High cost drugs pathway for psoriasis in adults

November 2019

Version 2.17
This supersedes version 2.1

Review due November 2022

Authors

Greater Manchester psoriasis working group

DOCUMENT CONTROL

REVISION DATE	ACTIONED BY	SUMMARY OF CHANGES	VERSION
July 2018	Prof Richard Warren S Jacobs	Version 1 updated in preparation for review by psoriasis working group.	2.2
August 2018	S Jacobs	Changes made to flow chart	2.3
September 2018	Psoriasis working group	Changes to recommendations for apremilast and dimethyl fumarate	2.4
September 2018	A Martin	Updated after meeting of psoriasis working group	2.5
September 2018	S Jacobs	Updated sections 10- 12	2.6
October 2018	S Jacobs	Changes following October working group	2.7
December 2018	A Martin	Changes following Consultants' comments	2.8
January 2019	A Martin	Changes following Commissioner's comments	2.9
January 2019	A Martin	Further changes following Commissioner's comments	2.10
February 2019	A Martin	Changes following comments received after 2.10 circulated	2.11
March 2019	A Martin	Changes following Commissioner's comments	2.12
March 2019	A Martin	Changes following comments received after 2.12 circulated	2.13
May 2019	A Martin	Updated with links to NICE TAs published April 2019	2.14
September 2019	RDTC	Updated to add risankizumab, and clarify commissioning position on 5-7th line biologics	2.15
September 2019	RDTC	Working group comments incorporated	2.16
November 2019	RDTC	Consultation comments incorporated	2.17
January 2020	RDTC	Update to add risankizumab to flowchart as an option where TB is a concern.	2.18

Main changes to version 2.18

- Addition of certolizumab pegol, guselkumab, tildrakizumab and risankizumab
- Biosimilar adalimumab positioning and dose optimisation
- 5th and 6th biologic option permitted, with MDT input, before an IFR is required
- Language and structure reviewed to ensure logical flow

Approvals

This document must be approved by the following before distribution:

TITLE	DATE OF ISSUE	VERSION
Psoriasis working group	November 2019	2.17
GMMMG High Cost Drugs Subgroup	November 2019	2.17
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Distribution

Final version available on GMMMG website

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Biologics pathway for psoriasis

1. Introduction

Psoriasis is a common chronic immune-mediated inflammatory skin disease. It typically follows a relapsing and remitting course that often persists throughout life. The prevalence of psoriasis is estimated to be around 1-2% in the UK with a significant proportion of patients (30%) having associated joint disease (psoriatic arthritis). Psoriasis can occur at any age, although is uncommon in children and the majority of cases occur before 35 years. Psoriasis for many people results in profound functional, psychological, and social morbidity, with consequent reduced levels of employment and income. The National Institute for Health and Care Excellence (NICE) has published individual Technology Appraisals (TAs) for the following licensed systemic biological therapies for psoriasis (see section 3);

Anti-TNFs:	Adalimumab, etanercept, certolizumab pegol, infliximab
IL-12/23 inhibitor:	Ustekinumab
IL-23 inhibitor:	Guselkumab, tildrakizumab, risankizumab
IL17 inhibitors:	Ixekizumab, secukinumab
IL-17 receptor antagonist:	Brodalumab

Apremilast, (oral phosphodiesterase 4 inhibitor) and dimethyl fumarate (oral fumaric acid ester) have also been approved by NICE, with similar requirements as for the biologic therapies for psoriasis, (see section 5 for further details).

NICE guidance allows treatment with 2 biologic drugs, after which supra-specialist advice from a clinician with expertise in biological therapy should be sought. However, as this is now dated and there is greater experience with biologics, this GMMMG pathway supports the routine commissioning of six different drugs with only the 5th and 6th line under supra-specialist advice from a multi-disciplinary team before submitting an individual funding request (IFR).

The vast majority of biologic prescribing for psoriasis within Greater Manchester is undertaken via the tertiary referral psoriasis clinic provided by Salford Royal Foundation Trust (SRFT).

All biologics can be used in accordance with NICE TAs, but the most cost effective treatment option should be selected, when suitable. For drugs where a biosimilar exists the best value biological medicine should be used in preference to the originator version, in line with NHSE commissioning framework. Specific treatment selection criteria are detailed in section 5.

