NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA199; Etanercept, Infliximab, and Adalimumab for the treatment of psoriatic arthritis, TA220; Golimumab for the treatment of psoriatic arthritis, and TA340; Ustekinumab for treating active psoriatic arthritis

TA199

This guidance was issued in August 2010.

The review date for this guidance is June 2013.

TA220

This guidance was issued in April 2011.

The review date for this guidance is June 2013.

TA340

This guidance was issued in June 2015.

The review date for this guidance is 3 years after publication.

1. Recommendation

TA199, TA220 and TA340 should be transferred to the ‘static guidance list’.

That we consult on this proposal.

2. Original remits

TA199

To review the Institute's earlier guidance on the clinical and cost-effectiveness of etanercept, infliximab and adalimumab*, in their licensed indications for the treatment of psoriatic arthritis.

* This appraisal will be a review of the following appraisals: NICE Technology Appraisal guidance No. 104 - Etanercept and infliximab for the treatment of psoriatic arthritis, July 2006 and NICE Technology Appraisal guidance No. 125 – Adalimumab for the treatment of psoriatic arthritis, Aug 2007.

TA220

To appraise the clinical and cost-effectiveness of golimumab, within its licensed indication, for the treatment of psoriatic arthritis.

TA340

To appraise the clinical and cost effectiveness of ustekinumab within its licensed indication for the treatment of active and progressive psoriatic arthritis.

3. Current guidance

TA199

1.1 Etanercept, infliximab and adalimumab are recommended for the treatment of adults with active and progressive psoriatic arthritis when the following criteria are met.

- The person has peripheral arthritis with three or more tender joints and three or more swollen joints, **and**

- The psoriatic arthritis has not responded to adequate trials of at least two standard disease-modifying antirheumatic drugs (DMARDs), administered either individually or in combination.

1.2 Treatment as described in 1.1 should normally be started with the least expensive drug (taking into account drug administration costs, required dose and product price per dose). This may need to be varied for individual patients because of differences in the method of administration and treatment schedules.

1.3 Etanercept, adalimumab or infliximab treatment should be discontinued in people whose psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 12 weeks. An adequate response is defined as an improvement in at least two of the four PsARC criteria, (one of which has to be joint tenderness or swelling score) with no worsening in any of the four criteria. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response at 12 weeks but whose PsARC response does not justify continuation of treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see 'Etanercept and efalizumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 103], 'Infliximab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 134] and 'Adalimumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 146] for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis).

1.4 When using the PsARC healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate.

TA220

1.1 Golimumab is recommended as an option for the treatment of active and progressive psoriatic arthritis in adults only if:

- it is used as described for other tumour necrosis factor (TNF) inhibitor treatments in Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (NICE technology appraisal guidance 199), **and**

- the manufacturer provides the 100 mg dose of golimumab at the same cost as the 50 mg dose.

1.2 When using the Psoriatic Arthritis Response Criteria (PsARC; as set out in NICE technology appraisal guidance 199), healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate

TA340

1.1 Ustekinumab is recommended as an option, alone or in combination with methotrexate, for treating active psoriatic arthritis in adults only when:

- treatment with tumour necrosis factor (TNF) alpha inhibitors is contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis and golimumab for the treatment of psoriatic arthritis) or

- the person has had treatment with 1 or more TNF–alpha inhibitors.

Ustekinumab is recommended only if the company provides the 90 mg dose of ustekinumab for people who weigh more than 100 kg at the same cost as the 45 mg dose, as agreed in the patient access scheme.

1.2 Ustekinumab treatment should be stopped if the person's psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 24 weeks. An adequate response is defined as an improvement in at least 2 of the 4 criteria (1 of which must be joint tenderness or swelling score), with no worsening in any of the 4 criteria. As recommended in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis, people whose disease has a Psoriasis Area and Severity Index (PASI) 75 response but whose PsARC response does not justify continuing treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see NICE technology appraisal guidance on ustekinumab for the treatment of adults with moderate to severe psoriasis).

