NHS
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Barts Health NHS Trust
Homerton Healthcare NHS Foundation Trust
Barking, Havering and Redbridge University Hospitals NHS Trust

High-Cost Drugs Treatment Pathway for Psoriasis (Adults)

North East London

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Authors and contributors	**NHS NEL ICB:** Commissioning and Contracting Pharmacist Joint Formulary Pharmacist QIPP Program Pharmacist **BHR University Hospitals NHS Trust:** Consultant Dermatologists Assistant Chief Pharmacist Clinical Services **Homerton Healthcare NHS Foundation Trust:** Consultant Dermatologists Lead Biologics Pharmacist **Barts Health NHS Trust:** Consultant Dermatologists Specialist Pharmacist – Dermatology
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Document Version History		
Date produced	**Version**	**Comment/Changes**
June 2023	1.2	Added Secukinumab and Ustekinumab into dose escalation
September 2023	1.3	Added Deucravacitinib to the pathway.
		Dose escalation updated for adalimumab inadequate response (primary and secondary failure)
		Appendix 1 updated to include route of administration

Contents

Definitions

a) **Very severe disease as per NICE eligibility criteria**
   i. Psoriasis Area and Severity Index (PASI) score of 20 or more
   ii. DLQI of ≥**18**
b) **Severe disease as per NICE eligibility criteria**
   i. Psoriasis Area and Severity Index (PASI) score of 10 or more
   ii. DLQI of **≥10**
c) **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

Scope

This document outlines the treatment pathway for adult patients in North East London diagnosed with Psoriasis using five modes of action.
It is to be used in conjunction with the National Institute for Health and Care Excellence (NICE) guidance and the published NICE Technology Appraisal (TA) guidance for each individual high cost drug. The pathway is intended to be adopted by all acute provider Trusts within North East London

NICE Guidance and Technology Appraisals

At the time of publication, this treatment pathway considers the following NICE clinical guideline:CG153
https://www.nice.org.uk/guidance/cg153

Table 1: NICE Technology Appraisals for Psoriasis

NICE Technology Appraisal Number	Title
TA146	Adalimumab for the treatment of adults with psoriasis
TA419	Apremilast for treating moderate to severe plaque psoriasis
TA723	Bimekizumab for treating moderate to severe plaque psoriasis
TA511	Brodalumab for treating moderate to severe plaque psoriasis
TA574	Certolizumab pegol for treating moderate to severe plaque psoriasis
TA475	Dimethyl fumarate for treating moderate to severe plaque psoriasis
TA103	Etanercept and efalizumab for the treatment of adults with psoriasis
TA521	Guselkumab for treating moderate to severe plaque psoriasis
TA134	Infliximab for the treatment of adults with psoriasis
TA442	Ixekizumab for treating moderate to severe plaque psoriasis

NICE Technology Appraisal Number	Title
TA596	Risankizumab for treating moderate to severe plaque psoriasis
TA350	Secukinumab for treating moderate to severe plaque psoriasis
TA575	Tildrakizumab for treating moderate to severe plaque psoriasis
TA180	Ustekinumab for the treatment of adults with moderate to severe psoriasis
TA907	Deucravacitinib for treating moderate to severe plaque psoriasis

At the time of publication, this treatment pathway considers the above NICE TAs

Principles

This document is based on current NICE TAs available for the management of psoriasis, with reference to the NCL psoriasis pathway and guideline.
The pathway is subject to change as new evidence, NICE TAs or local agreements are released or updated that will impact on the information outlined in this document. This includes changes in drug costs that may impact on cost-effectiveness and drug choice in the treatment pathway.
It is expected that drugs presenting best value are selected where clinically appropriate. For further prescribing information including contraindications and cautions, please refer to the relevant drug monograph in the latest version of the British National Formulary or the respective drug's Summary of Product Characteristics.

Definitions and Lines of therapy

NICE do not state a definitive maximum number of lines of therapy in their guidance. Therefore, taking into consideration the presence of multiple drugs recommended by NICE, the number of lines of therapy has been based on the number of different mechanisms of action of the recommended drugs (Table 2).

The ICB has recognised and adopted the recommendation set out by the Regional Medicines Optimisation Committee (RMOC) which recommends switching to a high cost drug with a new mechanism of action [1].
The drugs are categorised into 5 mechanisms of action which are independent of each other, and therefore each patient will have access to a maximum of 5 lines of therapy. Clinicians may start a drug from each mechanism of action for a patient, as outlined in the table below. There may be instances where multiple drugs are chosen from one mechanism of action as this is more appropriate for the patient based on their clinical presentation. A maximum of 5 lines of therapy would still apply for these patients.

