# Clinical Guideline

# North Central London

## High Cost Drug Treatment Pathway for Psoriasis

Guideline Summary
This clinical guideline outlines the high cost drug treatment pathway for adult patients with psoriasis.



June 2020

| Document Detail | |
|---|---|
| **Document Type** | Clinical Guideline |
| **Document Name** | North Central London High Cost Drug Treatment Guideline for Psoriasis |
| **Document Location** | https://www.ncl-mon.nhs.uk/faq/guidelines/ |
| **Version** | Version 1.1 |
| **Effective From** | June 2019 |
| **Review Due Date** | June 2022 |
| **Owner** | |
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| **Approved by, date** | NCL Joint Formulary Committee (June 2020)<br>NCL Heads of Medicines Management (July 2020) |
| **Superseded documents** | |
| **Related Documents** | |
| **Keywords** | Psoriasis, Guideline, Pathway, NICE |

| Change History | | |
|---|---|---|
| **Date** | **Change details since approved** | **Approved by** |
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| Review History | | |
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| **Date** | **Review Details** | **Approved by** |
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## Introduction

Psoriasis is a long-term inflammatory skin disorder affecting 2% of the population. Psoriasis is now recognised as a multi system disorder with increased risk of co-morbidities including cardiovascular disease, inflammatory bowel disease and depressive illness. Due to the visible nature of the lesions people with psoriasis may experience stigmatization and a negative impact on relationships, employment opportunities and social activities. The cumulative effect may be failure to achieve a 'full life potential'. It is therefore essential that patients with psoriasis receive timely effective treatment.[1,2]

This treatment pathway is based on the National Institute for Heath and Care Excellence (NICE) guidance, the British Association of Dermatologists (BAD) guidelines and locally and nationally agreed guidance for the use of biologics in adults with psoriasis.[1,2]

NICE has published guidance on the anti-TNF's adalimumab [3], certolizumab [4], etanercept [5] ,and infliximab [6], the IL12/23 inhibitor ustekinumab [7] and the IL 17A inhibitors brodalumab [8], ixekizumab [9] and secukinumab[10] and the IL 23 inhibitors guselkumab [11], risankizumab [12] and tildrakizumab [13] . Apremilast [14] (oral phosphodiesterase 4 inhibitor) and dimethyl fumarate [15] have also been approved by NICE with the same requirements as the biologic therapies for psoriasis and are also included in this guidance.

NICE guidance allows treatment with 2 biologic therapies after which supra-specialist advice should be sought [2]. This pathway supports the use of 5 lines of non-conventional DMARDs before submitting an individual funding request (IFR) with 3rd, 4th and 5th lines of treatment restricted to supra-specialist units. Supra-specialist units for this pathway are: Royal Free Hospital London NHS Trust, University College London Hospital and the Whittington Hospital.

## Aims of the North Central London (NCL) psoriasis high cost drugs pathway

**i.** To improve patient care by ensuring the appropriate use of high cost drugs for psoriasis
**ii.** To reduce variation across the region in the prescription of high cost drugs
**iii.** To reduce the number of Individual Funding Requests (IFR's) completed
**iv.** To enable effective treatment of people with high impact site psoriasis, a non-NICE approved indication
**v.** To promote cost containment by:
    i. Using the most appropriate biologic therapy
    ii. Supporting the use of biosimilar drugs
    iii. Dose reduction where appropriate.
**vi.** To improve drug efficacy and reduce time on treatment by promoting healthy lifestyle and patient wellbeing

## Definitions

**a. Very severe disease as per NICE eligibility criteria [2]**
    **i.** Psoriasis Area and Severity Index (PASI) score of 20 or more
    **ii.** DLQI of **≥18**

**b. Severe disease as per NICE eligibility criteria [2]**
    **i.** Psoriasis Area and Severity Index (PASI) score of 10 or more or
    **ii.** DLQI of ≥10

c. **High impact site psoriasis**
    i. Physician's global assessment (PGA) of severe or very severe on the PGA classification severity scale of clear, nearly clear, mild, moderate, severe or very severe
    ii. DLQI of ≥15

d. **Adequate response – severe or very severe psoriasis**
    i. A 75% reduction in PASI score from baseline or
    ii. 50% reduction in PASI score and a 5-point reduction in DLQI from start of treatment
    iii. Measured at designated time point for each individual drug as outlined by NICE

e. **Adequate response – high impact sites**
    i. PGA of clear, nearly clear or mild disease
    ii. DLQI ≤50% of baseline DLQI

f. **Inadequate response**
    i. Failure to achieve the above

g. **Primary failure**
    i. Inadequate response at the time point described in the NICE technology appraisals for the individual drug

h. **Secondary failure**
    i. An inadequate response after the patient's psoriasis initially responds adequately as detailed above

## Eligibility criteria for high cost drug therapy

i. **Methotrexate, ciclosporin and PUVA (Psoralen and ultraviolet-A light) have:**
    i. Failed or
    ii. Not tolerated or
    iii. Contraindicated

**AND**

j. **Psoriasis had a large impact on physical, psychological or social functioning**
    a. E.g. DLQI >10

**AND**

    b. Severe psoriasis (PASI ≥ 10 or BSA >10%)

## High Impact Site Psoriasis

NICE criteria for starting high cost drug treatment do not include high impact site psoriasis, yet this has a large impact on patients. 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). This has been specifically reviewed by NCL JFC and is approved under the following stipulations.

Adalimumab, apremilast or dimethyl fumarates may be considered in people psoriasis where the PASI is <10 when the following criteria are met:

- Physicians Global Assessment (PGA) of severe or very severe.
- At least one localised, high impact and difficult to treat site.
- DLQI ≥ 15
- Psoriasis cannot be controlled with optimised standard systemic therapy:
    - Acitretin
    - Ciclosporin
    - Subcutaneous methotrexate

## Pustular Psoriasis

This has not been reviewed or commissioned in NCL, therefore an IFR will be required for consideration of funding.

