NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINES

Psoriasis Treatment with Biological Agents

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Clinical Pathway: Psoriasis treatment with Biological Agents

This pathway is guidance only and is based on the clinical guidelines for treatment of Psoriasis with biological agents by the British Association of Dermatologists (BAD) which were produced based on best clinical evidence to date and on solid guidelines methodology. This is an updated version providing a summary of current BAD guidance last updated in 2020 to include new therapeutics and additional new agents approved and licensed since then.
It is the responsibility of clinicians who use biological agents to keep up to date with these guidelines, and to use their clinical judgement to guide appropriate treatment choice. The GG&C tertiary Psoriasis Service and clinic offer virtual advisory/discussion appointment slots for clinicians to discuss their patients. This is open and available for all Dermatologists prescribing treatments for Psoriasis.
This pathway is for non pregnant, adult patients. Some of the therapeutics are licensed for adolescents and children (see page 3). Treatment of those age groups should be undertaken by Dermatologists with experience in these age groups. For pregnant patients and patients with intention to conceive, please see advice on page 6.

There are multiple factors to be taken into consideration before choice of treatment:

- Patients with psoriasis (particularly severe psoriasis), can have many co-morbidities and be prescribed polypharmacy.
- Drug toxicities, contra-indications and drug interactions should be considered.
- Individual patient characteristics including; special site involvement, history of non adherence to treatment, family planning, needle-phobia, recurrent infections, lifestyle and profession.

Severity scores (**P**soriasis **A**rea **S**everity **I**ndex, **B**ody **S**urface **A**rea or **P**hysicians **G**lobal **A**ssessment), patient-reported scores of symptoms and impact on quality of life (**D**ermatology **L**ife **Q**uality **I**ndex) must be recorded to justify the use, and also to evaluate the response/outcome of treatment. All treatment discussions with the patient must be documented, and the reasons for any deviation from the current guideline recommendations must be recorded.

ELIGIBILITY:

Biological agents are approved for use in moderate-to-severe psoriasis:

a) Which has failed to respond to either methotrexate, ciclosporin or phototherapy.
b) If patients have contra-indications or have developed side effects to the above.
c) If patients have responded to ciclosporin but have exceeded the licensed duration of use (2 years).
d) If relapses happen within 3 months from completion of a treatment course e.g. phototherapy or a cyclosporine pulse
e) If there is co-morbid Psoriatic Arthritis, ciclosporin and phototherapy are not effective for the arthritis and after failure or contra-indication for methotrexate patients can be considered for biological agents.

Moderate-to-severe psoriasis is defined by PASI ≥10 + BSA >10% **or** PGA moderate-severe.

Biologic agents should also be considered for use in special/high impact site psoriasis: face, scalp, ano-genital area and palmo-plantar, which are areas particularly associated with severe impact on quality of life (DLQI ≥10).

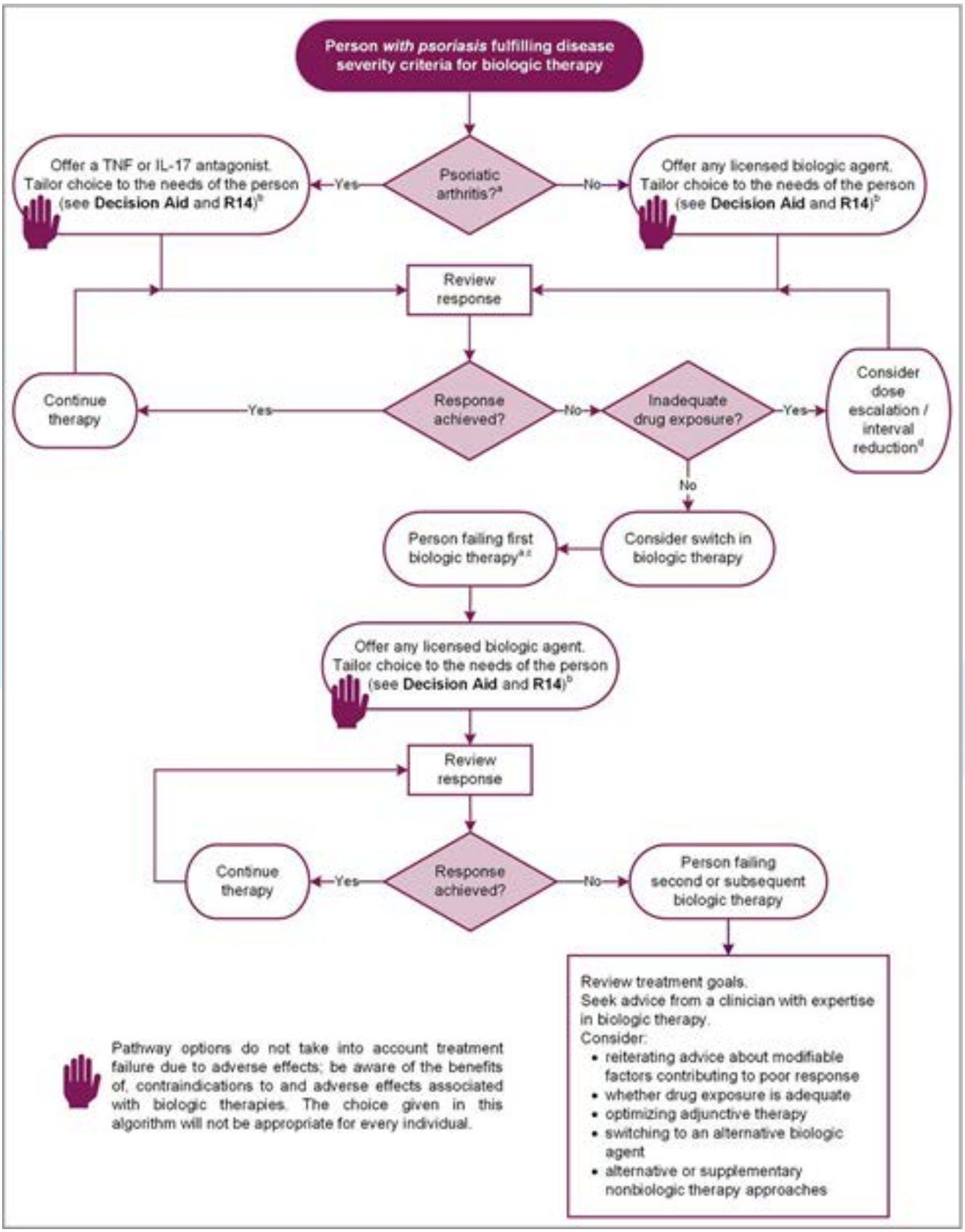
CHOICE OF AGENT:

