British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017

IMPLEMENTATION TOOLKIT

Table S1: SUMMARY OF LICENSED INDICATIONS AND POSOLOGY FOR BIOLOGIC THERAPY

Table S2: DECISION AID

This table supports the decision-making process during the consultation for patients and clinicians before the initiation of biologic therapy. It is complementary to the existing patient information leaflets (PILs; www.bad.org.uk/leaflets). All biologic therapies for the treatment of psoriasis require bloods tests before and during treatment. If you have psoriatic arthritis, your doctor will take this into consideration.

Table S3: SUGGESTED SCHEDULE FOR SCREENING AND MONITORING

S4: GROUPS AT INCREASED RISK OF TUBERCULOSIS, HEPATITIS B, HEPATITIS C AND HIV

Table S1.	Adalimumab (Humira)[I]	Etanercept (Enbrel, Benepali)[I]	Infliximab (Remicade, Inflectra, Remsima)[II]	Ixekizumab (Taltz)[I]	Secukinumab (Cosentyx)[I]	Ustekinumab (Stelara)[I]
Licensed indications and posology						
Adults	Moderate to severe chronic plaque psoriasis in adult patients who are candidates for systemic therapy	Moderate to severe plaque psoriasis …who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapy, including ciclosporin, methotrexate or psoralen and ultraviolet-A light (PUVA)	Moderate to severe plaque psoriasis …who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapy including ciclosporin, methotrexate or PUVA	Moderate to severe plaque psoriasis… who has not responded to standard systemic therapies, including ciclosporin, methotrexate or PUVA, or the person cannot have the treatment or it is not tolerated	Moderate to severe plaque psoriasis in adults who are candidates for systemic therapy	Moderate to severe plaque psoriasis …who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate (MTX) or PUVA (psoralen and ultraviolet A)
Children and young people	Severe chronic plaque psoriasis in children and adolescents from 4 years of age who have had an inadequate response to or are inappropriate candidates for topical therapy and phototherapies	Severe chronic plaque psoriasis in children and adolescents from the age of 6 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies (currently, the only licensed form of etanercept is Enbrel in children and young people)	Not licensed	Not licensed	Not licensed	Moderate to severe plaque psoriasis in adolescent patients from the age of 12 years and older, who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.
Dosing	Initial dose of 80 mg administered subcutaneously, followed by 40 mg subcutaneously	50 mg administered once weekly. Alternatively, 50 mg given twice weekly may be used for up to 12	5 mg/kg given as an intravenous infusion followed by additional 5 mg/kg infusion doses at 2	Initial dose of 160 mg administered subcutaneously, followed	The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at	45 mg (90 mg if >100 kg), administered subcutaneously, followed by a 45 mg (90 mg) dose 4

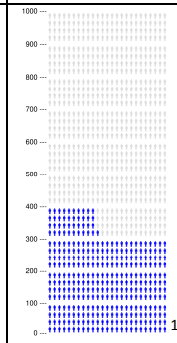
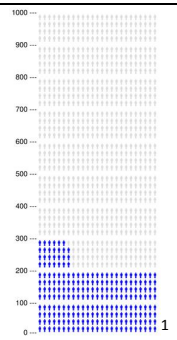
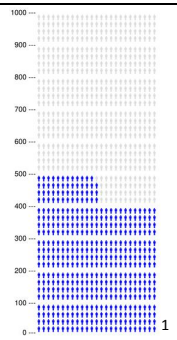
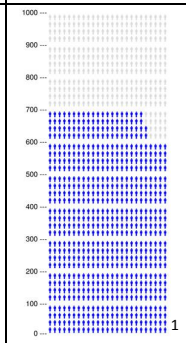
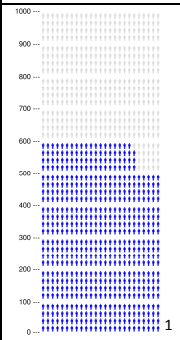
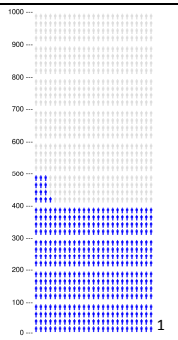
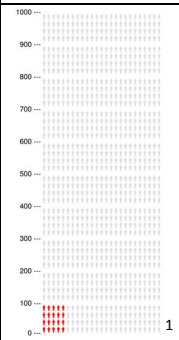
[I] NICE eligibility criteria: severe disease (PASI 10 or more and DLQI >10) and failed to respond to standard systemic therapies such as ciclosporin, methotrexate or PUVA (psoralen and long-wave ultraviolet radiation), or the person is intolerant to or has a contraindication to these treatments.