## NICE guidance for individual high cost drugs for psoriasis

| Medicine | TA number | Date | Recommendations | Dose |
|---|---|---|---|---|
| Adalimumab | TA146 | 25/06/2008 | | The recommended dosage for adalimumab is an initial 80 mg dose administered by subcutaneous injection, followed by 40 mg given subcutaneously every other week starting 1 week after the initial dose. |
| Apremilast | TA419 | 23/11/2016 | The company provides the drug with the discount agreed in the patient access scheme. | The recommended dosage is 30 mg twice daily after an initial titration schedule. A single 10 mg dose is given on the first day of treatment; this is titrated to 30 mg twice daily over 5 days |
| Brodalumab | TA511 | 21/03/2018 | The company provides the drug with the discount agreed in the patient access scheme. | The recommended dose is 210 mg administered by subcutaneous injection at weeks 0, 1 and 2, followed by 210 mg every 2 weeks. |

| | | | | |
|---|---|---|---|---|
| Certolizumab | TA574 | 17/04/2019 | The company has a commercial arrangement. It is the company's responsibility to let relevant NHS organisations know details of the arrangement. | The recommended starting dosage of certolizumab pegol for adults is 400 mg (given as 2 subcutaneous injections of 200 mg each) at weeks 0, 2 and 4. |
| Etanercept | TA103 | 26/07/2006 | | Etanercept is administered by subcutaneous injection at a dose of 25 mg twice weekly. Alternatively, 50 mg given twice weekly may be used for up to 12 weeks followed, if necessary, by a dose of 25 mg twice weekly |
| Guselkumab | TA521 | 13/06/2018 | The company provides the drug according to the commercial arrangement. | The recommended dosage of guselkumab is 100 mg by subcutaneous injection at weeks 0 and 4, followed by a 100 mg maintenance dose every 8 weeks. |
| Infliximab | TA134 | 23/01/2008 | | It is given as a 5-mg/kg intravenous infusion over a 2-hour period followed by additional 5-mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter. |
| Ixekizumab | TA442 | 26/04/2017 | The company provides the drug with the discount agreed in the patient access scheme. | By subcutaneous injection; 160 mg at week 0, followed by 80 mg every 2 weeks until week 12. After week 12, 80 mg every 4 weeks. |
| Risankizumab | NICE ID1398 | 21/08/2019 | It is likely that the company will provide the drug according to a commercially agreed arrangement to NHS trusts. | The recommended dose is 150 mg (two 75 mg injections) administered by subcutaneous injection at week 0, week 4, and every 12 weeks thereafter. |

| | | | | |
|---|---|---|---|---|
| Secukinumab | TA350 | 22/07/2015 | The company provides secukinumab with the discount agreed in the patient access scheme. | Secukinumab is given subcutaneously. The recommended dosage is 300 mg at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4. |
| Tildrakizumab | TA575 | 17/04/2019 | Tildrakizumab is available to the NHS at a commercially sensitive discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount. | The recommended dose of tildrakizumab is 100 mg at weeks 0 and 4 and every 12 weeks thereafter. In patients with certain characteristics (for example, high disease burden, body weight of 90 kg or more), a 200 mg dose may provide greater efficacy. |
| Ustekinumab | TA180 | 03/03/2009 | | The recommended dose of ustekinumab is 45 mg for people who weigh 100 kg or less, and 90 mg for people who weigh over 100 kg. An initial dose of ustekinumab is administered subcutaneously at week 0, followed by another dose at week 4, and then a further dose every 12 weeks. |

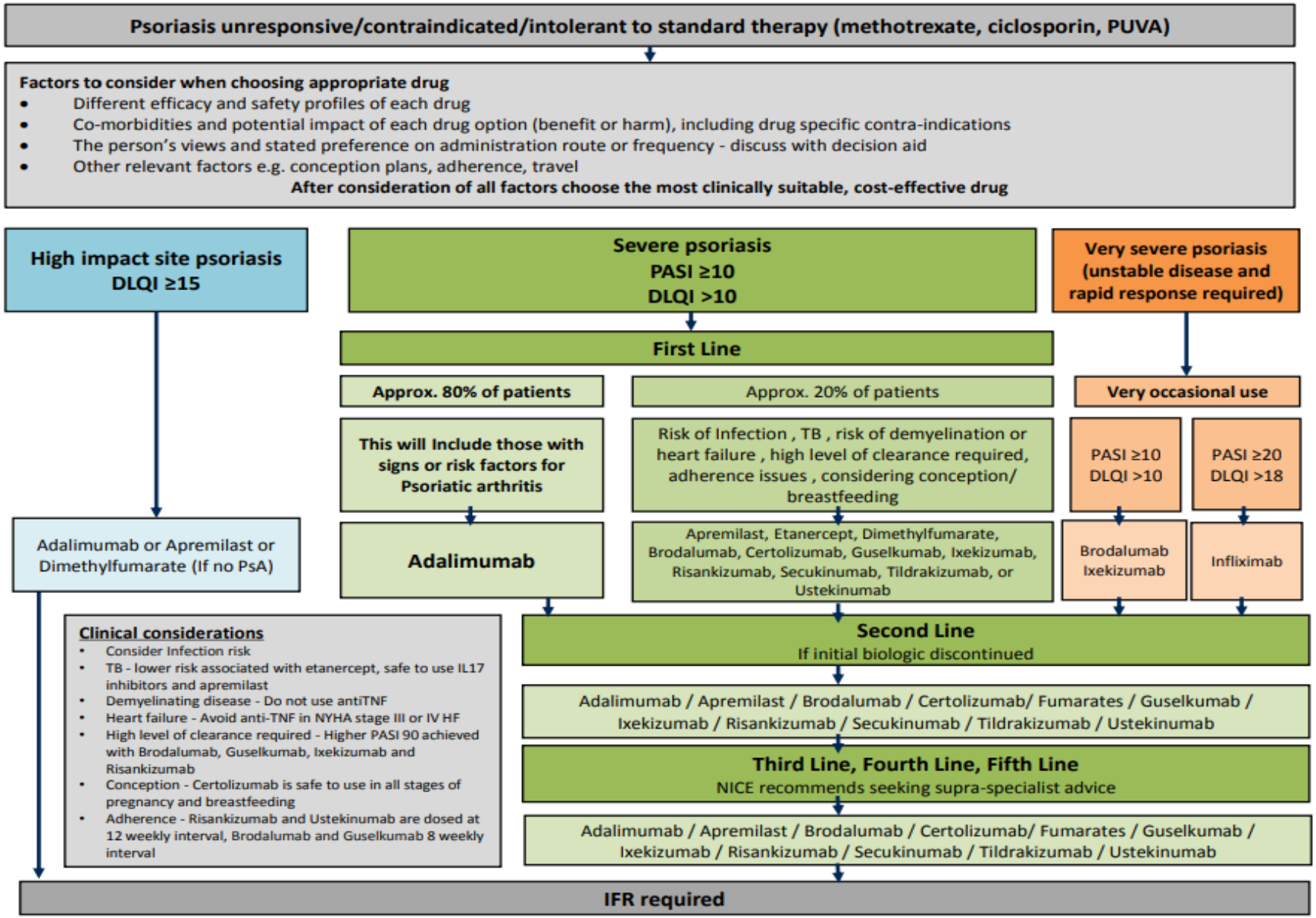
## Biosimilars

A biosimilar medicine is a biological medicine that is developed to be highly similar and clinically equivalent to an existing biological medicine.