If the responsible clinician deems the patient could still benefit from further HCD treatment, funding will need to be requested via an Individual Funding Request (IFR) to the patient's ICB.
Taken from the NEL IFR policy "*In order to support an IFR on the basis of failure to respond to standard care, the IFR Panel would normally need to be satisfied that the patient's inability to respond to, or be provided with, the usual treatment was a genuinely exceptional circumstance, which lies outside the natural history of the condition and is not characteristic of the relevant group of patients with the condition*".

The NICE committee considered that cost-effectiveness analyses for sequences should ideally be considered in decision making. But it acknowledged that there is no clinical data

on sequential effectiveness and the clinical rationale for using various sequences of treatments would be personalised to each person. Therefore, the committee concluded that analysis of treatment sequences would be uncertain.
It is expected that this pathway will impart a cost pressure which is why a maximum of three lines of therapy has been chosen. However, in the context of initiatives to utilise best value-value medicines, there is opportunity to formalise cost-effective prescribing through the pathway.

Table 2: Mechanisms of action

Mechanism of inhibition/Action				
Anti-TNF	**Anti IL12 / 23**	**IL17A**	**IL23**	**Small Molecule**
Adalimumab	Ustekinumab	Brodalumab	Guselkumab	Apremilast
Certolizumab		Ixekizumab	Risankizumab	Dimethyl fumarate
Etanercept		Secukinumab	Tildrakizumab	Deuvracacitinib
Infliximab		Bimekizumab		

Primary Failure
The patient's psoriasis does not demonstrate a response to therapy as outlined in the NICE TA.

Secondary Failure
The patient's psoriasis initially achieves a response to therapy which is subsequently not sustained, resulting in failure to maintain a response as outlined in the NICE TA.

Adverse Reaction
If the patient has an adverse event before the initial response assessment period it will not count as a line of therapy. If the adverse reaction occurs after the initial response assessment period, the patient must have shown a response to therapy with that biologic for it not to count as a line of therapy.

Treatment choice in pregnancy and breastfeeding

Certolizumab pegol is the drug of choice in women who are confirmed pregnant as it is compatible with all three trimesters of pregnancy [2,3]. If patient needs to be switched to certolizumab due to confirmation of pregnancy or pre-conception, and the drug is used for a finite duration with a planned exit strategy, this will **not** count as a line of therapy. The drug should be reviewed to stop post-parturition, reverting to the most clinically- and cost-effective agent as soon as is practicable.

The amount of certolizumab transferred from plasma to breast milk is expected to be minimal, therefore the associated risk is low.

Funding

Trusts are required to obtain funding for the use of bDMARDs and tsDMARDs in the management of Psoriasis via Blueteq prior to starting therapy and for continuation of therapy as described on the Blueteq forms.

With a view to support data-driven care, commissioners will be extracting outcome data from Blueteq. Blueteq must therefore be used for the management of **all funding requests**. This includes recording treatment switches and cessation because of clinical review and/or remission and drug switching for patients who are confirmed or planning for pregnancy.

Where Blueteq is not currently in use by the Trust, an alternative mechanism for requesting funding and monitoring (e.g clinical audit) will be agreed with commissioners.

Patients transferred from out of area or from overseas

For patients who have already commenced on their treatment for Psoriasis:

- If the current treatment is covered by a NICE TA, then the patient can continue their treatment as per the TA.
- If the treatment is not covered by a NICE TA, or this pathway, then an application to IFR must be submitted to continue the funding for therapy.

It is the responsibility of the specialist Dermatologist to ensure the patient's GP is informed that the patient is receiving treatment with a biologic. It will then be the responsibility of the GP to update a person's medical record with this biologic.

Dose escalation

For patients where there has been an inadequate response to treatment with adalimumab, dose escalation can be considered. Taking an anti-TNF level is recommended before starting dose escalation [4].

For patients where there has been an inadequate response to treatment with Secukinumab or Ustekinumab can also be considered.

The following table outlines the approved dose escalation for use across NEL by the North East London Formulary and Pathways group:

Table 3: Dose escalation

High Cost Drug	Dose Escalation	Licensed Use	Notes
Adalimumab 40mg fortnightly	Adalimumab 40mg weekly for 12 weeks and review Or Adalimumab 80mg fortnightly for 12 weeks and review (needle phobic patients)	Yes	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.
Secukinumab 300mg monthly	Secukinumab 300mg fortnightly (for patients > 90kg only) for 12 weeks and review	Yes	Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.
Ustekinumab 45mg 12 weeks or 90mg 12 weeks (if >100kg)	Ustekinumab up to 90mg every 12 weeks or 8 weeks (< 100kg) Or Up to 90mg 8 weeks (>100kg) for 24 weeks and review	No	

References

[1] Regional Medicines Optimisation Committee (RMOC) Advisory Statement: Sequential Use of Biologic Medicines. Available from: https://nras.org.uk/wp-content/uploads/sites/2/2021/04/Sequential-use-of-biologic-medicines-RMOC-v-2.0-1.pdf

[2] Summary of Product Characteristics, Cimzia 200mg solution for injection in pre-filled syringe. Last updated 28 July 2022. Available from: https://www.medicines.org.uk/emc/product/4450/smpc#PREGNANCY
[3] Owczarek W, Walecka I, Lesiak A et al. The use of biological drugs in psoriasis patients prior to pregnancy, during pregnancy and lactation: a review of current clinical guidelines. Postepy Dermatol Alergol; volume 36 (6): 2020 Dec.
[4] Smith, C., Yiu, Z., Bale, T., et al. 2020. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update. *British Journal of Dermatology*, 183(4), pp.628-637.