Table 1: Summary of available licensed biological agents for psoriasis and small molecules in groups according to mechanism of action

TNFa inhibition	IL12/23 (p40 subunit) inhibition	IL-17 pathway inhibition (Il-17 or IL-17 receptor inhibition)	IL-23 (p19 subunit) inhibition
Adalimumab	Ustekinumab	Secukinumab	Guselkumab
Etanercept		Ixekizumab	Risankizumab
Infliximab		Brodalumab	Tildrakizumab
Certolizumab		Bimekizumab	

All these agents are licensed only for plaque psoriasis. Other forms of psoriasis e.g. erythrodermic, pustular, unstable are not covered in this pathway.
In Scotland, Adalimumab is licensed for use in ages from 4 years and above, Ustekinumab is licensed for use in ages 12 and above. The rest of the above biologics are licensed for use in adults in Scotland.

At the time of creating this pathway the BAD guidelines are summarised in the following flowchart:



Smith CH, Yiu ZZN, Bale T, Burden AD, Coates LC, Edwards W, MacMahon E, Mahil SK, McGuire A, Murphy R, Nelson-Piercy C, Owen CM, Parslew R, Uthman OA, Woolf RT, Manounah L, Ezejimofor MC, Exton LS, Mohd Mustapa MF; British Association of Dermatologists' Clinical Standards Unit. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update. Br J Dermatol. 2020 Oct;183(4):628-637. doi: 10.1111/bjd.19039. Epub 2020 Jul 21. PMID: 32189327

The BAD guideline publication in full text including the above flowchart as well as the decision aid tool can be accessed through the link: onlinelibrary.wiley.com/doi/10.1111/bjd.19446
Dermatologists in Scotland follow recommendations of this flowchart based on guideline methodology. **When multiple agents are an appropriate choice, consider cost and show preference to the preparation with the lowest cost where possible**. **It is advisable that Adalimumab is considered as first line due to low cost in all cases with consideration of the clinical issues below**. When patients have co-morbid Psoriatic arthritis the treatment can be led by either Dermatology or Rheumatology depending on the severity of each disease and providing the two specialties are in communication. Using the BAD guidelines as reference, the cost for each drug and co-morbidity of psoriatic arthritis (PsA), the table of choices (in groups of mechanism of action) for treatment is:

All patients should be considered for Adalimumab (anti-TNFa) as a first line choice.
If clinical factors require a different choice then the following can be considered:

	Anti-TNFa	IL12/23 (p40 subunit) inhibition	IL-17 pathway inhibition (Il-17 or IL-17 receptor inhibition)	IL-23 (p19 subunit) inhibition
Psoriasis without Psoriatic arthritis				
Preferred drugs	Adalimumab	Ustekinumab	Secukinumab Ixekizumab Brodalumab Bimekizumab	Tildrakizumab Risankizumab Guselkumab
Less preferred drugs	Certolizumab* Infliximab Etanercept			
Psoriasis with co-morbid Psoriatic arthritis				
Preferred drugs	Adalimumab		Secukinumab Ixekizumab	Guselkumab Risankizumab
Less preferred option for Ps **with** PsA	Certolizumab* Infliximab Etanercept	Ustekinumab		

Certolizumab should be considered as first line for female patients with immediate intention to conceive.

SECOND LINE BIOLOGIC:

There is little evidence available to guide switching between biologics but there are arising publications. Choice of any licensed biological agent should take into consideration the above factors. Choice of different agents of a group with same or different mechanism of action is justified. Even agents with the same mode of action can have different effects, likely due to individual patient characteristics or different affinity to target. Some evidence in retrospective studies favouring this, is arising and increasing the choices available.

