have now been in use for over 10 years, and with accrued patient-years exposure and clinical experience, many areas that were covered in previous versions of the guideline are now part of the Summary of Product Characteristics (SPC) and/or routine care so that specific recommendations are redundant (see Toolkit A: Summary of licensed indications and posology for biologic therapy, in Supporting information 2). Therefore, in this update we focus on areas where there has been a major change in the evidence base or clinical practice, where practice is very varied and/or where clear consensus or guidelines are lacking (see section 3.1 in Supporting information 1).

This set of guidelines has been developed using the BAD’s recommended methodology1 with reference to the Appraisal of Guidelines Research and Evaluation (AGREE II) instrument [www.agreetrust.org]2 and the Grading of Recommendations Assessment, Development and Evaluation (GRADE). Recommendations were developed for implementation in the NHS (U.K.). Note that 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 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 statement4 and EMA guidelines.5 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.

To aid implementation, this executive summary contains only key clinical findings and recommendations (see Table 2) derived from systematic review of the evidence. The strength of recommendation is expressed by the wording and symbols featured in Table 1. Good practice point (GPP) recommendations are derived from informal consensus. A decision aid, informed by the evidence reviews, has been developed to help patients and clinicians choose the appropriate biologic therapy (see Table 3) and a suggested schedule for screening and monitoring (see Table 4) is also provided. The full version of the guideline is available online (Supporting information 1) and includes details on methodology, six systematic reviews with appraisal and discussion of the clinical evidence.
Table 1. Strength of recommendation ratings

### SUMMARY OF RECOMMENDATIONS

The evidence- and consensus-based (GPP) recommendations listed in Table 2 below should be implemented in the context of the evidence and discussions in the full version of the guideline.

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Strength</th>
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<tbody>
<tr>
<td><strong>Using biologic therapy</strong></td>
<td></td>
</tr>
<tr>
<td><strong>R1</strong></td>
<td>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 multi-morbidity in consultation with the relevant healthcare professionals.</td>
</tr>
<tr>
<td><strong>R2</strong></td>
<td>Agree and formalise arrangements for drug administration, monitoring and follow-up between health carers and the person receiving treatment</td>
</tr>
<tr>
<td><strong>R3</strong></td>
<td>Offer people with psoriasis who are starting biologic therapy the opportunity to participate in long-term safety registries (in the U.K. and Republic of Ireland the British Association of Dermatologists Biologic Interventions Register, BADBIR)</td>
</tr>
</tbody>
</table>

| **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 and the psoriasis has a large impact on physical, psychological or social functioning (for example, a DLQI or cDLQI of >10 or clinically relevant depressive or anxiety symptoms) and one or more of |  |

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2. Please see NICE guidelines CG153 for more information on contraindications and reviewing treatment response to phototherapy and systemic therapy

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the following disease severity criteria apply:
- the psoriasis is extensive (defined as BSA >10%, or a PASI ≥10, or at least ‘moderate’ on physician’s global assessment$^{III}$)
- the psoriasis is severe at localised 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)

$^{III}$ physician’s global assessment clear, nearly clear, mild, moderate, severe, very severe

$^{IV}$ Please see http://pathways.nice.org.uk/pathways/musculoskeletal-conditions#content=view-node%3Anodes-psoriatic-arthritis&path=view%3A/pathways/musculoskeletal-conditions/arthritis.xml

$^{V}$ Rapid relapse is defined as greater than 50% of baseline disease severity within 3 months of completion of any treatment (for example narrow band UVB)