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Psoriasis unresponsive/contraindicated/intolerant to standard therapy (methotrexate, ciclosporin, PUVA)

Factors to consider when choosing appropriate drug:

- Different efficacy and safety profiles of each drug
- Co-morbidities and potential impact of each drug option (benefit or harm), including drug specific contra-indications
- The persons view`s and stated preference on administration route or frequency – discuss with decision aid
- Other relevant factors e.g., conception plans, adherence (increased or decreased frequency should be discussed), travel

After consideration of all factors choose the most clinically suitable, best value drug

Clinical considerations

- Consider infection risk
- TB – lower risk associated with Etanercept, safe to use IL17 inhibitors and apremilast
- Demyelinating disease – do not use antiTNF
- Heart failure – avoid antiTNF in NYHA stage III or IV HF
- High level of clearance required – Higher PASI 90 achieved with Brodalumab, Guselkumab, Ixekizumab and Risankizumab
- Conception – Certolizumab is safe to use in all stages of pregnancy and breastfeeding
- Adherence – Risankizumab, Ustekinumab and Tildrakizumab are dosed at 12 weekly intervals, Bimekizumab and Guselkumab 8 weekly interval, Brodalumab is 2 weekly interval.
- Adherence – Oral vs Injection consideration. Apremilast, Deucravacitinib and Dimethylfumarate are given orally

Severe psoriasis
PASI ≥10 & DLQI ≥10

First line

Approximately 70% of patients

This will include those with signs or risk factors for psoriatic arthritis

Adalimumab

* Consider dose escalation if inadequate response, this may be due to insufficient drug dosing (recommend taking anti-TNF levels)

Approximately 30% of patients

Risk of infection, TB, risk of demyelination or heart failure, high level of clearance required, adherence issues, considering conception/breastfeeding

Apremilast/ Bimekizumab/ Brodalumab/ Certolizumab/ Dimethylfumarate/ Deucravacitinib/ Etanercept/ Guselkumab/ Infliximab/ Ixekizumab/ Risankizumab/ Secukinumab/ Tildrakizumab/

† Consider dose escalation if inadequate response with Secukinumab or Ustekinumab

Very severe psoriasis (unstable disease and rapid response required)

Very occasional use

PASI ≥ 10
DLQI > 10

Brodalumab
Guselkumab
Ixekizumab
Risankizumab

PASI ≥ 20
DLQI >18

Infliximab

Second line
if initial biologic discontinued

Adalimumab*/ Apremilast/ Bimekizumab/ Brodalumab/ Certolizumab/ Deucravacitinib/ Fumarates/ Etanercept/ Guselkumab/ Infliximab/ Ixekizumab/ Risankizumab/ Secukinumab†/ Tildrakizumab/ Ustekinumab†

Third line, Fourth line, Fifth line

Adalimumab*/ Apremilast/ Bimekizumab/ Brodalumab/ Certolizumab/ Deucravacitinib/ Fumarates/ Etanercept/ Guselkumab/ Infliximab/ Ixekizumab/ Risankizumab/ Secukinumab†/ Tildrakizumab/ Ustekinumab†

IFR required

* Consider dose escalation with adalimumab if inadequate response

† Consider dose escalation with Secukinumab or Ustekinumab if inadequate response

Appendix 1. Drug factors to consider (including modes of action)

The table below provides an approximate drug cost for each biologic based upon first year of therapy, with the loading dose schedule taken into consideration. The cost will vary depending upon commercial arrangements and access to short-term free of charge supplies, which has not been taken into consideration for this guidance.