1.3 When using the Psoriatic Arthritis Response Criteria (PsARC) healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate.

1.4 People whose treatment with ustekinumab is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue ustekinumab until they and their NHS clinician consider it appropriate to stop.

4. Rationale[1]

There remains an absence of evidence from head-to-head comparisons between biologic treatments in people with psoriatic arthritis. Regarding the research recommendations of TA199, TA220 and TA340 for data from registries of long-term outcomes and adverse events there was no new evidence that would change the recommendations. The availability of biosimilars of infliximab and etanercept will not change the recommendations.

5. Implications for other guidance producing programmes

There is a clinical guideline in development for spondyloarthritis, which is due to be published in March 2017. In the scope of the guideline, it was indicated that TA199 and TA220 will be incorporated into the guideline, whilst TA340 will be cross referred to. The Guideline Development Group may also wish to incorporate TA340 into the guideline, and would be able to if the guidance is moved to the static list.

6. New evidence

The search strategies from the original assessment reports were re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from April 2013 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

Changes to marketing authorisations, costs and introduction of biosimilars

Technology appraisal TA340 ustekinumab was published in June 2015, and the costs and marketing authorisation have not changed since.

The marketing authorisations for etanercept, infliximab, adalimumab and golimumab for the treatment of psoriatic arthritis have not changed since the publication of NICE TA199 and TA220 in August 2010 and April 2011, respectively. The companies have also confirmed that there are no proposed extensions to the marketing authorisation for these interventions in the treatment of psoriatic arthritis.

The list price of etanercept and infliximab are the same as published in NICE TA199. The list prices of adalimumab and golimumab have reduced marginally since the publication of NICE TA199 and TA220, respectively (see appendix 2). The company of golimumab also confirmed that the patient access scheme will continue to be available without any changes (that is, the 100 mg dose of golimumab is provided at the same cost as the 50 mg dose). Changes to the cost of treatment will not impact NICE TA199 and TA220 because the recommendations specify that 'treatment

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

should normally be started with the least expensive drug (taking into account drug administration costs, required dose and product price per dose)'.

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) recommended granting the marketing authorisations of the first 2 monoclonal-antibody biosimilars (based on infliximab), Inflectra and Remsima. In addition, there are also biosimilars for etanercept ([redacted]) and for adalimumabin development ([redacted]).

Previous NICE guidance and the upcoming MTA

Current practice for the management of psoriatic arthritis follows current NICE guidance: after initial treatment with non‑steroidal anti‑inflammatory drugs (NSAIDs) and disease‑modifying antirheumatic drugs (DMARDs), most people have treatment with a TNF-alpha inhibitor. TA199 recommends etanercept, infliximab or adalimumab when a person has peripheral arthritis with 3 or more tender joints and 3 or more swollen joints, and the psoriatic arthritis has not responded to at least 2 other DMARDs, given on their own or together. TA220 also recommends golimumab with the same criteria as TA199. Treatment should normally be started with the least expensive drug (taking into account administration costs, required dose and price per dose). The sequential use of TNF‑alpha inhibitors is established practice in the NHS. The recently published guidance for TA340 recommends ustekinumab when treatment with TNF-α inhibitors is contraindicated but would otherwise be considered, or when the person has had treatment with 1 or more TNF-α inhibitors.

Since the publications of TA199 and TA220, the only technology appraisal guidance for psoriatic arthritis to be issued is TA340. ApremilastTA372 for psoriatic arthritis the published final draft guidance does not recommend it. TA372 is subject to an ongoing rapid review [ID 1017].

There are also 2 NICE STAs in development for psoriatic arthritis to appraise certolizumab pegol and secukinumab.