The British Association of Dermatologists supports the use of biosimilars provided the following minimum set of standards is met [17] :

1. Biologic product (reference or biosimilar) is clearly identified by brand name.
    a. Batch numbers should also be recorded where possible
2. Robust safety monitoring of biosimilars is conducted post-marketing authorisation.
    a. all patients starting on or switching to biosimilars should be registered with the British Association of Dermatologists' Biologic Interventions Register (BADBIR).
3. Products (reference and biosimilars) are not considered interchangeable.
    a. If a particular product is not immediately available, the dispensing pharmacist must discuss appropriate action with the prescribing physician.
4. In NCL, all patients should be switched to a biosimilar within 3 months of availability unless a case to remain, based on exceptionality, can be made. No new patients can use originator if a biosimilar is available.

## Choice of High Cost Drug



## Assessment of response Continuation / Discontinuation Criteria

Discontinue if:

- Biologic or small molecule drug is not tolerated or becomes contraindicated
- Response is not adequate
    - Adequate response in severe or very severe psoriasis is:
        - A 75% reduction in PASI score from baseline or
        - 50% reduction in PASI score and a 5 point reduction in DLQI from start of treatment
    - Adequate response in high impact site psoriasis is:
        - PGA of clear, nearly clear or mild disease
        - DLQI ≤ 50% of baseline DLQI
- For primary response , assess response at time points specific for individual drugs as per NICE TA recommendations:

| Drug | Time point to assess primary efficacy |
|---|---|
| Adalimumab | 16 weeks |
| Apremilast | 16 weeks |
| Brodalumab | 12 weeks |
| Certolizumab | 16weeks |
| Dimethyl Fumarate | 16 weeks |
| Etanercept | 12 weeks |
| Guselkumab | 16 weeks |
| Ixekizumab | 12 weeks |
| Secukinumab | 12 weeks |
| Tildrakizumab | 28 weeks |
| Ustekinumab | 16 weeks |

- Review 3 monthly for first year and then 6 monthly if stable. If appropriate response NOT ACHIEVED discontinue treatment and consider 2$^{nd}$ line treatment.
- Blueteq continuation forms for funding update will be completed initially at the time point as per NICE recommendations and then annually thereafter.

## Choice of subsequent high cost drugs for NICE approved indications

a. **Reasons for discontinuation:**
    i. Primary failure
    ii. Secondary failure
    iii. First drug not tolerated or becomes contraindicated

b. **Subsequent drug and rationale for 5 lines of therapy**
    i. Choose the best value effective licensed NICE approved high cost drug for psoriasis
    ii. Consider
        1. Dose escalation as per NICE
        2. Disease severity
        3. Change in mode of action
            a. Consider mechanism of action of drug when switching treatments. It is strongly suggested switching to an alternative mode of action when switching agents (hence 5 lines of therapy)

| Modes of Inhibition / Action | | | | |
|---|---|---|---|---|
| **Anti-TNF** | **Anti IL12 / 23** | **IL17A** | **IL23 (p19)** | **Small Molecule** |
| Adalimumab | Ustekinumab | Brodalumab | Guselkumab | Apremilast |
| Certolizumab | | Ixekizumab | Risankizumab | Dimethyl fumarate |
| Etanercept | | Secukinumab | Tildrakizumab | |
| Infliximab | | | | |

        4. Use the BAD decision aid (see Appendix 4)
        5. Re-visit advice regarding maximising treatment response
        6. Cost of drug
        7. Considerations for choice of drug (see section 9)

## Dose escalation

Currently dose escalation is not routinely commissioned and this would require an IFR for funding application.

| High Cost Drug | Dose Escalation | Licenced Use |
|---|---|---|
| Adalimumab 40mg fortnightly | Adalimumab 40mg weekly for 12 weeks and review | Yes |
| Etanercept 50mg weekly | Etanercept 50mg twice weekly for 12 weeks and review | Yes |

## Free of charge (FOC) scheme

In NCL, all FOC schemes require sign off by the JFC. This is considered on a one to one basis. When this is signed off, all due process of the provider hospital is also required to be fulfilled.

New biologic and non-biologic DMARDs are often licensed and made commercially available many months before NICE are due to issue their NICE Technology Appraisal Guidance. Where this situation exists, individual dermatology departments may enter discussions with the pharmaceutical company to determine if a 'free of charge' (FOC) early access scheme is feasible. When a FOC is proposed it must satisfy the following criteria:

- Fund the treatment at zero cost to the NHS up to and for 90 days after the final positive NICE Technology Appraisal guidance.
- Continue to fund treatment in the event of a negative NICE Technology Appraisal Guidance until:
    - 90 days after a future positive NICE Technology Appraisal Guidance.
    - The dermatologists consider it no longer clinically appropriate to continue the drug.

## British Association of Dermatologists Biologic Interventions Register (BADBIR) and Biomarkers of Systemic Treatment Outcomes in Psoriasis (BSTOP)

All patients starting a biologic therapy should be given the opportunity to participate in BADBIR (a national long-term safety registry) and BSTOP within 6 months of initiation in accordance with NICE recommendations.

## Method of medication supply

Subject to local arrangements, patients may be offered a choice of method of supply.

a. A traditional homecare service.
b. Enhanced outpatient pharmacy service via outsourced outpatient pharmacies on main hospital sites.
c. Where there is agreement with pharmaceutical companies, unbundling of homecare and direct procurement via outsourced pharmacies may result in a reduction in the drug acquisition cost. This may further influence the biologic choice at local Trust level.

Subject to local arrangements, in order to reduce the time to biologic initiation, the first biologic doses (no more than 8 weeks) may be given in the infusion suite or dermatology day centre as part of an outpatient biologic initiation service.

a. The cost may incur VAT and this will be passed onto commissioners.