$^{VI}$ http://www.medicines.org.uk/emc/

$^{VII}$ http://www.bad.org.uk/healthcare-professionals/forms/downloads

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| R5 | Consider biologic therapy earlier in the treatment pathway (for example, if methotrexate has failed, is not tolerated or is contra-indicated) in people with psoriasis that fulfils the disease severity criteria and who also have active psoriatic arthritis$^{IV}$ or who have psoriasis that is persistent (i.e. that relapses rapidly off a therapy that cannot be continued long-term$^{V}$) |
| R6 | Be aware of the benefits of, contraindications to and adverse effects associated with biologic therapies and reference the drug-specific SPCs$^{VI}$ |
| R7 | Provide high-quality, evidence-based information to people being prescribed biologic therapies. Explain the risks and benefits to people undergoing this treatment (and their families or carers where appropriate), using absolute risks and natural frequencies when possible (see Table 3: Decision aid). Allow them adequate time to consider the information. |
| 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 |
| 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 (for example, every 6 months) |
| R10 | Review response to biologic therapy by taking into account: |
|    | - psoriasis disease severity compared with baseline (for example, Psoriasis Area and Severity Index [PASI] baseline to endpoint score$^{VII}$) |
|    | - 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 versus the risks of continued treatment |
|    | - the views of the person undergoing treatment (and their family or carers, where appropriate) |
|    | - adherence to the treatment |

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$^{VII}$ Rapid relapse is defined as greater than 50% of baseline disease severity within 3 months of completion of any treatment (for example narrow band UVB)

$^{VII}$ http://www.bad.org.uk/healthcare-professionals/forms-downloads

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| R11 | Assess whether the minimal response criteria have been met, as defined by:  
|     | • a 50% or greater reduction in baseline disease severity (for example, PASI 50 response, or % BSA where the PASI is not applicable) and  
|     | • clinically relevant improvement in physical, psychological or social functioning (for example, a 4-point or greater 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 | Take into account both psoriasis and psoriatic arthritis before initiating or making changes to biologic therapy, and:  
|     | • manage treatment in consultation with a rheumatologist or paediatric rheumatologist  
|     | • be aware that the presence of and phenotype of psoriatic arthritis (for example, peripheral versus axial disease) may influence access to, choice and dose of, biologic therapy |
| R14 | Tailor the choice of agent to the needs of the person and take into account the following factors (see Table 3: Decision aid):  

**Psoriasis factors**  
the goal of therapy (for example a PGA 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)  
outcomes to previous treatments for psoriasis  

**Other factors**  
person's age  
past or current co-morbid conditions (for example, inflammatory bowel disease, cardiovascular disease)  
conception plans  
body weight  
the person's views and any stated preference on administration route or frequency  
adherence  

| R15 | Be aware that the recommended first-line choice of biologic therapy will not be appropriate for every individual; use the decision aid and with reference to R14 to inform choice of alternative licensed biologic therapies. |

**Choice of biologic therapy in adults: first line**

| R16 | Offer ustekinumab as a first-line biologic agent to adults with psoriasis who fulfil the criteria for biologic therapy (see also R4 and R5) |
'Very severe' relates to the physician's global assessment or/and the NICE definition (PASI 20 or more and DLQI 18 or more) and failed to respond to standard systemic therapies such as ciclosporin, methotrexate or PUVA (psoralen and long-wave ultraviolet radiation), or the person is intolerant to or has a contraindication to these treatments.

Off-licence

R17 Offer adalimumab as a first-line biologic agent to adults with psoriasis particularly when psoriatic arthropathy is a consideration

R18 Consider secukinumab as a first-line biologic agent in adults with psoriasis, with or without psoriatic arthritis

Choice of biologic therapy in adults: second line

R19 Offer any of the currently licensed biologic therapies when psoriasis has not responded to a first biologic therapy. Use the decision aid (Table 3) and take into account all factors detailed in R14 to select the most appropriate agent.

Consideration

R20 Reserve infliximab for use in people with very severe disease VIII or where other available biologic agents have failed or cannot be used

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 biologic agent seek advice from a clinician with expertise in biologic therapy and consider any of the following strategies:

- reiterate advice about modifiable factors contributing to poor response (for example, obesity and poor adherence)
- optimise adjunctive therapy (for example, switch from oral to sub-cutaneous methotrexate)
- switch to an alternative biologic agent
- consider non-biologic therapy approaches (for example inpatient topical therapy, phototherapy or standard systemic therapy)

When to consider dose escalation

R22 Consider escalating the dose of biologic therapy in adults, where this is feasible and funded (see table below) when an inadequate primary response may be due to insufficient drug dosing (for example, in people who are obese or whose psoriasis relapses during the treatment cycle). Take into account that this may be associated with an increased risk of infection, and, depending on the drug, off-licence.