Certolizumab pegol has a marketing authorisation which was granted in November 2013 for adults with psoriatic arthritis when response to previous DMARD therapy has been inadequate. The company for certolizumab pegol has stated that it is now used in clinical practice, and it also has a similar cost and mechanism of action to the other TNF-alpha inhibitors already appraised by NICE (in TA199 and TA220). Secukinumab has a marketing authorisation alone or in combination with methotrexate, for the treatment of active psoriatic arthritis in adult patients when the response to previous disease modifying anti rheumatic drug (DMARD) therapy has been inadequate, which was granted in November 2015.

Clinical effectiveness evidence in TA199, TA220 and TA340

NICE TA199 and TA220 recommended etanercept, infliximab, adalimumab and golimumab for treating psoriatic arthritis after trials of 2 conventional DMARDs (see section 1). In the absence of head-to-head comparisons, the clinical evidence for these appraisals came from placebo controlled phase III trials. These included the GO-REVEAL trial (golimumab versus placebo); 2 RCTs comparing etanercept with placebo (Mease 2000 and Mease 2004); 2 RCTs comparing infliximab with placebo

(IMPACT and IMPACT 2); and 2 RCTs comparing adalimumab with placebo (ADEPT and Genovese 2007).

The Committees in TA199 and TA220 noted that there was insufficient evidence of superiority of any 1 treatment over the others. The Committees noted that in the Assessment Groups economic model, the Health Assessment Questionnaire (HAQ) response had a greater effect on utility than the Psoriasis Area and Severity Index (PASI), indicating that the calculated health-related quality of life benefit was mainly driven by the response in joint symptoms rather than skin disease. It concluded that the treatments had comparable safety profiles but uncertainty remained in the long-term. It was therefore suggested that registries gathering data on the long-term outcomes specific to psoriatic arthritis were collected.

The clinical evidence for recommending ustekinumab in TA340 when TNF-alpha inhibitors are contraindicated or when the person has had treatment with 1 or more TNF-α inhibitors came from 2 RCTS comparing ustekinumab with placebo (PSUMMIT 1 and PSUMMIT 2). PSUMMIT 2 in particular provided evidence in people with prior exposure to TNF-alpha inhibitors (equivalent evidence for second-line biologic use was not available for the TNF-alpha inhibitors appraised in TA199 or TA220). The Committee concluded from the results of the company's mixed treatment comparison that ustekinumab appeared to be less effective than TNF-alpha inhibitors for PASI 75, PASI 90 and PsARC response, particularly for the joint outcome. Regarding the need for further research, the Committee stated that there is a need forhead-to-head comparisons between biological treatments for psoriatic arthritis, particularly in people for whom treatment with tumour necrosis factor (TNF) alpha inhibitors has been unsuccessful.

Clinical effectiveness evidence since the issuing of TA199, TA220

There is no important new evidence regarding ustekinumab or apremilast (TA340 issued in June 2015 and TA372 issued November 2015); therefore searches carried out did not include ustekinumab or apremilast.

Since the publication of NICE TA199 and TA220, there is still an absence of evidence from head-to-head comparisons of the TNF-alpha inhibitors in people with psoriatic arthritis. The searches did not identify any studies that suggest the recommendations of NICE TA199 and TA220 need updating.

However, a number of studies have been published since NICE 199 and TA220 that support their recommendations.

- A recent systematic review and meta-analysis (Lemos et al. 2014) found no difference in efficacy and effectiveness among anti-TNFs; and another recent systematic review, network meta-analysis and economic evaluation (Cawson et al. 2014) which updated the previously developed models used in the NICE technology appraisals agreed with the conclusions from the previous models, in that biologics are cost-effective compared with the conventional management strategy.

- A long-term follow-up of the ADEPT study explored the relationship between PASI responses and radiographic progression after 144 weeks of adalimumab

treatment (Choy E et al. 2009). These post-hoc analyses on observed data suggest that patients who have PASI 50, PASI 75 and PASI 90 responses at 144 weeks (that is, improvement in psoriasis) also have inhibition of radiographic progression.