Mode of Action	Drug Name	Indicated for	TA (other indications)	Reviewed within	Drug cost
Anti-TNFα	Adalimumab biosimilar (subcutaneous injection)	(PASI) ≥10 and (DLQI) >10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and PUVA, OR systemic treatments are contraindicated or not tolerated	TA187 - Crohn's TA199 - Psoriatic arthritis TA195 - Rheumatoid arthritis TA329 - Ulcerative colitis TA373 - JIA TA375 - Rheumatoid arthritis TA383 – Ankylosing spondylitis and non-radiographic axial spondylitis TA392 - Hidradenitis suppurativa TA715 - Rheumatoid arthritis TA460 – Non-infectious uveitis	16 weeks	£
	Certolizumab (subcutaneous injection)	(PASI) ≥10 and (DLQI) >10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and phototherapy, OR systemic treatments are contraindicated or not tolerated	TA375 - Rheumatoid arthritis TA383 – Ankylosing spondylitis and non-radiographic axial spondylitis TA415 – Rheumatoid arthritis TA445 – Psoriatic arthritis	16 weeks	£££
	Etanercept (biosimilar) (subcutaneous injection)	(PASI) ≥10 and (DLQI) >10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and PUVA, OR systemic treatments are contraindicated or not tolerated	TA195 - Rheumatoid arthritis TA199 – Psoriatic arthritis TA373 – JIA TA375 - Rheumatoid arthritis TA383 – Ankylosing spondylitis and non-radiographic axial spondylitis TA715 - Rheumatoid arthritis	12 weeks	£
	Infliximab biosimilar (intravenous infusion or subcutaneous injection)	(PASI) ≥20 and (DLQI) >18 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and PUVA, OR systemic treatments are contraindicated or not tolerated	TA163 – Ulcerative colitis (acute) TA187 – Crohn's TA195 - Rheumatoid arthritis TA199 – Psoriatic arthritis TA 329 - Ulcerative colitis TA375 – Rheumatoid arthritis TA383 – Ankylosing spondylitis and non-radiographic axial spondylitis TA715 - Rheumatoid arthritis	10 weeks	£
Small-molecule inhibitor of	Apremilast (oral)	(PASI) ≥10 and (DLQI) >10 AND	TA443 – Psoriatic arthritis	16 weeks	£

Mode of Action	Drug Name	Indicated for	TA (other indications)	Reviewed within	Drug cost
phosphodiesterase 4 (PDE4)		Inadequate response to systemic treatments, including ciclosporin, methotrexate and PUVA, OR systemic treatments are contraindicated or not tolerated			
Small molecule	Dimethyl fumarate (oral)	(PASI) ≥10 and (DLQI) >10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and PUVA, OR systemic treatments are contraindicated or not tolerated		16 weeks	£
IL17 inhibitor	Bimekizumab (subcutaneous injection)	(PASI) ≥10 and (DLQI) >10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and phototherapy, OR systemic treatments are contraindicated or not tolerated		16 weeks	££
	Brodalumab (subcutaneous injection)	(PASI) ≥10 and (DLQI) >10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and PUVA, OR systemic treatments are contraindicated or not tolerated		12 weeks	£££
	Ixekizumab (subcutaneous injection)	(PASI) > and (DLQI) > 10 AND Inadequate response to systemic treatments i.e., ciclosporin, methotrexate and PUVA, OR systemic treatments are contraindicated or not tolerated	TA537 – Psoriatic arthritis TA718 – Axial spondyloarthritis	12 weeks	££
	Secukinumab (subcutaneous injection)	(PASI) > and (DLQI) > 10 AND Inadequate response to systemic treatments i.e., ciclosporin, methotrexate and PUVA, OR systemic treatments are contraindicated or not tolerated	TA407 – Ankylosing spondyloarthritis TA445 – Psoriatic arthritis TA719 – Non-radiographic axial spondyloarthritis	12 weeks	£££
IL-12 and IL-23 inhibitor	Ustekinumab (subcutaneous injection)	(PASI) > and (DLQI) > 10 AND	TA340 – Psoriatic arthritis TA456 – Crohn's disease TA633 – Ulcerative colitis	16 weeks	£££

Mode of Action	Drug Name	Indicated for	TA (other indications)	Reviewed within	Drug cost
		Inadequate response to systemic treatments, including ciclosporin, methotrexate and phototherapy, OR systemic treatments are contraindicated or not tolerated			
IL-23 inhibitor	Guselkumab (subcutaneous injection)	(PASI) > and (DLQI) > 10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and phototherapy, OR systemic treatments are contraindicated or not tolerated	TA711- Psoriatic arthritis	16 weeks	**££**
	Risankizumab (subcutaneous injection)	(PASI) ≥ and (DLQI) > 10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and phototherapy, OR systemic treatments are contraindicated or not tolerated	TA805 - Psoriatic arthritis TA888 – Crohn's disease	16 weeks	**££**
	Tildrakizumab (subcutaneous injection)	(PASI) ≥ and (DLQI) > 10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and phototherapy, OR systemic treatments are contraindicated or not tolerated		12 to 28 weeks	**££**
TYK2 inhibitor	Deucravacitinib (oral)	(PASI) ≥ and (DLQI) > 10 AND Inadequate response to systemic treatments, including ciclosporin, methotrexate and phototherapy, OR systemic treatments are contraindicated or not tolerated		16 to 24 weeks	**££**

**Prices are correct as of August 2023 and may be subject to change*