<table>
<thead>
<tr>
<th>Biologic agent</th>
<th>Suggested dose-escalation strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ustekinumab 45 mg every 12 weeks (&lt;100 kg)</td>
<td>Ustekinumab 90 mg every 12 weeks (&lt;100 kg) VIII</td>
</tr>
<tr>
<td>Ustekinumab 90 mg every 12 weeks (&gt;100 kg)</td>
<td>Ustekinumab 90 mg every 8 weeks (&gt;100 kg) VIII</td>
</tr>
<tr>
<td>Adalimumab 40 mg every other week</td>
<td>Adalimumab 40 mg weekly</td>
</tr>
<tr>
<td>Etanercept 50 mg once weekly</td>
<td>Etanercept 50 mg twice weekly</td>
</tr>
<tr>
<td>Infliximab 5 mg/kg every 8 weeks</td>
<td>Infliximab 5 mg/kg every 6 weeks IX</td>
</tr>
</tbody>
</table>

Choice of biologic therapy in children and young people

R23 Offer adalimumab (≥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)

R24 When a child’s or young person’s psoriasis responds inadequately to a first or subsequent...
Major congenital malformations reported in 3.6-5.0% of women exposed to anti-TNF compared with 1.5-4.7% in control groups (odds ratios [OR] = 1.32-1.64)

Biologic agent seek advice from a clinician with expertise in biologic therapy and consider any of the following strategies:
- reiterate advice about modifiable factors contributing to poor response (for example, obesity and poor adherence)
- optimise adjunctive therapy (for example, switch from oral to sub-cutaneous methotrexate)
- switch to an alternative biologic agent
- consider non-biologic therapy approaches (for example inpatient topical therapy or standard systemic therapy)

**Transitioning to/between biologic therapies**

**R25** 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 started and stopped (see Toolkit A: Summary of licensed indications and posology for biologic therapy, in Supporting information 2)
- the person’s clinical circumstances
- the person’s views on the risks and benefits of transitioning option(s)

**R26** Consider the following strategies when transitioning from standard systemic to biologic therapy:
- 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 (for example, in people for whom a disease flare would be severe or hazardous), rationalise use of therapy and stop as soon as possible (for example, when a minimum response has been achieved)

**R27** 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

**Conception and pregnancy**

**R28** Provide information about the possible effects of biologic therapy during conception and pregnancy including:
- the importance of controlling severe or unstable psoriasis to maintain maternal health
- that most pregnancies reported in women taking biologic therapy at conception and during pregnancy have successful outcomes
- that evidence about the effect of biologic therapy on conception and pregnancy mostly relates to TNF antagonists in women with rheumatological and inflammatory bowel disease; this evidence indicates a potential risk associated

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*X Major congenital malformations reported in 3.6-5.0% of women exposed to anti-TNF compared with 1.5-4.7% in control groups (odds ratios [OR] = 1.32-1.64)

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with exposure to TNF antagonists but is of low quality, and may relate to other factors (for example, other co-therapies or the underlying disease) that the risk of fetal abnormalities in women with psoriasis who conceive on biologic therapy has not been adequately studied and therefore cannot be quantified

- that maternal IgG, and therefore biologic drugs currently licensed for psoriasis, are actively transferred to the developing fetus during the second and third trimester and that the impact of this on fetal and neonatal development and risk of infection has not been adequately studied
- that live vaccines must be avoided in infants born to mothers taking biologic therapy beyond 16 weeks’ gestation
- relevant patient information resources\textsuperscript{xii}

| R29 | Advise women of child-bearing potential who are starting biologic therapy for psoriasis to use effective contraception\textsuperscript{xii} and discuss conception plans with the consultant supervising their care (see R30) |
| R30 | Discuss the risks and benefits of continuing versus stopping biologic therapy with women who are of child-bearing potential or who become pregnant. Offer advice on a case-by-case basis by taking into account the woman’s views and the:
  - course of psoriasis disease and the fetal outcome during any prior pregnancies
  - risk of severe or unstable psoriasis if the biologic therapy were stopped
  - physical, psychological and social functioning if the biologic therapy were stopped
  - options for alternative, non-biologic treatment strategies |
| R31 | Assess whether biologic therapy for psoriasis can be stopped in women who become pregnant. Ensure consultation and information-sharing across specialties 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 U.K. and Republic of Ireland. |
| R32 | Advise mothers who have received biologic therapy for psoriasis beyond 16 weeks’ gestation that their infants should not receive any live vaccinations until they have reached 6 months of age (for example, rotavirus and BCG) |