## Monitoring adherence with guideline

Adherence to this guideline will be reviewed in 6 monthly meetings with psoriasis lead clinicians from the Royal Free London NHS Trust, UCLH and the Whittington Hospital together with stakeholders from Camden CCG. Audits will be undertaken at the individual sites as required.

## Appendix 1: Recommendations on safe prescribing of high cost drugs

(Taken from BAD Biologics guidelines for psoriasis 2017)

### *Transitioning drug therapy*

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.
- the person's clinical circumstances.
- the person's views on the risks and benefits of transitioning option(s).

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 (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).

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.

| Biologic | Trade name | Half-life |
|---|---|---|
| Adalimumab | Humira, Hyrimoz, Amgevita | 12-14 days |
| Brodalumab | Siliq | 11 days |
| Certolizumab | Cimzia | 14 days |
| Etanercept | Enbrel | 3 days (approx. 70 hours) |
| Guselkumab | Tremfya | 15-18 days |
| Infliximab | Remicade, Remsima | 9 days |
| Ixekizumab | Taltz | 13 days |
| Risankizumab | Skyrizi | 28-29 days |
| Secukinumab | Cosentyx | Median half-life 27 days (18-46 days) |
| Tildrakizumab | Ilumetri | 23.4 days |
| Ustekinumab | Stelara | Median half-life 3 weeks (15-32 days) |

### *Cancer risk*

Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:

- Their past or current history of cancer and/or any future risk of cancer.
- Provide information to people with psoriasis about the importance of participating in national cancer screening programmes.

- Exercise caution and discuss with the relevant cancer specialist when prescribing biologics in people with psoriasis and:
    i. a history of cancer, particularly if this has been diagnosed and treated < 5 years previously and/or
    ii. where the baseline risk of skin cancer is increased (e.g. previously treated non-melanoma skin cancer).

***Infections***

Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:

- Risk factors for infection (e.g. comorbidities, co-therapy, lifestyle, and travel).
- Known infections (past or current).
- Signs or symptoms suggestive of infection.

**a) Chronic viral infections – hepatitis B, hepatitis C and HIV**

Test for

- Hepatitis B (surface antigen and core antibody),
- Hepatitis C (IgG)
- HIV (HIV-1 and HIV-2 antibodies and HIV-1 antigen)
- infection in people starting biologic therapy

- Consider on-going screening (e.g. annually) for hepatitis B, hepatitis C and HIV, particularly in people who belong to a group at increased risk of infection.
- Re-test 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 of HIV sero-conversion.
- Consult a hepatitis specialist when treating all people with biologic therapy who have hepatitis B or C infection, whether newly diagnosed or previously known.
- 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.

**b) Varicella zoster**

- 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.

**c)Tuberculosis**

- Screen for latent tuberculosis (TB) with an interferon-γ 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 NICE tuberculosis guideline).
- 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.

- 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 antagonist therapy is often disseminated and extra-pulmonary; symptoms may include unexplained weight loss, night sweats, non-resolving cough, haemoptysis and lymphadenopathy.
- 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.

### *Contraindications and cautions*

**Biological therapies**

- Hypersensitivity to the active substance or to any of the excipients
- 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.
- 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.
- Avoid **TNF antagonist** therapy in people with severe **cardiac failure** (NYHA class III and IV).
    - Assess people with well-compensated (NYHA class I and II) cardiac failure see the NICE pathway) and consult with a cardiology specialist before using TNF antagonist therapy.
    - Stop TNF antagonist therapy in the event of new or worsening pre-existing heart failure and seek specialist advice.
- Exercise caution and consult a gastroenterology specialist before using **IL17A inhibitors** in people with **inflammatory bowel disease**.

**Dimethyl fumarate**

- Hypersensitivity to the active substance or to any of the excipients.
- Severe gastrointestinal disorders.
- Severe hepatic or renal impairment.
- Pregnancy and breast-feeding.

**Apremilast**

- Hypersensitivity to the active substance or to any of the excipients
- Pregnancy.
    - Apremilast is classified as FDA pregnancy category C.
    - Apremilast should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.
- Breast-feeding - use with caution in breast-feeding women.
- History of depression or suicidal ideation - Apremilast treatment is associated with an increased risk of depression,
    - Use with caution in patients with a history of depression or suicidal ideation.

- Patients, as well as families and caregivers, should be advised to be alert for signs of depression, worsening of depression, suicidal thoughts, or other mood changes. If these reactions occur, prescribers should carefully evaluate the risks and benefits of continuing treatment.

- Renal failure, renal impairment.
  - The exposure to apremilast is increased in patients with renal failure or severe renal impairment and dosage reduction is required.
- Risk of dehydration.
  - Use with caution in patients at risk of dehydration as severe diarrhoea, nausea, and vomiting have been associated with apremilast therapy.

***Peri-operative risk***

Prevention of potential post-operative infection risk by temporarily stopping a patient's biologic treatment should be carefully balanced against the possibility of developing a peri-operative flare of psoriasis.

Should treatment be stopped prior to surgery, consider stopping the drug 3-5 times the half-life for the relevant drug (Level IV evidence, grade of recommendation C).

Biologic therapy should be recommenced post operatively once infection is excluded and the wound is healed (Level IV evidence, grade of recommendation C).

| Biologic | Half-life* | Time to stop treatment prior to surgery |
|---|---|---|
| Adalimumab | 12-14 days | 6 – 10 weeks |
| Certolizumab | 14days | 10 weeks |
| Etanercept | 3 days (approx. 70 hours) | 9- 15 days |
| Infliximab | 9 days | 4 – 7 weeks |
| Ixekizumab | 13 days | 6 – 10 weeks |
| Risankizumab | 28-29days | 20 weeks |
| Secukinumab | Median half-life 27 days (18-46 days) | 12 – 19 weeks |
| Tildrakizumab | 23 days | 15-16 weeks |
| Ustekinumab | Median half-life 3 weeks (15-32 days) | 9 - 15 weeks |

***Pregnancy and breast feeding***

**a) Pregnancy**

There is limited data for safety of biologic drugs in pregnancy and lactation. The decision to continue biologic agents in pregnancy needs to be individualised. This needs to take into account alternative therapies, the severity of the mother's condition prior to therapy, the risk of a disease flare by cessation of therapy, and the impact of a flare on the mother and the unborn child. This should be discussed by a multi-disciplinary team.

