Tillett, W., Allen, A., Tucker, L., Chandler, D., Ciurtin, C., Davis, C., Dick, A., Foulkes, A., Gullick, N., Helliwell, P., Jadon, D., Jones, G., Kyle, S., Madhok, V., McHugh, N., Parkinson, A., Raine, T., Siebert, S., Smith, C., & Coates, L. C. (2020). Treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs: British Society for Rheumatology guideline scope. *Rheumatology*, Article keaa526. Advance online publication. https://doi.org/10.1093/rheumatology/keaa526

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BRITISH SOCIETY FOR RHEUMATOLOGY

Guideline scope

Guideline for the treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs

The aim of this guideline is to provide an update on evidence-based recommendations for treatment of adult patients with PsA. The previous BSR guidelines for PsA were published in 2012 and since that time, there have been many new advanced therapies licensed for PsA. This update will provide practical guidance for clinicians on the optimal selection of advanced therapies taking into account different domains of PsA (arthritis, enthesitis, dactylitis, axial disease and psoriasis) and key associated comorbidities. It will also update guidance on treatment strategy including the use of a treat-to-target approach. The guideline will be developed using the methods and processes outlined in Creating Clinical Guidelines: Our Protocol.(1) This development process to produce guidance, advice and recommendations for practice has National Institute for Health and Care Excellence (NICE) accreditation.

1 Why the guideline is needed

The most recent BSR guidelines on psoriatic arthritis (PsA) were published in 2012.(2) Since that time, there have been significant advances in therapeutic options available for PsA. At the time of the last recommendations, they focused specifically on TNF inhibitors as they were the only biologic DMARDs (bDMARDs) available. Now there are drugs with different modes of action available including a new class of targeted synthetic DMARDs (tsDMARDs)

There are existing international treatment recommendations that may be applicable in the UK including those written by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in 2015 (due for update in 2020) and those written by the European League Against Rheumatism (EULAR) in 2020.(3, 4) However these are generic to many international health settings and do not provide specific guidance for the UK, taking account of the healthcare system and existing restrictions in prescribing of these drugs (technology appraisals from the National Institute of Health and Care Excellence). There are also patients with PsA who do not meet the standard criteria for the use of biologics under the NICE. This guideline aims to look at the evidence beyond current NICE technology appraisals to provide advice for the management of these patients.

Key facts and figures

Psoriasis is a skin condition that causes red, flaky, crusty patches of skin covered with silvery scale and affects some 2-3% of people in the UK. PsA is chronic, inflammatory, musculoskeletal disease associated with psoriasis.(5) An estimated prevalence of PsA in people with with psoriasis is 24%.(6) Musculoskeletal manifestations of PsA include peripheral arthritis, spondylitis, dactylitis (inflammation of the whole digit) and enthesitis (inflammation where a tendon, ligament or joint capsule inserts onto the bone). Skin manifestations of PsA include psoriasis (which has numerous phenotypes but the most common type associated with PsA is psoriasis vulgaris or plaque psoriasis) and nail disease. Whilst these are all considered key manifestations of the disease, different presentations are seen with a heterogeneous clinical picture. Interestingly, there is some differing evidence of efficacy for these drugs within the different domains of disease, so response in different

domains should be considered when choosing therapy for any individual. The majority of people have involvement in more than one domain when assessed, so this must be taken into account when choosing therapy.

Beyond the musculoskeletal and skin features, people with PsA experience fatigue, physical function limitations, sleep disturbance, as well as diminished work capacity and social participation.(7) In addition to the association with extra-articular manifestations such as uveitis and inflammatory bowel disease (IBD), PsA is also associated with several comorbidities including obesity and metabolic disease (diabetes, hypertension, hyperlipidaemia, fatty liver disease, cardiovascular outcomes), depression and anxiety.(8) All of these factors may play an important role in therapy selection.(3) In some cases, potentially modifiable risk factors such as obesity and smoking have an important impact on treatment response and prognosis so advice on these issues should be considered within a management plan.