[II] NICE eligibility criteria: very severe disease (PASI 20 or more and DLQI 18 or more) and failed to respond to standard systemic therapies such as ciclosporin, methotrexate or PUVA (psoralen and long-wave ultraviolet radiation), or the person is intolerant to or has a contraindication to these treatments.

	given every other week starting one week after the initial dose. Beyond 16 weeks, patients with inadequate response may benefit from an increase in dosing frequency to 40 mg every week.	weeks followed, if necessary, by a dose of 50 mg once weekly.	and 6 weeks after the first infusion, then every 8 weeks thereafter	by 80 mg every 2 weeks until week 12; 80 mg every 4 weeks after week 12	Weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at Week 4. Each 300 mg dose is given as two subcutaneous injections of 150 mg.	weeks later, and then every 12 weeks thereafter
Dosing (children and young people)	0.8 mg per kg body weight (up to a maximum of 40 mg per dose); dosing frequency as for adults.	0.8 mg/kg (up to a maximum of 50 mg per dose) once weekly for up to 24 weeks.	N/A	N/A	N/A	<60 kg: 0.75 mg/kg. Otherwise dosing as for adults.
Indications for stopping	Continued therapy beyond 16 weeks should be carefully reconsidered in a patient not responding within this time period	Treatment should be discontinued in patients who show no response after 12 weeks	If a patient shows no response after 14 weeks (i.e. after 4 doses), no additional treatment with infliximab should be given	Treatment should be discontinued If a patient shows inadequate response (PASI ≥75) at week 12	Not stated	Consideration should be given to discontinuing treatment in patients who have shown no response up to 28 weeks of treatment
Half life	Mean 14 days approx. (range 10 to 20 days)	Mean 3 days approx. (range 0.3 to 12.5 days)	Median 8 to 9.5 days	Mean 13 days	Mean 27 days (range 18 to 46 days)	Median 21 days (range15 to 23 days)
NICE timelines for evaluating response to therapy[III]	16 weeks	12 weeks	10 weeks	12 weeks	12 weeks	16 weeks

[III] To be discontinued if response criteria not met as defined by failure to achieve PASI 75 or PASI 50 and 5 point drop in DLQI

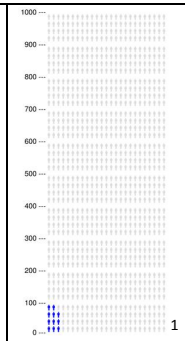
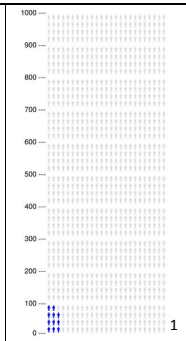
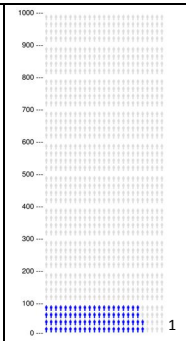
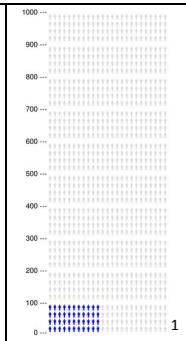
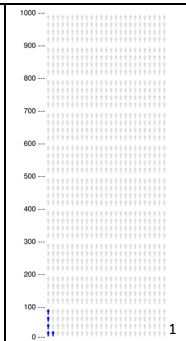
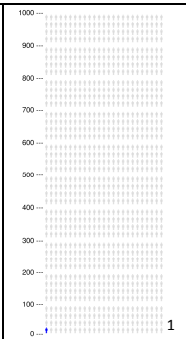
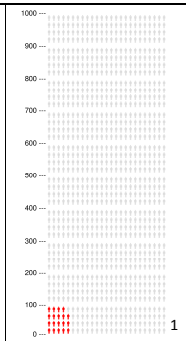
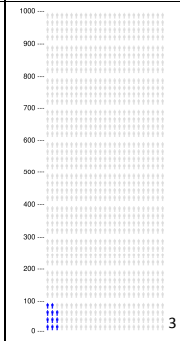
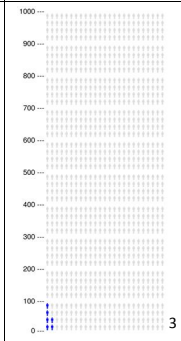
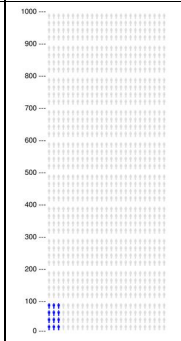
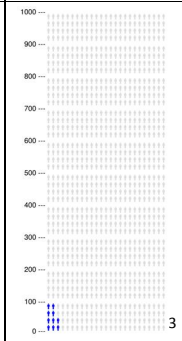
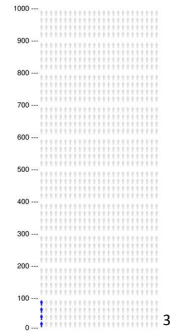
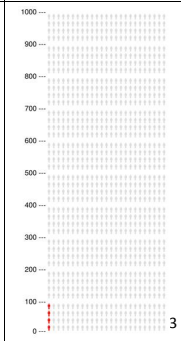
Table S2: DECISION AID