2. Aims

The aims of the biologics pathway for psoriasis are:

1. To give advice on the appropriate use of each biologic in order to enable consistent evidence based clinical practice.

2. To reduce the number of Individual Funding Requests (IFRs) across the region.

3. To illustrate particular instances where the use of a particular biologic drug may be preferred over another, based on mode of action and current safety data.

4. To promote cost containment by using the most appropriate biologic therapy, by supporting the use of best value biological medicine and by promoting dose reduction, where appropriate.

5. To improve patient care by ensuring appropriate and timely use of biologics, dose optimisation, and reducing the number of dermatology hospital admissions.

3. NICE guidance

Links to relevant NICE guidelines and technology appraisals are listed below. The NICE recommendations also apply to biosimilar products of the technologies that have a marketing authorisation, allowing the use of the biosimilar for the same indication.

NICE psoriasis pathways overview

3.1 Anti-TNFs

NICE TA146; Adalimumab for the treatment of adults with psoriasis; June 2008
Adalimumab is recommended as a treatment option for adults with plaque psoriasis only if:

- Their condition is severe as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more **and** a Dermatology Life Quality Index (DLQI) of more than 10 **and**
- their condition has not improved with other treatments such as ciclosporin, methotrexate **and** PUVA (psoralen and long-wave ultraviolet radiation), or they have had side effects with these in the past or there is a medical reason why they should not be given these treatments
- Adalimumab should be discontinued in people whose psoriasis has not responded adequately at 16 weeks. An adequate response is defined as either:
  - a 75% reduction in the PASI score (PASI 75) from when treatment started, **or**
  - a 50% reduction in the PASI score (PASI 50) and a five-point reduction in DLQI from when treatment started

NICE TA103: Etanercept (and efalizumab) for the treatment of adults with psoriasis; July 2006
As adalimumab, plus:

- the dose of etanercept should not exceed 25 mg twice weekly
- discontinue in people whose psoriasis has not responded adequately at 12 weeks

NB: Efalizumab is no longer marketed.

NICE TA134: Infliximab for the treatment of adults with psoriasis; Jan 2008
Infliximab, within its licensed indications, is recommended as a treatment option for adults with plaque psoriasis only when the following criteria are met.

- The disease is **very severe** as defined by a total PASI of ≥20 or more and a DLQI of >18.
- The psoriasis has failed to respond to standard systemic therapies such as ciclosporin, methotrexate or PUVA, or the person is intolerant to or has a contraindication to these treatments.
- Infliximab treatment should be continued beyond 10 weeks only in people whose psoriasis has shown an adequate response to treatment within 10 weeks. An adequate response is defined as either:
  - a 75% reduction in the PASI score from when treatment started (PASI 75) or
  - a 50% reduction in the PASI score (PASI 50) and a five-point reduction in the DLQI from when treatment started

NICE TA574 Certolizumab pegol for treating moderate to severe plaque psoriasis; April 2019
As adalimumab, plus

- the lowest maintenance dosage of certolizumab pegol is used (200 mg every 2 weeks) after the loading dosage and
- the company provides the drug according to the commercial arrangement (Patient Access Scheme, PAS)

Certolizumab pegol is also available at a dose of 400 mg. However, use of this strength is not supported by NICE, as above.
Note: from TA574 onwards (inclusive) the term “PUVA” has been replaced with “phototherapy”.

3.2 IL-12/23 inhibitor and IL-23 inhibitors:

NICE TA180: Ustekinumab for the treatment of adults with moderate to severe psoriasis; Sep 2009
As adalimumab

NICE TA521: Guselkumab for treating moderate to severe plaque psoriasis; June 2018
As adalimumab, plus:

- the company provides the drug according to the commercial arrangement (PAS)

NICE TA575 Tildrakizumab for treating moderate to severe plaque psoriasis; April 2019
As adalimumab, plus:

- Consider stopping tildrakizumab between 12 weeks and 28 weeks if there has not been at least a 50% reduction in the PASI score from when treatment started.
- Stop tildrakizumab at 28 weeks if the psoriasis has not responded adequately
- The company provides the drug according to the commercial arrangement (PAS)

Note: the tildrakizumab SPC allows for a 200mg dose to be used in patients with certain characteristics (e.g. high disease burden, body weight ≥ 90 kg); such use is approved within this pathway.