Current practice

PsA is a chronic condition and once diagnosed the aim of treatment is to achieve remission and slow progression. The current treatment follows a 'step up' approach using different conventional disease-modifying anti-rheumatic drugs (DMARDs) followed by biologics if people do not respond. The selection of drug is based on disease phenotype in the person.(9) Most physicians apply the same 'step up' therapy to all people given lack of comparative evidence in PsA. Typically single DMARDs are used initially with methotrexate being the most common first line therapy. If this is unsuccessful, then alternative single DMARDs or combinations of these standard DMARDs are used prior to biologics as people fail to respond to the previous treatment step.(3, 4) Treatment in England is governed by the NICE criteria for the use of these therapies, given the higher cost of bDMARDs and tsDMARDs. In addition to these drugs, non-steroidal anti-inflammatory drugs and corticosteroids are also used for short term relief throughout treatment as required. Whilst not optimal for long term use, these drugs do act quickly offering short term relief while other DMARDs have time to take effect.

Up to 50% of people with PsA require biologic therapy.(10) There are currently multiple advanced therapies available for the treatment of PsA, many of which have been licensed in recent years. These include

- TNF inhibitors
- IL12/23 inhibitors
- IL-17 inhibitors
- JAK inhibitors
- Apremilast (phosphodiesterase 4 inhibitor)

Response rates to most of these drugs are similar with 60-70% of people achieving a minimal response. In clinical practice, biologic therapies require use for a minimum of 12 (e.g. TNF inhibitors) or 16 weeks (e.g. IL-17A inhibitors) before response can be evaluated and assessment of a treatment target is later.(11) Unfortunately, a proportion of people do not respond to the first line drug chosen, known as primary non-response. Other people respond well initially to a therapy but subsequently lose response, known as secondary non-response. For these reasons, as well as adverse events suffered by some people, switching of therapies is required to achieve and maintain an optimal response. Although small case series have reported combinations of biologics or combinations with tsDMARDs, this is not usually funded in the UK.

2 Who the guideline is for

This guideline is for:

- Rheumatologists and other clinicians involved in the prescription of biologics and targeted synthetic DMARDs for people with PsA
- Specialist nurses and Allied Health Professionals (AHPs) on the application, assessment and monitoring of PsA treatment
- People with PsA who are receiving or moving towards to biologic DMARD treatment

Equality considerations

- None known

3 What the guideline will cover

3.1 Who is the focus?

Groups that will be covered

- Adult with psoriatic arthritis affecting any domains

Groups that will not be covered

- Biological therapies for juvenile idiopathic arthritis
- Biological therapies for people with psoriatic disease confined to the skin
- Use of conventional DMARDs

3.2 Settings

Settings that will be covered

- Secondary care rheumatology settings (in collaboration with dermatology)

3.3 Activities, services or aspects of care

Key areas that will be covered

We will look at evidence in the areas below when developing the guideline, but it may not be possible to make recommendations in all the areas.

Treatment of people with:

1. Peripheral arthritis (mono, oligo and polyarthritis)
2. PsA with axial disease
3. PsA with enthesitis
4. PsA with dactylitis
5. PsA with uvetis
6. PsA with inflammatory bowel disease (IBD)

Treatment strategy:

7. Drug sequencing and switching
8. Concomitant DMARDs
9. Biosimilars
10. Tapering

11. Treat to target

    Risk factors:
12. Obesity
13. Smoking

Areas that will not be covered

For data on safety in pregnancy and breastfeeding, refer to existing BSR guidelines

Related guidance

- BSR and BHPR guideline for the treatment of axial spondyloarthritis (including ankylosing spondylitis) with biologics(12)
- The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis-Executive summary(13)
- BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids(14)
- American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis(15)
- European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update(4)
- Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 Treatment Recommendations for Psoriatic Arthritis(3)

3.4 Key issues and draft questions

While writing this scope, we have identified the following key issues and draft questions related to them. The key issues and draft questions will be used to develop more detailed review questions, which guide the systematic review of the literature.

Treatment of people with:

Peripheral arthritis (mono, oligo and polyarthritis)

1. In people with active peripheral psoriatic arthritis, what is the clinical effectiveness of TNF inhibitors, IL12/23 inhibitors, IL17 inhibitors, abatacept, apremilast or JAK inhibitors, in comparison to each other or placebo?
2. In adults with active psoriatic arthritis using a TNF inhibitor, what is the clinical effectiveness of switching to an alternate TNF inhibitor or to an alternate targeted biological agent (e.g. IL17i, IL12/23i, JAKi, abatacept)?