Patients who stop therapy during pregnancy should be re-loaded with biological therapy soon after delivery.

Consideration should be given to stopping biologic therapy in a woman who becomes pregnant as listed below:

| Biologic | Compatible with 1st trimester | Compatible with 2nd / 3rd trimester |
|---|---|---|
| Adalimumab | Yes | Second but not third |
| Certolizumab | Yes | Yes |
| Etanercept | Yes | Second but not third |
| Infliximab | Yes | Stop at 16 weeks |
| Ixekizumab | Limited data | Limited data |
| Ixekizumab | Limited data | Limited data |
| Risankizumab | No data | No data |
| Secukinumab | No data | No data |
| Tildrakizumab | No data | No data |
| Ustekinumab | No data | No data |

To ensure low/no levels of drug in cord blood at delivery, etanercept and adalimumab should be avoided in the third trimester and infliximab stopped at 16 weeks. If these drugs are continued later in pregnancy to treat active disease, then live vaccines should be avoided in the infant up to 6 months of age.

**b) Breast feeding**

There is insufficient information on the excretion of biologics in breast milk. Since immunoglobulins are excreted into human breast milk, a risk to the breastfeeding child cannot be excluded. A decision on whether to breastfeed or to continue/discontinue therapy should be made taking into account the benefit of breastfeeding to the child and the benefit of therapy to the woman.
The manufacturers recommend the following in relation to biologics in breastfeeding.

| Biologic | Compatible with Breastfeeding |
|---|---|
| Adalimumab | Yes |
| Certolizumab | Yes |
| Etanercept | Yes* |
| Infliximab | Manufacturers advise wait 6 months until after stopping to breastfeed |
| Ixekizumab | Risk vs benefit. Wait 6-10 weeks until after stopping to breastfeed |
| Risankizumab | Limited data – risk vs benefit |
| Secukinumab | Risk vs. benefit. Wait 20 weeks until after stopping to breastfeed |
| Tildrakizumab | Limited data – risk vs. benefit |
| Ustekinumab | Risk vs. benefit. Manufacturers suggest wait 15 weeks until after stopping to breastfeed |

* Limited data. Immunoglobulins, in common with many medicinal products, can be excreted in human milk a decision must be made whether to discontinue breast-feeding or to discontinue etanercept therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

## *Vaccinations*

Vaccination requirements should be reviewed and brought up to date prior to initiation of biologic therapy with reference to Department of Health Guidance.

- **Vaccination of Infants**

Any infant who has been exposed to immunosuppressive treatment from the mother either in utero during pregnancy or via breastfeeding should have any live attenuated vaccination deferred for as long as a postnatal influence on the immune status of the infant remains possible.
In the case of in utero exposure to an anti-TNF and other biological medicines, this period should be until the infant is up to 6 months of age, after which time vaccination should be considered.
MHRA has received 4 Yellow Card reports regarding neonates who have died from disseminated BCG or tuberculosis infection after exposure to an anti-TNF in utero.
The risk of a natural rotavirus infection is high. Although the vaccine is a live attenuated virus, with the exception of severe combined immune-deficiency (SCID), the benefit from vaccination may exceed any risk in other forms of immunosuppression. Therefore, there are very few infants who cannot receive rotavirus vaccine. Vaccination should be discussed on an individual basis.

- **Live vaccines**

The administration of live vaccines is contraindicated in patients on biologic agents. Patients should be counselled on the need to avoid live vaccines and the implication that may have for travelling.

It is safe to administer a live vaccine 4 weeks prior to commencing biologic therapy, when necessary.

There is no contra-indication for the administration of live vaccines to relatives or friends of patients on biologic or immunosuppressant drugs.

The table below shows all live vaccines available in the UK.

| Live Vaccine | Brand Name |
|---|---|
| BCG | Bacillus Calmette-Guerin Vaccine |
| Live Influenza vaccine | Fluenz Tetra® |
| Measles, Mumps and Rubella combined vaccine (MMR) | MMRvaxPRO®, Priorix® |
| Poliomyelitis (Live oral vaccine) | Poliomyelitis Vaccine, live (oral) GSK OPV |
| Rotavirus (Live oral vaccine) | Rotarix® |
| Typhoid (Live oral vaccine) | Vivotif® |
| Varicella-Zoster Vaccine | Varilrix®, Varivax®, Zostavax® |
| Yellow Fever | Stamaril® |

For patients on established conventional DMARD treatment, immunosuppression treatment should be stopped for 6 months before administration of a live vaccine. Therapy may then be restarted 2 to 4 weeks after the administration of the live vaccine.
When a live vaccine is required by a patient on a biologic, the cessation of treatment may permit a necessary vaccination to be administered. The table below shows the time period required to elapse off each biologic therapy, prior to the administration of a live vaccination.

| Biologic | Time to elapse before giving a live vaccine |
|---|---|
| Adalimumab | 3 months |
| Certolizumab | 10 weeks |
| Etanercept | 1 month |
| Infliximab | 2 months |
| Ixekizumab | 6 months |
| Risankizumab | 21 weeks |
| Secukinumab | 6 months |
| Tildrakizumab | 17 weeks |
| Ustekinumab | 6 months |

- **Non-live vaccines**

Non-live vaccines are deemed safe to administer to people on immunosuppressant and on biologic therapies.
Pneumococcal vaccine should be given 2-4 weeks before starting a biologic as response after starting

treatment can be poor.
The table below gives a list of non-live vaccines available in the UK.

| Vaccine | Brand Name |
|---|---|
| Cholera Vaccine (Oral preparation only) | Dukural® |
| Diphtheria | Given as combined adsorbed diphtheria (low dose), tetanus and inactivated poliomyelitis preparation. |
| Hepatitis A | Avaxim®, Epaxal®, Havrix Monodose®, Vaqta Paediatric® |
| Hepatitis B | Engerix®, Fendrix®, HBvaxPRO® |
| Hepatitis A and B Combined | Ambrix®, Twinrix® |
| Influenza | Agrippal®, Begrivac®, Enzira®, Fluarix®, Fluvirin®. Imuvac®, Influvac® Sub-unit, Mastaflu®, Optaflu® and Viroflu® |
| Pneumococcal | Pneumovax II® (Adults and children over 5), Prevenar® (Primary childhood immunisation. |
| Poliomyelitis (Injection) | Inactivated Poliomyelitis Vaccine (non-proprietary) IPV |
| Meningococcal Group C | Menjugate Kit®, NeisVac-C® |
| Meningococcal polysaccharide A,C, W135 and Y vaccine | ACWY Vax® |
| Rabies | Rabipur® |
| Tetanus | *Single preparation no longer available. Combined Adsorbed diphtheria (low dose), tetanus and inactivated poliomyelitis preparation given. |
| Tick-borne encephalitis | TicoVac® |
| Typhoid (Polysaccharide injection for vaccination) | Typherix®, Typhim Vi® |

