

British Association of Dermatologists
Guidelines for use of biological interventions in psoriasis 2005
Summary of recommendations and quick reference

Smith CH, Anstey AV, Barker JN, Burden AD, Chalmers RJ, Chandler D, Finlay AY, Griffiths CE,
Jackson K, McHugh NJ, McKenna KE, Reynolds NJ, Ormerod AD; Br J Dermatol. 2005
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Full text access on <http://www.bad.org.uk/healthcare/guidelines/>

Eligibility criteria

Patients must have:

- (a) **Severe disease** is defined as a PASI score of 10 or more (or a BSA of 10% or greater where PASI is not applicable) *and* a DLQI > 10. Disease should have been severe for 6 months, resistant to treatment and the patient should be a candidate for systemic therapy. In exceptional circumstances (for example, disabling acral disease), patients with severe disease may fall outside this definition but may be considered for treatment. (*Strength of recommendation D, level of evidence 3*).

AND

- (b) **Fulfil at least one of the following clinical categories** (*Strength of recommendation B, level of evidence 1++ and formal consensus*):

- (i) have developed or are at higher than average risk of developing clinically important drug-related toxicity and where alternative **standard therapy**^a cannot be used
- (ii) are or have become intolerant to or cannot receive standard systemic therapy
- (iii) are or have become **unresponsive to standard therapy**^b
- (iv) have disease that is only controlled by repeated inpatient management
- (v) have significant, coexistent, unrelated co-morbidity which precludes use of systemic agents such as ciclosporin or methotrexate
- (vi) have severe, unstable, life-threatening disease (erythrodermic or pustular psoriasis)
- (vii) have psoriatic arthritis fulfilling the British Society for Rheumatology (BSR) eligibility criteria for treatment with anti-TNF agents, in association with skin disease (<http://rheumatology.oupjournals.org/cgi/content/full/44/3/390/>)

^a**standard systemic therapy** includes acitretin, ciclosporin, methotrexate, narrowband ultraviolet (UV) B and psoralen + UVA photochemotherapy (PUVA)

^b**unresponsive to standard therapy** is defined as an unsatisfactory clinical response (a less than 50% improvement in baseline PASI score or percentage BSA where the PASI is not applicable, and a less than 5-point improvement in DLQI) to at least 3 months of treatment in the therapeutic dose range to the following treatments: ciclosporin 2.5–5 mg kg⁻¹ daily; methotrexate single weekly dose (oral, subcutaneous, intramuscular) 15 mg, max 25–30 mg; acitretin 25–50 mg daily; narrowband UVB or psoralen photochemotherapy (nonresponse, rapid relapse or exceeding recommended maximum doses) 150–200 treatments for PUVA, 350 treatments for narrowband UVB.

Which Biological?

- Choice of agent efalizumab, etanercept or infliximab, will depend on the clinical pattern of psoriasis, pre-existing comorbidity, patient preference, prescriber preference and local facilities.
- Etanercept should be considered first choice for patients with significant, uncontrolled psoriatic arthritis (refer to BSR guidelines if joint disease identifies patient need <http://rheumatology.oupjournals.org/cgi/content/full/44/3/390/>) (*Strength of recommendation D, level of evidence 4*).
- For patients with stable psoriasis where a decision has been made to treat with an anti-TNF agent, etanercept should be used unless there are clear reasons not to do so. (*Strength of recommendation D, level of evidence 4*).
- Infliximab is useful in clinical circumstances requiring rapid disease control, e.g. in unstable erythrodermic or pustular psoriasis, due to its very rapid onset of action and high response rate. (*Strength of recommendation D, level of evidence 4*).

- For patients with a high risk of latent tuberculosis (and therefore requiring tuberculosis prophylaxis) or with evidence of demyelinating disease, efalizumab should be considered first choice. (*Strength of recommendation D, level of evidence 4*).

Etanercept

Etanercept is effective in the treatment of chronic plaque psoriasis with 38% and 54% of patients clear or nearly clear of disease after 12 weeks of treatment (25mg twice weekly, 50mg twice weekly, respectively). (*Strength of recommendation A level of evidence 1++*)

The current licence recommends intermittent courses no longer than 24 weeks with the time to relapse being variable (around 12 weeks) and with similar response rates achieved with repeat dosing.

Treatment should normally be initiated at 25mg subcutaneously, twice weekly. However, response is dose dependent and the chances of responding to treatment are greater with 50mg twice weekly. The choice of the higher dose should be made based on an individual patient basis. (*Strength of recommendation B extrapolated from level of evidence 1++*).