NICE TA596 Risankizumab for treating moderate to severe plaque psoriasis; August 2019
As adalimumab, plus:

- The company provides the drug according to the commercial arrangement

3.3 IL17 inhibitors and IL-17 receptor antagonist:

NICE TA350: Secukinumab for treating moderate to severe plaque psoriasis; July 2015
As adalimumab, plus:

- The company provides secukinumab with the discount agreed in the PAS
- Secukinumab treatment should be stopped in people whose psoriasis has not responded adequately at 12 weeks.

NICE TA442: Ixekizumab for treating moderate to severe plaque psoriasis; April 2017
As secukinumab.

NICE TA511: Brodalumab for treating moderate to severe plaque psoriasis; March 2018
As secukinumab.

3.4 Non-biologic drugs:

NICE TA419: Apremilast for treating moderate to severe plaque psoriasis; Nov 2016
As adalimumab plus:

- The company provides apremilast with the discount agreed in the PAS.

NICE TA475; Dimethyl fumarate (Skilarence®) for treating moderate to severe plaque psoriasis; September 2017
As adalimumab.

4. Sequential use of biologic drugs

- The core biologic drugs fall into 4 categories, targeting different cytokines, or having varying affinity or avidity where the target is the same cytokine.

- It is likely that the key driver of any individual's disease is one of these cytokines. Lack of response to one biological agent in the management of psoriasis is therefore not predictive of a patient's likely response to alternative agents in an alternative class

- Although all biologics are highly efficacious in the short term, biologic drugs have an attrition rate year on year of approximately 15%+, such that changes to therapy are required for longer term disease control for what is a life-long condition. (3)

- Consideration can be given to escalating the dose of biologic therapy in adults when feasible when an inadequate primary response may be due to insufficient drug dosing, for example in obese patients or when psoriasis relapses during the treatment cycle. Take into account that this may be associated with an increased risk of infection. See section 5.2.

- Data on all patients will be made available annually to support the sequential use of biologics via the GMMMG High Cost Drugs Subgroups.

- Advice on switching between biologics is available in the British Association of Dermatologists guidelines for biologic therapy for psoriasis, 2017. The risk of a disease flare should be balanced against safety considerations.

5. Drug considerations and positioning

Systemic biological therapies are reserved for when a patient's psoriasis has not improved with other treatments such as ciclosporin, methotrexate **and** PUVA, or these options are contraindicated or not tolerated.

It is expected that methotrexate (oral and / or injectable) has been offered as the first choice of systemic agent for people with psoriasis unless contra-indicated.

There are numerous factors which would influence the choice of which biologic drug should be used at which point in the pathway. The choice of treatment between biological therapies should be made on an individual basis after discussion between the patient and their clinician about the advantages and disadvantages of the treatments available. Where more than one agent is clinically appropriate the most cost-effective drug should be chosen, in line with NICE guidance. Clinicians should contact pharmacy for advice on the relative cost-effectiveness of these drugs.

See section 10 for a flowchart summarising the treatment pathway.

5.1 First line biologics

Adalimumab (biosimilar, usually considered 1st line, including patients with psoriatic arthritis): If patients and their clinicians consider adalimumab to be one of a range of suitable treatment options it should be chosen first line as, in line with NICE guidance, it is the least costly.

Infliximab (biosimilar) is now only used for patients who have unstable disease and where rapid control is required.

5.2 Dose optimisation

Dose escalation is licensed for several drugs:

Drug	Usual dose	Escalated dose
Adalimumab	40 mg every 2 weeks	40 mg every week or 80 mg every 2 weeks
Certolizumab pegol	200 mg every 2 weeks	400 mg every 2 weeks
Tildrakizumab	100 mg every 12 weeks	200 mg every 12 weeks

If, after 16 weeks, patients prescribed best value adalimumab have an inadequate response to 40mg every other week, as per the licence the dose may be increased to 40 mg every week or 80 mg every other week. If adequate response is achieved with 40 mg every week or 80 mg every other week, the dosage may subsequently be reduced to 40 mg every other week, if considered clinically appropriate.