**B) Vaccination scheduling during biologic therapy**
Influenza vaccine – receive annually
Pneumococcal vaccine – receive once. Check titres every 5-10 years

## Appendix 2. BAD schedule for monitoring

| SUGGESTED SCHEDULE FOR SCREENING AND MONITORING | | Baseline | Monitoring |
|---|---|---|---|
| **History/symptom enquiry** | | | |
| Psoriasis | Disease phenotype; course (stable/unstable); response & adverse effects to prior therapies | Yes | Ongoing |
| Psoriatic arthritis | Screen for psoriatic arthritis (e.g. using the PEST questionnaire); for people with psoriatic arthritis symptom enquiry to assess control | Yes | Every 12 months |
| Identification of contraindications to therapy and/or development of therapy-induced toxicity | Thorough history, symptom enquiry | Yes | Every 3-6 months |
| Infection | Any past or current chronic infection including tuberculosis, candidiasis | Yes | Every 3-6 months |
| | Identify risk factors for tuberculosis, hepatitis B, C and HIV | | |
| | Ascertain history for chickenpox | | N/A |
| Alert card | Ensure people carry an alert card with them at all times in line with MHRA guidance | Yes | At each review appointment |
| Cardiovascular assessment | Include symptom enquiry about heart failure<br>[NYHA III. Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation or dyspnoea. 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.] | Yes | Clinical assessment every 3-6 months |
| Neurological assessment | Past or current history or symptoms of demyelinating disease | Yes | Every 3-6 months |
| Gastrointestinal assessment | Past of 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 | | |

| SUGGESTED SCHEDULE FOR SCREENING AND MONITORING | | Baseline | Monitoring |
|---|---|---|---|
| **History/symptom enquiry** | | | |
| | Gynaecological review of patients with history of cervical dysplasia | | |

| **BADBIR** | | | |
|---|---|---|---|
| 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 group at increased risk of infection[X] |
| | Human immunodeficiency virus (HIV-1 and HIV-2 antibody, and HIV-1 antigen) | | If clinically indicated, e.g. symptoms of seroconversion, or |

| | | | |
|---|---|---|---|
| | | | ongoing (annually) in people who belong to a group at increased risk of infection[X] |
| | Autoantibodies (anti-nuclear antibodies, anti-nuclear double-stranded DNA antibodies) | | If symptoms or signs suggest development of autoimmune phenomena, e.g. transaminitis (raised ALT and/or AST) |
| | Test for varicella zoster 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[XIV] |
| Tuberculosis | Interferon-gamma release assay and chest X-ray | Yes | If clinically indicated, e.g. symptoms or signs of tuberculosis, new exposure to tuberculosis or residence in high-incidence setting |
| Urine | Urine analysis | Yes | If clinically indicated |
| | Urine pregnancy test | | |

## Appendix 3: UK Biologics Check list

# UK Biologics Checklist

**Patient Details:** **Date:**

**Consultant & Nurse:** **Diagnosis:**

**Previous systemic therapy:**

**Other medication:**

| | | | | | |
|---|---|---|---|---|---|
| **Baseline PASI** | | **Baseline DLQI** | | **Baseline PEST** | |

| **Medical History** | | | **Comments** |
|---|---|---|---|
| Demyelinating disease in person or family, i.e. first-degree relative (e.g. MS: optic neuritis) | Y | N | |
| Signs and symptoms of active TB<br>Past H/O TB or close family member contact with active TB | Y<br>Y | N<br>N | |
| H/O Hep B, Hep C, HIV | Y | N | |
| H/O allergies (e.g. latex, egg) | Y | N | |
| Past history of malignancy (except NMSC) | Y | N | |
| H/O cardiac failure | Y | N | |
| H/O heavy smoking (>20/day) | Y | N | |
| Planned surgery (if yes, follow guidelines) | Y | N | |
| Contraception (if relevant, follow guidelines) | Y | N | |
| Immunosuppression in last 3 months | Y | N | |
| **Phototherapy**<br>• >200 PUVA<br>• >350 UVB | <br>Y<br>Y | <br>N<br>N | |

| **Vaccination and Screening** | | | **Comments** |
|---|---|---|---|
| H/O BCG vaccination | Y | N | |
| **Recommend pre-treatment vaccinations (if serology -ve and delay acceptable)**<br>• Influenza<br>• Pneumococcal<br>• varicella zoster | <br>Y<br>Y<br>Y | <br>N<br>N<br>N | |
| Mammogram (if relevant) | Y | N | Date: |
| Last cervical smear (if relevant) | Y | N | Date: |

| **Clinical Examination** | | | **Comments** |
|---|---|---|---|
| Height | Y | N | |
| Weight | Y | N | |
| Waist measurement | Y | N | |

| | | | |
|---|---|---|---|
| Baseline BP | Y | N | |
| Full skin examination | Y | N | |
| Lymphadenopathy | Y | N | |
| Hepatosplenomegaly | Y | N | |

| Screening Investigations | | Date | Results |
|---|---|---|---|
| **TB Screening**<br>• CXR and tuberculin skin test (TST or Mantoux) if NO immunosuppression in last 3 months<br>• CXR and IGRA (TB ELISpot/QuantiFERON®-TB gold test) if immunosuppressed<br>• Refer ALL patients to local TB service with a H/O previously treated TB, or who have had close contact with a case of active TB | | | |
| **Bloods**<br>• FBC/ESR<br>• Renal function<br>• LFT<br>• Hep B/Hep C<br>• HIV<br>• VZV serology<br>• ANA/dsDNA<br>• Fasting lipids/glucose | | | |
| • Urinalysis<br>• Pregnancy test (if relevant) | | | |