**Biologic therapy and cancer risk**

| R33 | Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:
  - their past or current history of cancer (see R35) and/or
  - any future risk of cancer |
| R34 | Provide information to people with psoriasis about the importance of participating in national cancer screening programmes |
| R35 | 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 <5 years previously and/or
  - where the baseline risk of skin cancer is increased (for example, previously treated non-melanoma skin cancer (NMSC)) |

\textsuperscript{xii} For example, http://www.medicinesinpregnancy.org/Medicine--pregnancy

\textsuperscript{xii} There are no known interactions between biologic therapies and contraceptive methods (see drug-specific SPCs)

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<table>
<thead>
<tr>
<th>Biologic therapy and infections</th>
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</table>
| R36  | Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:  
|      |  - risk factors for infection (for example, co-morbidities, co-therapy, lifestyle and travel)  
|      |  - known infections (past or current)  
|      |  - signs or symptoms suggestive of infection  
| R37  | Test for hepatitis B (surface antigen and core antibody), hepatitis C (IgG) and HIV (HIV-1 and HIV-2 antibody and HIV-1 antigen) infection in people starting biologic therapy  
| R38  | Consider ongoing screening (for example annually) for hepatitis B, hepatitis C and HIV, particularly in people who belong to a group at increased risk of infection (see Toolkit B: Groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV, in Supporting information 2)  
| R39  | Retest for viral hepatitis in any person who develops unexplained transaminitis (raised ALT and/or AST); retest for HIV infection in any person who has symptoms of HIV seroconversion.  
| R40  | Consult a hepatitis specialist when treating all people with biologic therapy who have hepatitis B or C infection, whether newly-diagnosed or previously known  
| R41  | 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 ART before considering biologic therapy.  
| R42  | Test for varicella zoster (VZ) virus antibody in people with a negative or uncertain history for chickenpox; consider varicella vaccination in those who are not varicella-immune and seek expert advice. Be aware of the indications for using VZ immunoglobulin in VZ-susceptible individuals.  

<table>
<thead>
<tr>
<th>Biologic therapy and chronic viral infections – hepatitis B, hepatitis C and HIV</th>
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</thead>
</table>
| R43  | Screen for latent TB with an interferon-gamma release assay. Arrange a plain chest radiograph 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 Tuberculosis NICE guideline)  
| R44  | 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’ treatment before commencing biologic therapy  
| R45  | Any symptoms or signs suggestive of TB, or new exposure to TB or prolonged residence in a high-incidence setting should prompt further clinical assessment and investigation, including a repeat interferon-gamma release assay. Be aware that active TB on TNF  

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XIII HIV testing and prevention: People who should be offered an HIV test (NICE and BHIVA guidelines); Offering and providing hepatitis B and C tests (NICE guidance) and BHIVA guidelines for routine investigation and monitoring of adult HIV-1-infected individuals www.bhiva.org/documents/Guidelines/Monitoring/160606-Monitoring-gl-draft-for-Consultation.pdf

XIV Good Practice Point (GPP)