Off-label dose optimisation of other biologics can occur where there is evidence to support safety and efficacy, and where there is no financial cost to the NHS, e.g. ustekinumab 90 mg every 12 weeks in patients weighing <100 kg. Cost neutral options may be available for other agents; please contact pharmacy for advice. At time of publication, evidence review identified evidence that ixekizumab and ustekinumab may have increased efficacy when used at doses higher or more frequent than licensed. No major safety concerns were identified. It should be noted that the evidence base is evolving rapidly in this area, as experience is gained.

Dose reduction may be considered on a case-by-case basis, following discussion between the patient and their clinician. Consideration should be given to the risks and benefits for each patient, and to factors such as degree of disease control, consequences of a disease flare, and patient preferences.

5.3 Treatment failure

NICE CG153: Psoriasis: Assessment and management Sept 2017 recommends considering changing to an alternative biological drug in adults if:

1. Primary failure: the psoriasis does not respond adequately to a first biological drug within the timescales defined in NICE technology appraisals (see section 3)

   or
2. Secondary failure: the psoriasis initially responds adequately but subsequently loses this response

   or
3. The first biological drug cannot be tolerated or becomes contraindicated.

Where patients discontinue a drug due to adverse effects or the drug becoming contraindicated during the timescales for the assessment of efficacy defined in the respective NICE technology appraisals, this will not be regarded as one of the sequential treatment options in the patient's pathway. Similarly, if a drug becomes contraindicated during successful treatment due to a newly identified safety issue, switching to a new agent will not be regarded as one of the sequential treatment options in the patient's pathway.

5.4 Choosing an alternative biologic

The NICE-approved agents for the management of psoriasis have different mechanisms of action, so using an agent with a different mechanism of action to the failed therapy may result in disease control.

The choice of an alternative agent should be taken following review by a specialist, with consideration given to the mechanism of action of the previous agent, disease severity, current level of disease control, and the presence of co-existing PsA, as well as the patient's past medical history and contraindications and precautions to individual agents. If patients also have psoriatic arthritis, use a biologic that is approved for use by the GMMMG High Cost Drugs Pathway for Psoriatic Arthritis. Where more than one agent is considered clinically appropriate consideration should be given to drug cost (discuss with pharmacy).

Patients must meet the criteria laid out in the relevant NICE Technology Appraisal for initiation of alternative biologic therapy.

Brodalumab would not routinely be considered an early treatment option due to safety issues concerning the risk of suicide; see summary of product characteristics for more detail.

Certolizumab pegol: Consider for first line use in women who are pregnant or breast-feeding, or who are likely to become pregnant during treatment. Adalimumab remains first line for women of child-bearing potential who do not anticipate becoming pregnant. See section 12 for advice on prescribing in pregnancy and breast-feeding.

Etanercept is not routinely used. In line with the NICE TA, it is available as an option but as it is less effective than the other biologics, it is no longer included in this pathway as a routine treatment option.

Guselkumab: NICE has stated that guselkumab provides substantially greater clinical benefits compared with adalimumab, etanercept, infliximab and ustekinumab, and is likely to provide similar benefits to secukinumab and ixekizumab. It should be noted that emerging evidence may alter this balance over time. As experience is gained this might be considered an alternative second line option with increasing frequency.

Ixekizumab / secukinumab: These agents would only be considered where there are concerns or potential problems with adalimumab / ustekinumab e.g. demyelination risk / tuberculosis risk.
The presence of inflammatory bowel disease would warrant caution when using secukinumab, ixekizumab and brodalumab. Brodalumab is contraindicated in patients with active Crohn's disease.

Risankizumab: NICE has stated that risankizumab provides substantially greater clinical benefits compared with adalimumab and ustekinumab. There is evidence from a very small number of patients (n=31) that use of risankizumab in people with latent tuberculosis who were not receiving any prophylaxis did not result in active TB infection after a mean 55 weeks follow-up. As experience is gained this might be considered an alternative second line option with increasing frequency.

Tildrakizumab: Starting dose should take into account patient characteristics such as disease burden and body weight.