IMPORTANT CONSIDERATIONS FOR CHOICE:

- For Adalimumab and Infliximab **biosimilars** of the reference product are available.
- When multiple agents are an appropriate choice, **consider cost** and show preference to the one with the lowest cost where possible.
- When patients have **co-morbidities that share common treatments with psoriasis**, e.g. Psoriatic Arthritis or Inflammatory Bowel Disease, consider rationalising medication for patient by choosing agents that can target all co-morbidities.
- Consider **immunogenicity** (development of neutralising antibodies) against anti-TNFa agents.
- Consider special groups of patients:
    - **Needle-phobia**: a less frequent dosing regimen may be preferred (ustekinumab, tildrakizumab, risankizumab, guselkumab, bimekizumab).
    - **History of non compliance** to treatment: less frequent dosing regimens (ustekinumab, tildrakizumab, risankizumab, guselkumab, bimekizumab) and/or controlled administration by nurse. (ustekinumab, tildrakizumab, risankizumab, guselkumab, infliximab, bimekizumab).
    - **Obesity**: biologics with weight-based dosing regimens are preferred: ustekinumab, infliximab, secukinumab and bimekizumab.
    - **Heart failure NYHA Class III/IV**: avoid anti-TNFa. For heart failure of lower class consider consulting a Cardiologist
    - **Demyelination** in patient or first degree relative (multiple sclerosis): relative contra-indication of TNFa inhibitors.
    - Co-morbid **Inflammatory Bowel Disease**: avoid IL-17 inhibition.
    - History of **recurrent thrush** and difficult to treat without other risk factors: avoid IL-17 inhibition.
    - Intent for pregnancy: preferred Certolizumab and second line other TNFa inhibitors. Consider co-morbidities and unstable versus stable disease.
    - **Lifestyle/**professional commitments demanding patient to travel frequently: consider less frequent dosing regimens.

Multi-disciplinary input must be considered for the following groups:

- **Co-morbid Psoriatic Arthritis**: input by Rheumatologist.
- **Co-morbid Inflammatory Bowel Disease**: input by Gastroenterologist/Surgeon.
- **Malignancy**: input by Oncologist and other specialists using these biological agents
- **Latent TB**: input by Respiratory/Infectious Diseases physicians. TNFa inhibitors and IL23/12 are contra-indicated if there is no evidence of previous treatment until they are treated by the Respiratory/Infectious Diseases physicians. IL-17 and IL-23(p19) inhibitors may not reactivate latent TB but the advice of the Respiratory/ID physicians is strongly advised before any treatment initiation.
- **Chronic infections** (HIV, viral Hepatitis): input by managing Physician.
- **Obesity**: input by weight management team to optimise response to treatment.
- Intention for conception and pregnancy: discuss with Obstetrics/Pre-conception advice

Monitoring:

Patients established on biologic therapy require regular clinic follow up and routine blood monitoring (haematology and biochemistry every 3-6 months depending also on co-morbidities).

It is advised that monitoring is co-ordinated with other clinical specialties involved in the patients care to avoid unnecessary hospital appointments.

There is no requirement for routine therapeutic drug monitoring. At present therapeutic drug monitoring and measurement of anti-drug antibodies is available routinely for adalimumab and infliximab.

DISCONTINUATION/SWITCHING TREATMENT:

Consider changing to an alternative therapy, including another biologic agent if any of the following apply:

- There is no response or suboptimal response (<PASI75 or absolute PASI>3 and <5 points reduction in DLQI) after 16 weeks of treatment with adalimumab or other anti-TNFa agents, after 12 weeks with IL-17 inhibitors and after 4-6 months with ustekinumab or IL-23p19 inhibitors
- The psoriasis initially responds but subsequently loses this response (secondary failure).
- The current biologic therapy cannot be tolerated or becomes contraindicated.

Factors which should be considered before deciding to continue or change biological agents are:

- Response in special /high impact sites (palmo-plantar disease, face, ano-genital area).
- Response of Psoriatic Arthritis (if present).
- Tolerability and side effects.
- Treatment alternatives.
- Patient views.
- Maximization of dose: Adalimumab 40mgr Sc once weekly; Ustekinumab from 45mgr to 90mgr every 12 weeks or 90mgr every 8 weeks Sc; Infliximab Iv or Sc every 6 weeks; Tildrakizumab from 100mgr to 200 mgr every 12 weeks; Ixekizumab 80mgr from every 4 weeks to every two weeks. Secukinumab 300mgr every 2 weeks and Bimekizumab 160mgr every 4 weeks. Please consider cost and possible increased risk of infections. Please refer to prescribing guidance for these agents (summary of product characteristics)

RESEARCH RECRUITMENT:

For all patients starting biologic therapy it is strongly recommended that they are registered with BADBIR (British Association of Dermatologists Biologics and Immunomodulators Registry) in terms of providing information/evidence for developing the BAD guidelines, clinical standards and continuing pharmacovigilance for these agents. The tertiary Psoriasis clinic at the West Glasgow ACH is a recruiting centre for BADBIR.