XV NICE guidelines. Tuberculosis NG33 https://www.nice.org.uk/guidance/ng33

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<table>
<thead>
<tr>
<th><strong>antagonist therapy</strong> is often disseminated and extrapulmonary; symptoms may include unexplained weight loss, night sweats, non-resolving cough, haemoptysis and lymphadenopathy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>R46 Inform people that they should seek medical advice if symptoms of tuberculosis develop during or after treatment with a biologic therapy and issue a patient alert card in line with MHRA guidance</td>
</tr>
<tr>
<td><strong>Biologics and vaccination</strong></td>
</tr>
<tr>
<td>R47 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</td>
</tr>
<tr>
<td>R48 Stop biologic therapy for at least 6 months before giving live vaccines, and for 12 months in the case of Shingles (herpes zoster) vaccine. In general, biologic therapy can be started 4 weeks after administration of a live vaccine. Refer to the drug-specific SPC and Green Book (Immunisation against infectious disease) for further information.</td>
</tr>
<tr>
<td>R49 Provide people on biologic therapy information on safe use of vaccinations including which vaccination should be used and which to avoid (see BAD Patient Information Leaflet on immunisation and the Green Book, with reference to the clinical risk category ‘immunosuppression’)</td>
</tr>
<tr>
<td>R50 Where possible, complete all required vaccinations prior to initiation of biologic therapy and review vaccination requirements during therapy with reference to the Green Book and the clinical risk category ‘immunosuppression’</td>
</tr>
<tr>
<td><strong>Important contraindications to biologic therapies (Good Practice Point, GPP)</strong></td>
</tr>
<tr>
<td>R51 Do not use TNF antagonists in people with demyelinating diseases and review alternative interventions in people who have an affected first-degree relative with demyelinating disease</td>
</tr>
<tr>
<td>R52 Stop treatment and seek specialist advice if neurological symptoms suggestive of demyelinating disease develop during TNF antagonist therapy</td>
</tr>
<tr>
<td>R53 Avoid TNF antagonist therapy in people with severe (NYHA class III and IV) cardiac failure</td>
</tr>
<tr>
<td>R54 Assess people with well-compensated (NYHA class I and II) cardiac failure and consult with a cardiology specialist before using TNF antagonist therapy</td>
</tr>
<tr>
<td>R55 Stop TNF antagonist therapy in the event of new or worsening pre-existing heart failure and seek specialist advice</td>
</tr>
<tr>
<td>R56 Exercise caution and consult a gastroenterology specialist before using secukinumab or ixekizumab in people with inflammatory bowel disease</td>
</tr>
<tr>
<td>R57 In people undergoing elective surgery balance the potential benefit of preventing post-operative infection by stopping biologic therapy against the risk of developing severe or unstable disease. Advise stopping biologic therapy 3 to 5 times the half-life of the drug in</td>
</tr>
</tbody>
</table>

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**xviii** www.bad.org.uk/leaflets

**xix** 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's symptom); please see NICE guidelines CG186 www.nice.org.uk/guidance/cg186

**xx** Please see NICE Pathway 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

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Question (see Toolkit A: Summary of licensed indications and posology for biologic therapy, in Supporting information 2) 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 post-operatively. Restart biologic therapy postoperatively if there is no evidence of infection and wound healing is satisfactory.

Table 2. List of key recommendations

![Algorithm diagram]

Pathway algorithm to guide Choice of Biologic therapy in Adults with Psoriasis

Please use in conjunction with the summary of recommendations.

1. Offer biologic therapy to people fulfilling eligibility criteria
2. Tailor choice of agent to the needs of the person (see decision aid)
3. Consider switch in biologic therapy
4. Consider dose escalation
5. Consider re-iterating advice about modifiable factors contributing to poor response (e.g.: obesity / poor adherence) and optimising adjunctive therapy
6. Consider switching to an alternative biologic therapy or non biologic therapies
NOTES

1. Take into account psoriasis factors (the goal of therapy e.g. PGA clear/nearly clear; disease phenotype and pattern of activity; disease severity and impact; presence of psoriatic arthritis; outcomes of previous treatment for psoriasis) and other factors (age; past or current co-morbid conditions; conception plans; body weight).

2. Take 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 versus axial disease) may influence access to, choice and dose of, biologic therapy.

3. Consider 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).

4. Consider escalating the dose of biologic therapy in adults (R22) when an inadequate primary response may be due to insufficient drug dosing (for example, in people who are obese or whose psoriasis relapses during the treatment cycle). Take into account that dose escalation may be associated with an increased risk of infection, and, depending on the drug, off-licence and not funded. Currently, a dose-escalation strategy is not applicable to secukinumab or ixekizumab.

5. This guidance applies to biosimilars, subject to recommendations given within the BAD position statement and EMA guidelines.\textsuperscript{4,5}
DECISION AID
This table supports the decision-making process during the consultation for patients and clinicians before the initiation of biologic therapy. It is complementary to the existing patient information leaflets (PILs; www.bad.org.uk/leaflets). All biologic therapies for the treatment of psoriasis require bloods tests before and during treatment. If you have psoriatic arthritis, your doctor will take this into consideration.