Ustekinumab: Ustekinumab has been shown to be safe and effective in the long-term and remains a 2nd line treatment option when adalimumab is not suitable. Ustekinumab has 2 dosing regimens; patients >100kg require the higher dose of drug and this dose may also be of relevance for heavier patients weighing <100kg, though such use would be off-label.

5.5 Third line and subsequent treatment

- NICE CG 153 states that for adults in whom there is an inadequate response to a 2nd biological drug, seek supra-specialist advice from a clinician with expertise in biological therapy.
- However, within Greater Manchester, it is considered appropriate for those clinicians with specialist skills, who are familiar with the mechanisms of action of the biologics, to prescribe 3rd line agents.
- The use of a 5th line treatment or beyond should be initiated at a tertiary referral psoriasis centre. For Greater Manchester registered patients this is currently provided by dermatologists at SRFT.
- Use of 5th or 6th line biologics is subject to Multi-Disciplinary Team (MDT) approval at a tertiary centre, with agreement from ≥3 consultants, including input from other specialties as required (e.g. rheumatology).
- Considerations should be given to the different mechanisms of action of the various treatments available.

5.6 Apremilast and dimethyl fumarate

These "small molecule", non-biologic treatments can be used at any stage of the pathway when clinical scenarios make their use preferable to biologics, but should not be used in preference to a biologic where a biologic is considered more clinically appropriate. Use will not be regarded as one of the sequential treatment options in the patient's pathway.

5.6.1 Apremilast

- Apremilast is a phosphodiesterase type-4 inhibitor.
- It can be considered as an alternative to biologics for patients with either psoriasis alone or psoriasis in combination with PsA:
    - in patients with significant comorbidities and therefore at higher risk of developing adverse effects to biologics OR
    - when laboratory parameters may preclude other therapies

5.6.2 Dimethyl fumarate

- Dimethyl fumarate is an oral fumaric acid ester.
- When compared indirectly, dimethyl fumarate is less effective than systemic biologic therapies but is generally less costly.
- It can be considered as an alternative to biologics for treatment of moderate to severe psoriasis in the absence of psoriatic arthritis:
    - In patients with a significant risk of infection or significant comorbidities, such as demyelination, OR
    - when laboratory parameters may preclude other therapies
- The licensed preparation Skilarence® should be prescribed. Unlicensed Fumaderm® should no longer be initiated.

5.7 Data requirements and audit

- Full clinical details regarding patients on high cost drugs – disease scores at initiation and continuation, reasons for change of treatment and all previously tried drugs – must be made available to commissioners. This is expected to be via Blueteq; see section 5.8.
- All use drugs in line with this pathway will be monitored in line with the accompanying monitoring framework. The Greater Manchester High Cost Drug Subgroups will provide assurance on the commissioned pathways to the Greater Manchester Clinical Standards Board (GMMMG CSB).

5.8 Blueteq

Blueteq forms which comply with this pathway are available. Where Blueteq has been introduced to the Trust as part of the contractual arrangements, funding approval for the PbR excluded high cost drugs will be made by meeting the accepted criteria outlined on completion and submission of a Blueteq form.

5.9 Route of supply

Opportunities to supply biologics (and non-biologic PbRe drugs) via VAT-exempt routes should be maximised where appropriate.

6. Biosimilars

A Prescribing of high cost biosimilar biological medicines position statement has been approved by **GMMMG** and makes the following recommendations:

6.1 Initiating treatment with a biologic

- If patients and their clinicians consider adalimumab to be one of a range of suitable treatments, in line with NICE guidance it should be chosen as it is the least costly. The rationale for choice should be documented on Blueteq.
- **If more than one treatment is suitable, the least expensive should be chosen** (taking into account administration costs, dosage and price per dose). This is currently biosimilar adalimumab.
- If the least expensive product is not prescribed, the reasons why must be documented on Blueteq form and made available to commissioners if required.

- Where NICE has already recommended the originator biological medicine, the same guidance will apply to the biosimilar medicine.
- In line with MHRA guidelines: biologics, including biosimilars, must be prescribed by brand name to support on-going pharmacovigilance of the individual products.