| | | | |
|---|---|---|---|
| **Entry into BADBIR** | **Y** | **N** | |

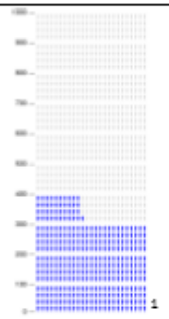
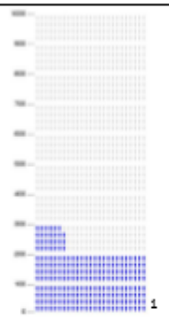
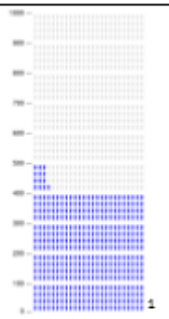
| | | |
|---|---|---|
| **Doctor discussed side effects/patient leaflet with patient:** | **Sign:** | **Date:** |
| **Risk of infection, malignancy, demyelination:**<br>**Advise on avoiding live vaccines 2 weeks before, during and 6 months after** | | |
| **Consent of the patient:** | **Sign:** | **Date:** |

| **Monitoring** | **Months** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | **3** | **6** | **12** | **18** | **24** | **30** | **36** | **42** | **48** | **54** | **60** |
| FBC<br>LFT<br>Renal<br>Fasting lipids/glucose<br>PASI<br>DLQI<br>PGA<br>Contraception | | | | | | | | | | | |
| Date | | | | | | | | | | | |
| ANA<br>TB ELISpot<br>Flu vaccine<br>Cancer screening*<br>PEST<br>Weight | | | | | | | | | | | |
| Date | | | | | | | | | | | |
| Pneumovax® | | | | | | | | | | | |
| Date | | | | | | | | | | | |

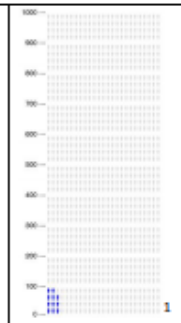
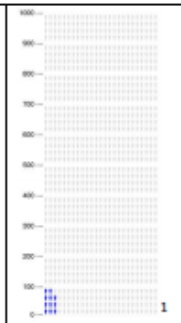
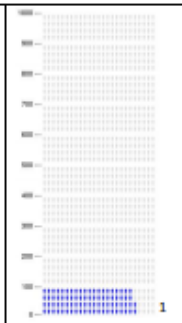
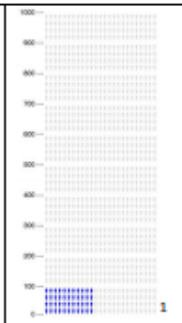
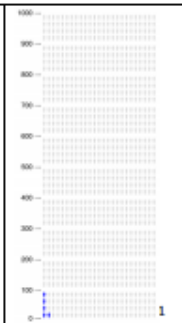
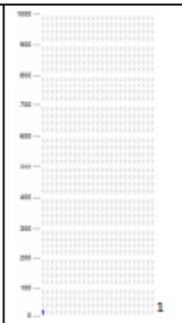
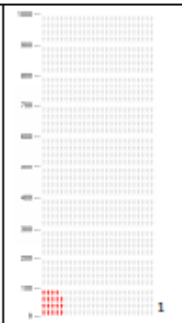
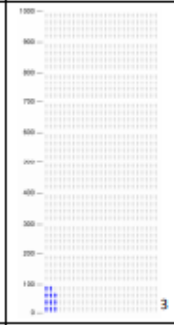
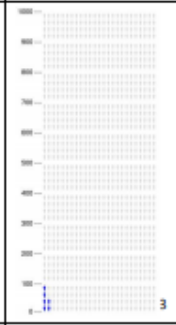
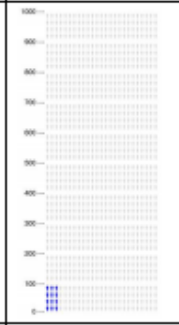
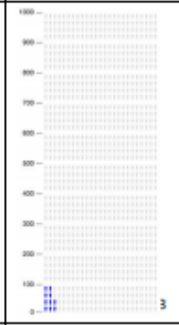
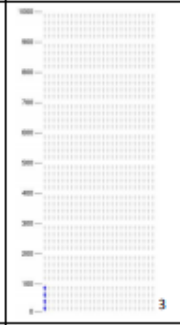
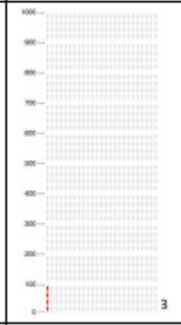
*Disclaimer: this checklist was developed by the Therapy & Guidelines sub-committee with inputs from the Biologics Register Steering sub-committee and the wider BAD membership during a consultation period, and is based on the BAD clinical guidelines for biologic interventions for psoriasis 2009 (Smith et al.). This checklist will be reviewed once the biologic guideline is updated; please forward any comments that you may have to clinicalstandards@bad.org.uk for consideration at that stage*

**age & gender - national prog*

## Appendix 4: Patient decision aid

| *Questions you might want to ask* | **Adalimumab** | **Etanercept** | **Infliximab** | **Ixekizumab** | **Secukinumab** | **Ustekinumab** | **No active treatment** |
|---|---|---|---|---|---|---|---|
| **How often do I need to inject the treatment?** | 1 injection under the skin<br>Every other week | 1 injection under the skin<br>Once or twice a week | 1 injection in the vein<br>Every 8 weeks | 1 injection under the skin<br>Every 2 weeks for the first 3 months, every 4 weeks thereafter | 2 injections under the skin<br>Every month | 1 injection under the skin<br>Every 12 weeks | Does not apply |
| **Who gives the treatment?** | 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. | You or your carer will learn to give the injection after training. | You will need to go to hospital where the injection will be given by a healthcare professional. | You or your carer will learn to give the injection after training | You or your carer will learn to give the injection after training. | 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. | Does not apply |
| **How long has this treatment been around for?**[IV] | Since 2008 | Since 2004 | Since 2006 | Since 2016 | Since 2015 | Since 2009 | Does not apply |
| **On average, for every 1000 people how many become clear or nearly clear of psoriasis (PASI90) because of this treatment after 3-4 months?**[V] |  |  |  |  |  |  |  |
| **In U.K. clinical practice, what is the likelihood of staying on this treatment past 1 year?**[VI] | 77-81% chance[2] | 67-73% chance[2] | 54-74% chance[2] | Not known at present | Not known at present | 86-92% chance[2] | Does not apply |

[IV] First approval of the drug for moderate to severe plaque psoriasis
[V] The evidence is drawn from clinical trials including a mixed biologic-naïve and experienced population
[VI] The evidence is drawn from a real-world UK biologic-naïve population; it may not apply to biologic choice for subsequent lines of treatment