<table>
<thead>
<tr>
<th>Frequently Asked Questions</th>
<th>Adalimumab</th>
<th>Etanercept</th>
<th>Infliximab</th>
<th>Ixekizumab</th>
<th>Secukinumab</th>
<th>Ustekinumab</th>
<th>No active treatment</th>
</tr>
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<tbody>
<tr>
<td>How often do I need to inject the treatment?</td>
<td>1 injection under the skin Every other week</td>
<td>1 injection under the skin Once or twice a week</td>
<td>1 injection in the vein Every 8 weeks</td>
<td>1 injection under the skin Every 2 weeks for the first 3 months, every 4 weeks thereafter</td>
<td>2 injections under the skin Every 4 weeks</td>
<td>1 injection under the skin Every 12 weeks</td>
<td>Does not apply</td>
</tr>
<tr>
<td>Who gives the treatment?</td>
<td>You or your carer will learn to give the injection after training.</td>
<td>You or your carer will learn to give the injection after training.</td>
<td>You will need to go to hospital where the injection will be given by a healthcare professional.</td>
<td>You or your carer will learn to give the injection after training.</td>
<td>You or your carer will learn to give the injection after training.</td>
<td>You may choose to have the injection given to you by a nurse in your home. Alternatively, you or your carer may learn to give the injection after training.</td>
<td>Does not apply</td>
</tr>
<tr>
<td>How long has this treatment been around for?</td>
<td>Since 2008</td>
<td>Since 2004</td>
<td>Since 2006</td>
<td>Anticipated to be available in 2017</td>
<td>Since 2015</td>
<td>Since 2009</td>
<td>Does not apply</td>
</tr>
<tr>
<td>How many people become clear or nearly clear of psoriasis because of this treatment?</td>
<td>Around 341 per 1000 people after 3-4 months of treatment</td>
<td>Around 227 per 1000 people after 3-4 months of treatment</td>
<td>Around 451 per 1000 people after 3-4 months of treatment</td>
<td>Around 682 per 1000 people after 3-4 months of treatment</td>
<td>Around 579 per 1000 people after 3-4 months of treatment</td>
<td>Around 413 per 1000 people after 3-4 months of treatment</td>
<td>Roughly 20 per 1000 people become clear or nearly clear with placebo (sham injection) after 3-4 months</td>
</tr>
</tbody>
</table>

*XXI The evidence is drawn from clinical trials including a mixed biologic-naïve and experienced population
In U.K. clinical practice, what are the chances of staying on this treatment past 1 year?<sup>XXII</sup>

<table>
<thead>
<tr>
<th>How many people experience unwanted effects that are serious enough to stop the treatment?&lt;sup&gt;XXII&lt;/sup&gt;</th>
<th>77-81% chance&lt;sup&gt;7&lt;/sup&gt;</th>
<th>67-73% chance&lt;sup&gt;7&lt;/sup&gt;</th>
<th>54-74% chance&lt;sup&gt;7&lt;/sup&gt;</th>
<th>Not known at present</th>
<th>Not known at present</th>
<th>86-92% chance&lt;sup&gt;7&lt;/sup&gt;</th>
<th>Does not apply</th>
</tr>
</thead>
<tbody>
<tr>
<td>How many people experience an infection serious enough to lead to admission into hospital because of this treatment?&lt;sup&gt;XXIII&lt;/sup&gt;</td>
<td>Up to 2 per 1000 people after 3-4 months of treatment&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Up to 10 per 1000 people after 3-4 months of treatment&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Up to 82 per 1000 people after 3-4 months of treatment&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Up to 39 per 1000 people after 3-4 months of treatment&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Up to 5 per 1000 people after 3-4 months of treatment&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Up to 1 per 1000 people after 3-4 months of treatment&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Roughly 19 per 1000 people taking a placebo (sham injection) withdraw after 3-4 months of monitoring&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>What conditions would make your doctor hesitant about giving you the treatment?</td>
<td>Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis)</td>
<td>Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis)</td>
<td>Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis)</td>
<td>Inflammatory bowel disease (i.e. Crohn’s disease or ulcerative colitis), recurrent candida infection (i.e. thrush)</td>
<td>Inflammatory bowel disease (i.e. Crohn’s disease or ulcerative colitis), recurrent candida infection (i.e. thrush)</td>
<td>No particular condition</td>
<td>Does not apply</td>
</tr>
</tbody>
</table>