6.2 Changing from originator to a biosimilar

- There is evidence that patients who are in a stable clinical response or remission may be changed over to the biosimilar at the same dose and dose interval. This should be done after discussion and agreement with individual patients.
- Changing a patient on a biologic originator medicine to a biosimilar should be done at the point of prescribing and in discussion with the hospital pharmacy department.
- There should be no automatic substitution of a biologic with a biosimilar at the point of dispensing.

7. Individual Funding Requests (IFR)

- Up to six biologics for treatment of psoriasis will be commissioned routinely, if prescribed in accordance with this pathway. IFRs will not be required for up to six biologics, or for apremilast and dimethyl fumarate. However, where available, Blueteq forms must be completed for these patients. See section 5.8, above.
- All other treatment options outside of this pathway will require an IFR to be approved prior to treatment being started. When submitting an IFR, exceptionality should be demonstrated; exhausting the treatment options in this pathway does not automatically establish exceptionality.
- IFRs for sequential use of 7th line and beyond biologics must include details of all previous treatments with responses and reasons for discontinuation.

8. Free of Charge Schemes

All free of charge schemes should be approved in accordance with trust guidance and GMMMG Free of Charge guidance. Approval should be agreed at the trust's medicines management committee.

There must be clear exit criteria that do not place financial burden on commissioners and do not raise patients' expectations of continuation of treatment.

9. Research Recruitment

9.1 Clinical trials

Where possible, consideration should be made to entering patients into observational/clinical studies. Some sites host early and later phase clinical trials of biologic therapies, both biologic naïve and biologic experienced.

9.2 Biologics registers

Clinicians are strongly encouraged to offer people with psoriasis who are starting treatment with a systemic non-biological or biological drug the opportunity to participate in long-term safety registries (for example the British Association of Dermatologists Biologic and Immunomodulators Register, BADBIR).

10. Greater Manchester Biologics Pathway for psoriasis: flow chart

Severe psoriasis despite conventional DMARDs (i.e. ciclosporin, methotrexate and PUVA)
See section 14 for biologic screening questions for pre-admission

Severe psoriasis (PASI ≥10 and DLQI >10)

First line

Adalimumab (biosimilar) (see 5.1). Optimise dose prior to switching, if possible

Alternatives

- if adalimumab unsuitable: **guselkumab or risankizumab**
- if demyelination or TB: **ixekizumab, risankizumab** or **secukinumab**

Very severe psoriasis (PASI ≥20 and DLQI >18)

First line

Infliximab (biosimilar) if unstable disease and rapid control required

Alternatives

- Consider an IL-17 modulator, e.g. secukinumab, ixekizumab or brodalumab.

Second and Third line

If initial biologics discontinued, choose the next most appropriate. Please refer to sections 5.4 & 5.5 for guidance.

Adalimumab / brodalumab / certolizumab pegol / guselkumab / ixekizumab / risankizumab / secukinumab / tildrakizumab / ustekinumab

Fourth line

Where there is inadequate response to prior treatment a 4th-line treatment can be initiated by a clinician with appropriate specialist skills. Choice depends on previous biologics used and comorbidities of the patient. Please refer to section 5.4 for guidance.

Fifth and sixth line

Subject to Multi-Disciplinary Team (MDT) approval at tertiary centre, with agreement from ≥3 consultants, including input from other specialties as required (e.g. rheumatology).

Seventh line

Individual Funding Request (IFR) required. IFR must include full clinical history and disease scores.

Notes

For all drugs, discontinue if:

- the biologic is not tolerated or becomes contra-indicated (see section 5.3).
- response is not adequate at the review date (see section 3) or there is loss of response

Adequate response is defined as either:

- 75% reduction in the PASI score from the start of treatment **or**
- 50% reduction in the PASI score **and** a 5 point reduction in the DLQI from the start of treatment

Apremilast or dimethyl fumarate may be used at any stage of the pathway when clinical scenarios make their use preferable to biologics. Use of these agents will not count as one of the sequential choices prior to requiring an IFR.

11.1. Cautions and contraindications

Cautions, contraindications, and special warnings to use of systemic agents for psoriasis are detailed in the individual summaries of products characteristics (SPCs), which are available from www.medicines.org.uk. Prescribers should consult the relevant SPC to inform clinical decision-making for individual patients.