- Psoriatic arthritis patients treated with etanercept in the open-label Mease 2004 follow-up study achieved significant improvements in physical functioning (Mease PJ et al. 2010). The improvement was reported to be approximately 10 times that observed in patients treated with placebo and was also maintained for up to 2 years.

- The 5-year results from the GO-REVEAL extension study are now published in a peer review journal (Kavanaugh A et al. 2014). This publication suggests continued clinical efficacy is demonstrated over 5 years and the overall safety profile of golimumab is similar to the other TNF inhibitors. Patient attrition was noted by the authors to be low, with the study retaining more than two-thirds of randomised patients through 5 years. The data suggest golimumab treatment provides long-term maintenance of clinically meaningful responses in the arthritic and skin components of psoriatic arthritis, improved physical function and inhibition of radiographic progression. No apparent differences between the long-term efficacy and safety of the 2 golimumab doses were observed.

The literature searches identified little evidence to address the research recommendations of NICE TA199 and TA220 to 'collect further data within registries of patients receiving biological treatments for psoriatic arthritis to obtain information on long-term outcomes, including adverse events', in the UK healthcare setting. Results from a UK retrospective audit of 548 patients with psoriatic arthritis presented at a conference by Jani et al. (2013) provided some evidence supporting the effectiveness of switching between anti-TNFs. In healthcare settings outside the UK, a number of long-term observational studies including patients with psoriatic arthritis, rheumatoid arthritis and ankylosing spondylitis have shown that the treatments are not associated with safety issues that were not already identified from previous short term studies. An Italian registry reported there was no increased risk of malignancies. One Canadian registry (RemiTRAC) reported that infusion reactions associated with infliximab were uncommon and mild to moderate in nature. Another ongoing prospective Canadian registry (BioTRAC) found a high durability of treatment with infliximab.

The registered and unpublished trials listed in Appendix 2 are not expected to impact the recommendations or address the uncertainties and research recommendations of NICE TA199 and TA220. However, there is a phase 4 RCT (NOR-SWITCH) expected to complete in May 2016 that is evaluating the safety and efficacy of switching from innovator infliximab to biosimilar infliximab in patients with rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease and chronic plaque psoriasis. The results of this study should be reviewed if the wording of the recommendations of TA199 and TA220 are amended to reflect the introduction of biosimilars.

Since the publication of NICE TA199, TA220 and TA340, there is still an absence of evidence from head-to-head comparisons of the TNF-alpha inhibitors in people with

psoriatic arthritis. The searches did not identify any studies that suggest the recommendations of NICE TA199, TA220 and TA340 need updating.

Recommendations

There is still an absence of evidence from head-to-head comparisons between biologic treatments in people with psoriatic arthritis. With regard to the research recommendations of TA199,TA220 and TA340 for data from registries of long-term outcomes and adverse events there was no new evidence found that would change the recommendations.

Ustekinumab has evidence in the second-line biologic setting, but there is no equivalent evidence for the TNF-alpha inhibitors, so it will be difficult to determine the relative effectiveness, and therefore it is unlikely based on the available evidence that an explicit recommendation on sequential use could be supported. There have been no changes to the marketing authorisations and no major changes to the list prices of the technologies appraised in TA199 and TA220. It is therefore proposed that the upcoming MTA does not include any of the technologies from TA199 or TA220.

The recent introduction of biosimilars based on infliximab has important cost implications. However, it is not anticipated that changes to the cost of treatment are likely to impact NICE TA199 and TA220 because the recommendations specify that treatment should normally be started with the least expensive drug. It is proposed that the wording of the recommendations of TA199 and TA220 should be changed to reflect the availability of infliximab biosimilars and that, based on the above information, the guidance should then be transferred to the 'static guidance list'.

8. Implementation

No submission was received from Implementation.

9. Equality issues

In TA199, TA220 and TA340 the Committee concluded that, when using the PsARC, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate. This potential equality issue was incorporated in the guidance recommendations (see NICE TA199 section 1.4 and NICE TA220 section 1.2).