<sup>XXII</sup> The evidence is drawn from a real-world UK biologic-naive population; it may not apply to biologic choice for subsequent lines of treatment

<sup>XXIII</sup> The figures are drawn from the upper limit of the 95% confidence interval from a meta-analysis of clinical trials and reflect the risk that has been excluded; differences amongst biologic therapies should be interpreted with caution

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| What if I want to have children? | Women and men have had children on this treatment. The risk to the baby is unknown. Your dermatologist will discuss this with you. | Women and men have had children on this treatment. The risk to the baby is unknown. Your dermatologist will discuss this with you. | Women and men have had children on this treatment. The risk to the baby is unknown. Your dermatologist will discuss this with you. | The risk to the baby is unknown. Your dermatologist will discuss this with you. | The risk to the baby is unknown. Your dermatologist will discuss this with you. | The risk to the baby is unknown. Your dermatologist will discuss this with you. | During pregnancy, psoriasis may get better, stay the same, or become worse |

Table 3. Decision aid. NICE eligibility criteria, infliximab: PASI ≥20, DLQI >18; other biologic therapies: PASI ≥10, DLQI >10
<table>
<thead>
<tr>
<th><strong>History/symptom enquiry</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psoriasis</strong></td>
<td>Disease phenotype; course (stable/unstable); response &amp; adverse effects to prior therapies</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Psoriatic arthritis</strong></td>
<td>Screen for psoriatic arthritis (e.g. using the PEST questionnaire); for people with psoriatic arthritis symptom enquiry to assess control</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Identification of contraindications to therapy and/or development of therapy-induced toxicity</strong></td>
<td>Thorough history, symptom enquiry</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>Any past or current chronic infection including tuberculosis, candidiasis</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Identify risk factors for tuberculosis, hepatitis B, C and HIV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ascertain history for chickenpox</td>
<td></td>
</tr>
<tr>
<td><strong>Alert card</strong></td>
<td>Ensure people carry an alert card with them at all times in line with MHRA guidance</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Cardiovascular assessment</strong></td>
<td>Include symptom enquiry about heart failure [NYHA III. Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation or dyspnea. NYHA IV. Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.]</td>
<td>Yes</td>
</tr>
</tbody>
</table>

---

XXIV Additional assessment and monitoring may be required in patients on concomitant therapy or in certain clinical circumstances

XXV www.bad.org.uk/healthcare-professionals/forms-downloads

XXVI See Toolkit B: Groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV, in *Supporting information 2*


XXVIII Evidence of demyelination/heart failure may preclude use of TNF antagonists

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| Neurological assessment<sup>XXVIII</sup> | Past or current history or symptoms of demyelinating disease<sup>XXVIII</sup> | Yes | Every 3-6 months |
| Gastrointestinal assessment<sup>XXIX</sup> | Past or current history or symptoms of inflammatory bowel disease | Yes | Every 3-6 months |
| Malignancy | Any past or current malignancy (including skin cancer) | Yes | Every 3-6 months |
| Ensure concordant with national cancer screening programmes | | | |
| Gynaecological review of patients with history of cervical dysplasia | | | |
| BADBIR | Offer the opportunity to participate | Yes | Every 6 months (to complete follow-up data) |

**Clinical assessments**

| Psoriasis disease severity assessment | Goal of therapy, e.g. a PGA of clear or nearly clear | Yes | To establish disease response; every 6 months thereafter |
| | PASI (or BSA if PASI not applicable) | | |
| | DLQI | | |
| Skin cancer | Full skin examination | Yes | As indicated by risk at baseline and in the context of immunosuppression |
| Psoriatic arthritis | Consult with a rheumatologist | Yes | To establish disease response; every 3-6 months thereafter and/or as clinically indicated |
| General physical examination | To identify contra-indications to therapy and/or development of therapy-induced toxicity | Yes | As indicated by history/symptom enquiry |