11.2. Additional safety considerations

The MHRA has published Drug Safety Updates relating to several of the drugs included in this pathway, all of which are available from www.gov.uk/drug-safety-update:

- Tumour necrosis factor alpha inhibitors; December 2014
- Ustekinumab (Stelara): risk of exfoliative dermatitis; January 2015
- Apremilast (Otezla▼): Risk of suicidal thoughts and behaviour; Feb 2017
- Live attenuated vaccines: avoid use in those who are clinically immunosuppressed; April 2016

12. Special Situations

12.1. Peri-operative risk

Reduction of potential post-operative infection risk by temporarily stopping a patient's biologic treatment should be carefully balanced against the possibility of a peri-operative flare of psoriasis. Where infection risk is high, or where infection would be catastrophic, consider stopping treatment 3-5 half-lives prior to surgery (see table below). Treatment should be recommenced post-operatively once infection is excluded and the wound is healed.

Where infection risk is low, or the risk of disease flare is high, consider continuing treatment. If possible, surgery may be scheduled at a time where drug levels are expected to be low.

For further guidance, see British Association of Dermatologists guidelines for biologic therapy for psoriasis, 2017.

Biologic	Mean half-life*	Time to stop treatment prior to surgery (3-5 half-lives)
Etanercept	3 days (approx. 70 hours)	9- 15 **days**
Adalimumab	2 weeks	6 – 10 weeks
Infliximab	Median 8-9.5 days	4 – 7 weeks
Ustekinumab	Median 3 weeks (range 15-32 days)	7 – 23 weeks
Secukinumab	27 days (range 18-46 days)	8 – 33 weeks
Ixekizumab	13 days	6 – 10 weeks
Brodalumab	11 days	5 – 8 weeks
Certolizumab pegol	14 days	6 – 10 weeks
Guselkumab	15-18 days	7 – 13 weeks
Tildrakizumab	23 days	10 – 17 weeks
Risankizumab	28-29 days	12 – 21 weeks

*summary of product characteristics (SPCs), www.medicines.org.uk

12.2. Pregnancy and breast feeding

12.2.1. Pregnancy

There are limited data on the safety of biologic drugs in pregnancy and lactation. The decision to continue biologic agents in pregnancy needs to be individualised, taking 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 may, if needed, be re-loaded with biological therapy soon after delivery. Information to support this decision is available in the individual Summaries of Product Characteristics (available from www.medicines.org.uk), and from the UK Teratology Information Service (UKTIS) website at http://uktis.org/html/exposures_abc.html.

Exposures in pregnancy should be reported to the UKTIS by use of their online reporting form

(http://www.uktis.org/html/reporting.html) or by contacting 0344 892 0909 (available 9am-5pm, Monday – Friday). UKTIS are commissioned by Public Health England to perform national surveillance of known and emerging human teratogens across the United Kingdom.

Advice and risk assessment for individual patients may also be available by contacting a local Medicines Information service via Trust pharmacy departments, or by discussing directly with UKTIS on 0344 892 0909.

12.2.2. Breast feeding

There is very limited information on the excretion of biologics in breast milk. Since immunoglobulins are excreted into human breast milk, a risk to the breastfeeding child cannot always 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.

Information on manufacturers' recommendations on use in lactation is available from the individual Summaries of Product Characteristics (available from www.medicines.org.uk), and further information may be available from the Specialist Pharmacy Service (SPS) website at www.sps.nhs.uk.

Advice and risk assessment for individual patients may also be available by contacting a local Medicines Information service via trust pharmacy departments.

12.3. Vaccination of Infants

If a biologic has been continued in pregnancy after 16 weeks gestation, live vaccines should be avoided in the infant until they reach 6 months of age, after which time vaccination should be considered. The live vaccinations currently included in the childhood vaccination schedule for infants aged <1 year are:

- Rotavirus – all infants
- Tuberculosis – infants living in areas of the country with incidence ≥40/100,000, and infants with a parent or grandparents born in a country with incidence ≥40/100,000 (see www.gov.uk/government/publications/tuberculosis-tb-by-country-rates-per-100000-people).