GE paper sign off: Frances Sutcliffe 21 June 2016

Contributors to this paper:

Information Specialist: Paul Levay

Technical Lead: Chris Chesters

Programme Manager: Andrew Kenyon

CCP input Rupert Franklin

Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the [specify STA or MTA] process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	Yes

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Psoriatic arthritis in adults: certolizumab pegol (2014) NICE evidence summary of new medicines 42.

Musculoskeletal conditions overview (2015) NICE pathway.

In progress

Spondyloarthritis: diagnosis and management of spondyloarthritis. NICE guideline. Publication expected December 2016.

Apremilast for treating active psoriatic arthritis after inadequate response to disease modifying anti-rheumatic drugs. NICE technology appraisals guidance. Publication expected October 2015. ID682

Certolizumab pegol and secukinumab for treating active psoriatic arthritis after disease-modifying anti-rheumatic drugs. NICE technology appraisals guidance. Publication expected May 2017. ID579

Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
Adalimumab (Humira), Abbvie Adalimumab is licensed for the treatment of active and progressive psoriatic arthritis in adults when the disease has not responded adequately to previous DMARD therapy. The acquisition cost of adalimumab is £357.50 per 40-mg prefilled pen or prefilled syringe (exc VAT; BNF 58).	Indication: no change. The manufacturer has no proposed extensions to the current marketing authorisation. Sources: SPC (August 2015) and letter to NICE (July 2015) Net price 40-mg prefilled pen or prefilled syringe = £352.14; Source: BNF (August 2015)
Etanercept (Enbrel), Pfizer Etanercept is licensed for the treatment of active and progressive psoriatic arthritis in adults whose disease has not responded adequately to previous DMARD therapy. The acquisition cost of etanercept is £89.38 per 25-mg prefilled syringe or 25-mg vial with powder for reconstitution (with solvent), and £178.75 per 50-mg prefilled syringe (excluding VAT; BNF 58)	Indication: no change. The manufacturer has no proposed extensions to the current marketing authorisation. Source: SPC (April 2015) and letter to NICE (July 2015) Net price 25-mg prefilled syringe = £89.38; 50-mg prefilled pen or prefilled syringe = £178.75 Source: BNF (August 2015)

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
Golimumab (Simponi), MSD Golimumab has a marketing authorisation for the treatment of active and progressive psoriatic arthritis (alone or in combination with methotrexate) in adults when the response to previous disease-modifying antirheumatic drug (DMARD) therapy has been inadequate. The cost of golimumab is £774.58 for a 50 mg pre-filled injection pen (excluding VAT, 'MIMS' February 2011 edition) The manufacturer of golimumab has agreed a patient access scheme with the Department of Health, in which the 100 mg dose of golimumab will be available to the NHS at the same cost as the 50 mg dose.	Indication: no change. The manufacturer has no proposed extensions to the current marketing authorisation. Source: SPC (July 2015) and letter to NICE (August 2015) Net price 50-mg prefilled pen or prefilled syringe = £762.97. Source: BNF (August 2015)
Infliximab (Remicade), MSD Infliximab is licensed for the treatment of active and progressive psoriatic arthritis in adults when the disease has not responded adequately to previous DMARD therapy. Infliximab should be administered: in combination with methotrexate, **or** alone in people who show intolerance to methotrexate or for whom methotrexate is contraindicated. The acquisition cost of infliximab is £419.62 per 100-mg vial with powder for reconstitution (excluding VAT; BNF 58)	Indication: no change. The manufacturer has no proposed extensions to the current marketing authorisation. Source: SPC (May 2015) Net price 100-mg vial = £419.62 Source: BNF (August 2015)
	Inflectra [infliximab biosimilar] (Hospira) is indicated for treatment of active and progressive psoriatic arthritis in adult patients when the response to previous DMARD therapy has been inadequate. Inflectra should be administered in combination with methotrexate; or alone in patients who show intolerance to methotrexate or for whom methotrexate is contraindicated. Source: SPC (June 2015) Net price 100-mg vial = £377.66 Source: MIMS (August 2015)
	Remsima [infliximab biosimilar] (Napp) is indicated for treatment of active and