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **At worst, for every 1000 people how many experience unwanted effects that are serious enough to stop the treatment after 3-4 months?** [V, VII] |  |  |  |  |  |  |  |
| **At worst, for every 1000 people how many experience an infection serious enough to lead to admission into hospital because of this treatment after 3-4 months?** [VII] |  |  | Cannot be estimated |  |  |  |  |
| **What conditions would make your doctor hesitant about giving you the treatment?** | Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis) | Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis) | Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis) | Inflammatory bowel disease (i.e. Crohn's disease or ulcerative colitis), recurrent candida infection (i.e. thrush) | Inflammatory bowel disease (i.e. Crohn's disease or ulcerative colitis), recurrent candida infection (i.e. thrush) | No particular condition | Does not apply |
| **What is known about these medicines in conception and pregnancy?** | 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 |

NICE eligibility criteria, infliximab: PASI ≥20, DLQI >18; other biologic therapies: PASI ≥10, DLQI >10. Images created by Iconarray.com; Risk Science Center and Center for Bioethics and Social Sciences in Medicine, University of Michigan; accessed 21st June 2017.

[VII] 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

## Appendix 5: Supra-specialist unit

Any patient whose skin condition cannot be managed by a generalist will need to be referred for specialist care (Level 3; secondary care) and/or supra-specialist services (Level 4; tertiary care)[2]. Supra-specialist care usually takes place entirely within an acute hospital and is carried out by:

- Consultant dermatologists
- A range of other healthcare professionals with special skills in the management of complex and/or rare skin disorders.

For the purpose of this pathway, Royal Free London NHS Trust, UCLH and the Whittington shall be regarded as supra specialist centres

## Appendix 6: Recommended letter to GP

Your patient has been started on a biologic treatment …….. to treat their psoriasis. There are some important aspects regarding their on-going care that we would like to bring to your attention.

**1**. Please could their **medical record** be updated to state that they are receiving treatment with this biologic therapy.

**2. Vaccinations:**
Live vaccinations should not be given to people on biologic therapy.
Inactivated vaccines are safe to administer concurrently with biologic therapy.
Patients should receive annual influenza vaccine (intramuscular only) and pandemic influenza vaccine when recommended.
Pneumococcal vaccination should be given prior to biologic therapy.

**3. Increased risk of infection (TB, skin and soft tissue)**
Patients on biologic therapy are at an increased risk of infection including TB skin and soft tissue. There should be a high index of suspicion if a patient on biologic therapy presents with signs or symptoms of the above infections. Any symptoms or signs suggestive of TB, or new exposure or prolonged residence in a high-incidence setting should prompt further clinical assessment and investigation. Active TB on TNF-antagonist therapy is often disseminated and extrapulmonary; symptoms may include unexplained weight loss, night sweats, non-resolving cough, haemoptysis and lymphadenopathy.

**4. Pregnancy**
If the patient is receiving biologic therapy or has recently stopped therapy (within 16 weeks of gestation) reports a pregnancy, please inform the dermatology unit as soon as possible to arrange urgent follow-up and monitoring.

**5. Elective Surgery**
If the patient is due to have elective surgery, please advise them to contact the dermatology unit for advice on when/if to stop therapy prior to surgery. Biologic therapy can be re-started post-operatively if there is no evidence of infection and wound healing is satisfactory

## References


1. British Association of Dermatologists' guidelines for biologic interventions for psoriasis 2017. C.H. Smith, Z.K. Jabbar-Lopez, Z.Z. Yiu, T. Bale, A.D. Burden, L.C. Coates, M. Cruickshank, T. Hadoke, E. MacMahon, R. Murphy, C. Nelson-Piercy, C.M. Owen, R. Parslew, E. Peleva, E. Pottinger, E.J. Samarasekera, J. Stoddart, C. Strudwicke, V. A. Venning, R.B. Warren, L.S. Exton and M.F. Mohd Mustapa. Br J Dermatol 2017; 177: 628-136.
2. National Institute for Health and Care Clinical Excellence Psoriasis: assessment and Management Clinical guideline [CG153]. Last updated September 2017.
3. Adalimumab for the treatment of adults with psoriasis (2008) NICE technology appraisal guidance 146
4. Certolizumab pegol for treating moderate to severe plaque psoriasis (2019) NICE technology appraisal guidance 574
5. Etanercept and efalizumab for the treatment of adults with psoriasis (2006) NICE technology appraisal guidance 103
6. Infliximab for the treatment of adults with psoriasis (2008) NICE technology appraisal guidance 134
7. Ustekinumab for the treatment of adults with moderate to severe psoriasis (2009 updated 2017) NICE technology appraisal guidance 180
8. Brodalumab for treating moderate to severe plaque psoriasis (2018) NICE technology appraisal guidance 511
9. Ixekizumab for treating moderate to severe plaque psoriasis (2017) NICE technology appraisal guidance 442
10. Secukinumab for treating moderate to severe plaque psoriasis (2015) NICE technology appraisal guidance 350
11. Guselkumab for treating moderate to severe plaque psoriasis (2018) NICE technology appraisal guidance 521
12. Risankizumab for treating moderate to severe plaque psoriasis (2019) NICE technology appraisal guidance 596
13. Tildrakizumab for treating moderate to severe plaque psoriasis (2019) NICE technology appraisal guidance 575
14. Apremilast for the treatment of adults with psoriasis (2016) NICE technology appraisal guidance 419
15. Dimethylfumrate for the treatment of adults with psoriasis (2017) NICE technology appraisal guidance 475
16. British Association of Dermatologists' – Position statement on biosimilars updated September 2017
17. Summary of Product Characteristics Cosentyx 150mg solution for injection in pre-filled pen.
18. Department of Health Immunisation against Infectious disease –The Green Book https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book#thegreen-book
19. Warren RB, Smith CH, Yiu ZZ, Ashcroft DM, Barker JN, Burden AD, Lunt M, McElhone K, Ormerod AD, Owen CM,Reynolds NJ, Griffiths CE. Differential Drug Survival of Biologic Therapies for the Treatment of Psoriasis: AProspective Observational Cohort Study from the British Association of Dermatologists Biologic InterventionsRegister (BADBIR). J Invest Dermatol. 2015 Jun 8. doi: 10.1038/jid.2015.208.
20. Summary of product characteristics for all drugs available at www. Medicines.org