Treatment may be continued according to clinical need, although long term efficacy is only established in psoriasis for up to 2 years. (*Strength of recommendation D level of evidence 3*)

Efalizumab

Efalizumab is effective in the treatment of moderate to severe chronic plaque psoriasis, with approximately one third of patients treated becoming clear or almost clear after 12 weeks. (*Strength of recommendation A, level of evidence 1++*).

Duration of remission is variable on discontinuing therapy and may be associated with disease rebound. (*Strength of recommendation D, level of evidence 4*).

Therapy may be continued according to clinical need although data on long-term efficacy are limited to 27 months. (*Strength of recommendation D, level of evidence 4*).

Infliximab

Infliximab is effective in the treatment of chronic plaque psoriasis, with 90% of patients becoming clear or minimally affected at 10 weeks following 5 mg kg¹ at weeks 0, 2 and 6. (*Strength of recommendation A, level of evidence 1++*).

Infliximab therapy may be initiated at a dose of 5 mg kg¹ at weeks 0, 2 and 6 and subsequent maintenance infusions (either 5 mg kg¹ or 3 mg kg¹) given at 8-week intervals depending on clinical need and circumstances. (*Strength of recommendation A, level of evidence 1++*).

In those patients who respond to therapy, regular maintenance infusions may avoid the risk of loss of efficacy seen in some patients receiving intermittent as-required repeat infusions on disease relapse. (*Strength of recommendation D, level of evidence 3*).

Infliximab may also be of value in recalcitrant or unstable disease and in generalized pustular psoriasis. (*Strength of recommendation D, level of evidence 3*).

Concomitant systemic therapies may be indicated for some patients with very severe or unstable psoriasis, although doses of these should be minimized. (*Strength of recommendation D, level of evidence 3*).

Withdrawal of therapy

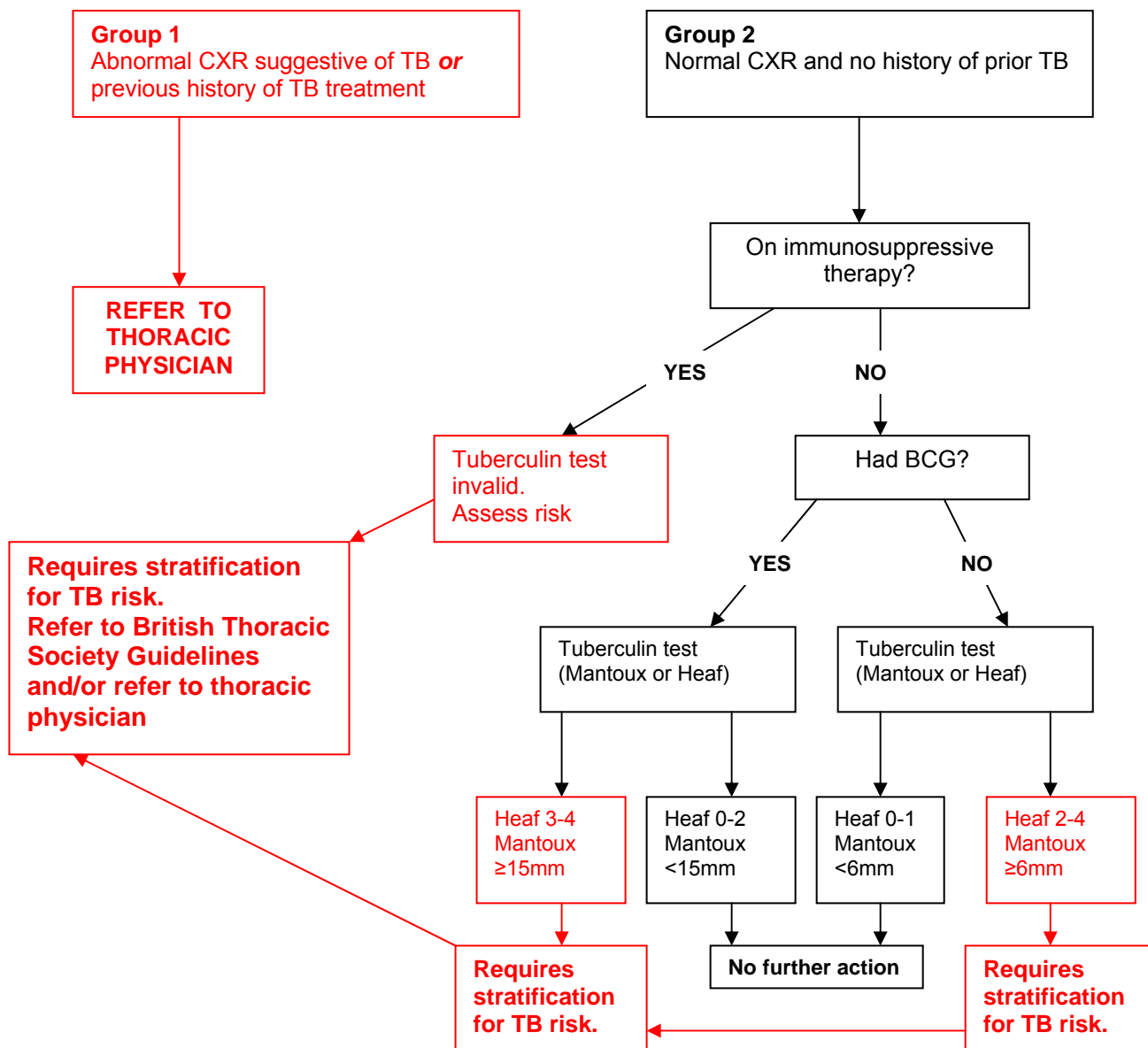
Therapy should be withdrawn after 3 months if there has not been at least a 50% improvement in baseline PASI score (or percentage BSA where the PASI is not applicable) and a 5-point or greater improvement in DLQI. Withdrawal of therapy is also indicated due to the development of a serious adverse event. eg malignancy (excluding nonmelanoma skin cancer); severe drug-related toxicity; pregnancy (temporary withdrawal); severe intercurrent infection (temporary withdrawal); major surgical procedures (temporary withdrawal in accordance with updated BSR guidelines).