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 Every other week	1 injection under the skin Once or twice a week	1 injection in the vein Every 8 weeks	1 injection under the skin Every 2 weeks for the first 3 months, every 4 weeks thereafter	2 injections under the skin Every month	1 injection under the skin 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]	 1	 1	 1	 1	 1	 1	 1
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]	 3	 3	Cannot be estimated		 3	 3	 3
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

Table S3: SUGGESTED SCHEDULE FOR SCREENING AND MONITORING		**Baseline**[VIII]	**Monitoring**[VIIII]
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[IX]); 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[X]		
	Ascertain history for chickenpox		N/A
Alert card[XI]	Ensure people carry an alert card with them at all times in line with MHRA guidance	Yes	At each review appointment
Cardiovascular assessment[XII]	Include symptom enquiry about heart failure [NYHA III. Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation or dyspnea. 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[XII]	Past or current history or symptoms of demyelinating disease[XII]	Yes	Every 3-6 months
Gastrointestinal assessment[XIII]	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		

[VIII] Additional assessment and monitoring may be required in patients on concomitant therapy or in certain clinical circumstances
[IX] www.bad.org.uk/healthcare-professionals/forms-downloads
[X] See S4: Groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV
[XI] https://www.gov.uk/drug-safety-update/tumour-necrosis-factor-alpha-inhibitors
[XII] Evidence of demyelination/heart failure may preclude use of TNF antagonists
[XIII] Exercise caution using secukinumab in people with inflammatory bowel disease

	Gynaecological review of patients with history of cervical dysplasia		
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		

[XIV] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/559469/VZIG_ChickenPox_v4.pdf

S4. Groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV

Groups at increased risk of tuberculosis[4] include:

a) People classified as under-served, e.g. people who are homeless, people who misuse substances, prisoners, vulnerable migrants
b) people identified as contacts according to the case-finding recommendations
c) new entrants from high-incidence countries
d) people who are immunocompromised

Groups at increased risk of hepatitis B[5] include:

a) people born or brought up in a country with an intermediate or high prevalence (2% or greater) of chronic hepatitis B; this includes all countries in Africa, Asia, the Caribbean, Central and South America, Eastern and Southern Europe, the Middle East and the Pacific islands
b) babies born to mothers infected with hepatitis B
c) people who have ever injected drugs
d) men who have sex with men
e) anyone who has had unprotected sex, particularly, people who have had multiple sexual partners, people reporting unprotected sexual contact (https://pathways.nice.org.uk/pathways/hepatitis-b-and-c-testing#glossary-sexual-contact) in areas of intermediate and high prevalence, people presenting at sexual health and genitourinary medicine clinics, people diagnosed with a sexually transmitted disease, commercial sex workers
f) looked-after children and young people, including those living in care homes
g) prisoners, including young offenders
h) immigration detainees
i) close contacts (https://pathways.nice.org.uk/pathways/hepatitis-b-and-c-testing#glossary-close-contacts) of someone known to be chronically infected with hepatitis B

Groups at increased risk of hepatitis C[5] include:

a) people who have ever injected drugs
b) people who received a blood transfusion before 1991 or blood products before 1986, when screening of blood donors for hepatitis C infection, or heat treatment for inactivation of viruses were introduced
c) people born or brought up in a country with an intermediate or high prevalence (2% or greater) of chronic hepatitis C; for practical purposes this includes all countries in Africa, Asia, the Caribbean, Central and South America, Eastern and Southern Europe, the Middle East and the Pacific islands
d) babies born to mothers infected with hepatitis C
e) prisoners, including young offenders
f) looked-after children and young people, including those living in care homes
g) people living in hostels for the homeless or sleeping on the street
h) HIV-positive men who have sex with men
i) close contacts of someone known to be chronically infected with hepatitis C

Groups at increased risk of HIV[6,7] include:

a) men who have sex with men, with frequent partner change or practicing ‘chemsex’
b) intravenous drug users with chaotic lifestyle
c) commercial sex worker
d) people who frequently use intranasal cocaine
e) recent tattoo
f) recent blood transfusion abroad
g) other risks

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