Rotavirus is the most common cause of gastroenteritis in infants in the UK.. Although there is limited evidence of safety and efficacy in infants with immunosuppression the vaccine may be considered by the treating consultant following careful consideration of the risks and benefits, and following specialist consultation as appropriate. This does not include infants with severe combined immune deficiency.

If breastfeeding, the BCG vaccination should not be given until 6 months after finishing breastfeeding. For advice on other live vaccinations following exposure to biologics in breast milk, healthcare professionals should contact the relevant specialist for advice.

Current vaccination strategies with non-live vaccines for infants who have been exposed to biologic medicines in utero do not differ from those for unexposed infants.

13. Vaccinations

Where possible, vaccination requirements should be reviewed and brought up to date prior to initiation of biologic therapy, with reference to Department of Health Guidance. During biologic therapy, patients should receive (inactivated) influenza vaccine annually and pneumococcal vaccine once.

13.1. Live vaccines

The administration of live vaccines is contraindicated in patients on biologic agents. 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
Influenza	Fluenz Tetra®
Measles, Mumps and Rubella combined vaccine (MMR)	MMRvaxPRO®, Priorix®
Rotavirus (Live oral vaccine)	Rotarix®
Typhoid (Live oral vaccine)	Vivotif®
Varicella-Zoster Vaccine	Varilrix®, Varivax®, Zostavax®
Yellow Fever	Stamaril®

When a live vaccine is required by a patient on a biologic, stopping treatment (following careful assessment of the risks and benefits) may enable a necessary vaccination to be administered. For advice on the appropriate interval between stopping biologic therapy and administering live vaccines please consult:

- relevant summaries of products characteristics, www.medicines.org.uk
- the Green Book, https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book
- specialist advice

13.2. Non-live vaccines

Non-live vaccines are deemed safe to administer to people on immunosuppressant and on biologic therapies, though they may elicit a lower response than in immunocompetent individuals.

Non-live vaccines should be given 2-4 weeks before starting immunosuppressant therapy, as response after starting treatment can be poor.

For information on specific vaccines please refer to the appropriate Summary of Product Characteristics (www.medicines.org.uk) or the Green Book: Immunisation against infectious disease (https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book).

14. Checklist for patient screening on pre-admission for biologic agents

Name:…… **Number:**…… **Consultant:**……..

Screening Investigations Requested in Clinic			
	Y/N	**Initial**	**Results/Details**
FBC/U&E/LFT/ESR/CRP			
ANA *(If positive also order ENA/dsDNA/C3/C4)*			
HIV, HBV *(surface antigen, core antibody)**, **HCV** *(antibody test) If positive result please refer to Hepatology/GUM* * Reactivation has been reported in HBsAg-ve as well as HbsAg +ve patients stressing the importance of measuring not only HBsAg but also antibodies against HBc antigen to identify positive carrier status			
Varicella Zoster IgG (If negative inform GP and patient)			
TB screening *(g-IFN testing)* *If positive refer to respiratory*			
Chest X-Ray *(within the last 6 months)* *(± pulmonary function tests/HRCT thorax)* **CXR checked by/date**			
Screening questions asked in clinic			
	Y/N	**Initial**	**Details**
Previous TB/TB contact (*details*)			
Recent travel abroad *(i.e. TB high risk countries)* *Which Country/Dates*			
History of heart failure (NYHA class III or IV) *(details)*			
History of recurrent infection *(details)*			
History of interstitial lung disease *(details such as extent of ILD [21])*			
History of cancer *(Type/Date when occurred/Date of all clear)*			
Date of last mammogram (50yr +) *(Encourage patient to visit GP if >3 years)*			
Date of last smear (25yr +) *(Encourage patient to visit GP if >3 years)*			
History of infusion reaction to any agent *(To what/type of reaction)*			
Allergy (*details)*			
Education and funding			
	Initial	**Details**	
Blueteq form completed			
Pregnancy/breastfeeding advice given			
Annual influenza vaccination advice given			
Pneumococcal vaccination advice given			
Patient counselled and educated			
Patient education pack given			
Patient consent to be approached for research			

Completing Clinician Signature…… **Date**…….....

Nurse Practitioner Signature…… **Date**…….....

15. **References**

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