   PsA with axial disease
3. In adults with active psoriatic arthritis-related axial disease that is not responding to NSAIDs, what is the clinical effectiveness of TNF inhibitors, IL12/23 inhibitor, IL17 inhibitors, JAK inhibitors, apremilast or abatacept, in comparison to each other or placebo?

   PsA with enthesitis
4. In adults with active psoriatic arthritis-related enthesitis what is the clinical effectiveness of TNF inhibitors, IL12/23 inhibitors, apremilast, IL17 inhibitors or JAK inhibitors, in comparison to each other or placebo?

   PsA with dactylitis
5. In adults with active psoriatic arthritis-related dactylitis, what is the clinical effectiveness of TNF inhibitors, IL12/23 inhibitors, apremilast, IL17 inhibitors or JAK inhibitors, in comparison to each other or placebo?

PsA with uvetis

6. In adults with active psoriatic arthritis and uveitis, what is the clinical effectiveness of TNF inhibitors, IL12/23 inhibitors, IL17 inhibitors, apremilast or JAK inhibitors, in comparison to each other or placebo?

PsA with inflammatory bowel disease

7. In adults with active psoriatic arthritis and IBD, what is the clinical effectiveness of TNF inhibitors, IL12/23 inhibitors, IL17 inhibitors, apremilast or JAK inhibitors, in comparison to each other or placebo?

Treatment strategy:

Treat to target

8. In adults with active psoriatic arthritis, what is the clinical effectiveness of a treat to target strategy compared to a not treat to target strategy compared with usual care?

Tapering

9. In adults with psoriatic arthritis, who have achieved clinical remission, what is the impact of bDMARD or tsDMARD tapering/dose reduction?

Biosimilars

10. In adults with psoriatic arthritis, who have achieved clinical remission what is the clinical effect of switching to a biosimilar drug compared to remaining on the originator drug

Concomitant DMARDS

11. In adults with active psoriatic arthritis commencing b/ts DMARDS, what is the clinical effect of concomitant conventional synthetic DMARD use compared to monotherapy.

DMARD sequencing

12. In adults with PsA who have had an inadequate response to, or failed treatment with, one or more biologic or targeted synthetic DMARDs, which biologic and targeted synthetic DMARDs are most clinically and cost effective as subsequent treatment?

Risk factors:

Obesity

13. In adults with active psoriatic arthritis who are overweight, what is the clinical effectiveness of TNF inhibitors, IL12/23 inhibitors, IL17 inhibitors, apremilast or JAK inhibitors, in comparison to each other or placebo?
14. In adults with active psoriatic arthritis who are overweight and using biologics, what is the clinical effectiveness of weight loss compared with no weight loss?

Smoking

15. In adults with active psoriatic arthritis who are smokers, what is the clinical effectiveness of TNF inhibitors, IL12/23 inhibitors, IL17 inhibitors, apremilast or JAK inhibitors, in comparison to each other or placebo?
16. In adults with active psoriatic arthritis who are smokers and using biologics, what is the clinical effectiveness of giving up smoking versus continuing to smoke?

The guideline is expected to be published in [EXPECTED PUBLICATION DATE]

4 Guideline working group constituency

Laura Coates (co-chair) – rheumatologist

William Tillett (co-chair) – rheumatologist

Laura Tucker – rheumatology fellow

David Chandler – patient representative and head of PAPAA

Charlotte Davis – specialist nurse

Amy Foulkes – dermatologist

Nicola Gullick – rheumatologist

Tina Hawkins – pharmacist

Philip Helliwell – rheumatologist

Deepak Jadon – rheumatologist

Gareth Jones – rheumatologist and epidemiologist

Stuart Kyle - rheumatologist

Vishnu Madhok – GP

Neil McHugh – rheumatologist

Andrew ~~Parkes~~ Parkinson – patient representative

Stefan Siebert – rheumatologist

Catherine Smith – dermatologist

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