Exclusion criteria for Biologicals

Pregnant or breast feeding
Active infections. High risk include:
chronic leg ulcers
persistent or recurrent chest infections
indwelling urinary catheter
Latent tuberculosis ^a (see Fig.)
Malignancy or premalignancy states <i>excluding</i> :
adequately treated non-melanoma skin cancer
malignancies diagnosed and treated more than 10 years previously (where the probability of cure is very high)
Demyelinating disease ^a
Congestive cardiac failure ^a (New York Heart Association grade III or IV)
Relative contraindications:
Psoralen + ultraviolet A therapy > 200 treatments, especially when followed by ciclosporin therapy
Human immunodeficiency virus-positive or AIDS
Hepatitis B or C virus-positive
^a These apply to anti-TNF agents only.

Recommended pre-treatment & monitoring investigations		Pretreatment ^a	Monitoring ^a
Disease severity assessment			
Skin	PASI	Yes	At 3 months, then every 6 months
	DLQI		
Joints (where applicable)	Follow recommended BSR guidelines for psoriatic arthritis	Yes	At 3 months, then every 6 months
General health (symptom)	Infection	Yes	At 3–6-monthly intervals
Enquiry and clinical examination)	Demyelination ^b Heart failure ^b		
	Malignancy (including skin)		
Latent Tb ^b	See Fig.		
Blood tests	Full blood count	Yes	Efalizumab: monthly for the first 3 months, then every 3 months Tumour necrosis factor blockers: at 3 months, then every 6 months
	Creatinine, urea and electrolytes, liver function tests	Yes	At 3 months, then every 6 months
	Hepatitis B and C	Yes	–
	Human immunodeficiency virus	Consider testing in those at risk	–
Urine	Autoantibodies ^b (antinuclear antibodies, anti-double-stranded DNA antibodies)	Yes	–
	Urine analysis	Yes	At 3 months, then every 6 months
Radiology	Chest X-ray	Yes	–
^a Additional assessment and monitoring may be required in patients on concomitant therapy or in certain clinical circumstances. ^b Applies to tumour necrosis factor blockers only.			

Figure. Screening for Tuberculosis risk before starting TNF alpha antagonist for full guideline follow links from http://www.brit-thoracic.org.uk/guidelines_before_1997.html.



Adapted from guidelines issued by Joint Tuberculosis Committee of the British Thoracic Society⁴²

Notes

1. The three most important risk factors for TB infection are ethnicity, age (>55) and for those born outside the UK, the length of time since first entry to the UK.
2. Although the SPC for infliximab (but not that for etanercept) recommends skin testing prior to therapy, tuberculin skin testing may be unreliable (ie falsely negative) in those who are immunocompromised and/or systemically unwell. In this instance the risk of chemoprophalaxis (principally hepatitis) has to be balanced against the risk of developing TB during the therapy and should be assessed by a thoracic or infectious disease physician.
3. Clinical awareness of the possibility of TB should be maintained throughout anti-TNF therapy and for a period of 6 months after cessation.

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