**Investigations**

| Blood tests | Full blood count; creatinine and electrolytes; liver function tests | Yes | At 3-4 months; every 6 months thereafter and/or as clinically indicated |
| | Hepatitis B (surface antigen and core antibody) hepatitis C (IgG) | | If clinically indicated, e.g. transaminitis (raised ALT and/or AST), or ongoing (annually) in people who belong to a |

<sup>XXVII</sup> Exercise caution using secukinumab in people with inflammatory bowel disease

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<table>
<thead>
<tr>
<th>Group at increased risk of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>If clinically indicated, e.g. symptoms of seroconversion, or ongoing (annually) in people who belong to a group at increased risk of infection</td>
</tr>
<tr>
<td>If symptoms or signs suggest development of autoimmune phenomena, e.g. transaminitis (raised ALT and/or AST)</td>
</tr>
<tr>
<td>Consider varicella vaccination in those who are not varicella-immune and seek expert advice; be aware of the indications for using VZ immunoglobulin in VZ-susceptible individuals</td>
</tr>
</tbody>
</table>

**Human immunodeficiency virus (HIV-1 and HIV-2 antibody, and HIV-1 antigen)**

**Autoantibodies (anti-nuclear antibodies, anti-nuclear double-stranded DNA antibodies)**

**Test for varicella zoster virus antibody in people with a negative or uncertain history for chickenpox**

**Tuberculosis**

- Interferon-gamma release assay and chest X-ray

**Urine**

- Urine analysis
- Urine pregnancy test

<table>
<thead>
<tr>
<th>Table 4. Suggested schedule for screening and monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

**Tuberculosis**

- Interferon-gamma release assay and chest X-ray

**Urine**

- Urine analysis
- Urine pregnancy test

| Yes |

**Tuberculosis**

- Interferon-gamma release assay and chest X-ray

**Urine**

- Urine analysis
- Urine pregnancy test

| Yes |

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AUDIT STANDARDS, DATA ITEMS AND DATA COLLECTION METHODOLOGY

Dermatology teams involved in prescribing biologic 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. See Toolkit C: Audit standards, data items and data collection methodology, in Supporting information 2, for further details.

STAKEHOLDER INVOLVEMENT AND PEER REVIEW

The full version of the guideline 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 Appendix F, in Supporting information 1, for the full list of stakeholders), comments from whom were actively considered by the GDG. Following further review, the finalized version was peer-reviewed by the Clinical Standards Unit of the BAD, made up of the Therapy & Guidelines Subcommittee (T&G), 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 this may exclude some important information published in other languages.

PLANS FOR GUIDELINE REVISION

This 2017 guideline updates the previous version. 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.

SUPPORTING INFORMATION

The full version of this guideline is available in the online Supporting information 1 document, which includes tables linking evidence to recommendations (LETR), details of the network meta-analysis, summary of included studies, forest plots, GRADE evidence profiles, PRISMA flow diagrams, list of excluded studies and search strategies. Supporting information 2 contains toolkits to aid implementation.

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- BAD Therapy & Guidelines sub-committee
- Giulia Zuodar, Document editor, NGC
- Andrew Brain, BAD Clinical Standards Administrator

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• All individuals/stakeholders who commented on the draft during the consultation period

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FOOTNOTE
This is an updated guideline prepared for the BAD Clinical Standards Unit, which includes the Therapy & Guidelines sub-committee. Members of the Clinical Standards Unit that have been involved are: PM McHenry [Chairman T&G], K Gibbon [BAD Assistant Honorary Secretary], DA Buckley, TA Leslie, EC Mallon, S Wakelin, S Ungureanu, RYP Hunasehally, M Cork, GA Johnston, J Natkunarajah, FS Worsnop, N Chiang, GP Petrof, J Donnelly [British National Formulary], C Saunders [British Dermatological Nursing Group], AG Brain [BAD Scientific Administrator], LS Exton [BAD Information Scientist], MF Mohd Mustapa [BAD Clinical Standards Manager].

CONFLICTS OF INTEREST
Details of declarations of interests (cumulative, throughout the project) can be found in the full version of the guideline (Appendix A, in Supporting information 1) and are consistent with NICE Accreditation policy.

REFERENCES