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
	progressive psoriatic arthritis in adult patients when the response to previous DMARD therapy has been inadequate. Remsima should be administered in combination with methotrexate; or alone in patients who show intolerance to methotrexate or for whom methotrexate is contraindicated. Source: SPC (February 2015) NHS list price = £377.66 per 100mg vial [redacted] Source: letter to NICE (August 2015)
Ustekinumab (Stelara), Janssen Ustekinumab has a marketing authorisation in the UK for use alone or in combination with methotrexate for the treatment of active psoriatic arthritis in adult patients when the response to previous non-biological disease-modifying antirheumatic drug (DMARD) therapy has been inadequate. The list price for ustekinumab is £2147 per 45-mg vial (excluding VAT; British national formulary online [accessed February 2015]).	No change Source: SPC (June 2015) Net price 0.5-mL (45-mg) prefilled syringe = £2147.00 Source: BNF (August 2015)

Details of new products

Drug (company)	Details (phase of development, expected launch date)
Abatacept (Orencia), Bristol-Myers-Squibb - Psoriatic arthritis after failure of a DMARD - SC formulation	Phase 3 clinical trials [redacted]
Brodalumab (AMG827), AstraZeneca	Phase 3 clinical trials [redacted]
Ixekizumab (LY2439821), Eli Lilly	Phase 3 clinical trials [redacted]

Tofacitinib (Xeljanz), Pfizer		Phase 3 clinical trials [redacted]
Adalimumab (Humira) - new formulation, Abbvie		Recently approved by the EMA
Adalimumab biosimilars	ABP 501, Amgen	[redacted]
	BI-695501, Boehringer Ingelheim	[redacted]
	CHS-1420, Coherus Biosciences	[redacted]
	GP2017, Sandoz	[redacted]
	M923, Baxter	[redacted]
	ONS-3010, Oncobiologics	[redacted]
	PF-06410293, Pfizer	[redacted]
	SB5, Merck	[redacted]
Etanercept biosimilars	CHS-0214, Baxter	[redacted]
	GP2015, Sandoz	[redacted]
	HD203, Merck	[redacted]
	SB4	[redacted]
Infliximab biosimilars	ABP-710, Amgen	[redacted]
	BOW-015, EPIRUS Biopharmaceuticals	[redacted]
	PF-06438179, Pfizer	[redacted]

	SB2, Biogen	[redacted]

Registered and unpublished trials

Trial name and registration number	Details
A randomized, double-blind, parallel-group study to evaluate the safety and efficacy of switching from innovator infliximab to biosimilar infliximab compared with continued treatment with innovator infliximab in patients with rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease and chronic plaque psoriasis NOR-SWITCH Phase 4 NCT02148640	Enrolment: 500 Start date: October 2014 Estimated completion: May 2016
REmoval of Treatment for patients in REmission in psoriatic ArThritis - Feasibility study RETREAT UKCRN 13690 UKCRN 13916	A randomised controlled trial to compare withdrawal of therapy versus continuing therapy in low disease states in psoriatic arthritis Status: open Enrolment: 30 Closure: August 2013
Evaluation of clinical value of standardized protocol for dose-reduction in patients with spondylarthropathies and clinical remission with anti-tnf therapy: open-label, controlled, randomized, multicenter trial Phase 4 NCT01604629	Purpose: to demonstrate that patients with spondylarthropathies in remission under antiTNF therapy, can maintain the remission with a maintenance dose inferior to the currently recommended dose schedule Enrolment: 190 Start date: July 2012 Estimated completion: September 2015
A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, an Anti-TNFα Monoclonal Antibody, Administered Intravenously, in Subjects With Active Psoriatic Arthritis Phase 3 NCT02181673	Enrolment: 440 Start date: April 2014 Estimated completion: April 2017

Trial name and registration number	Details
A Multicenter Double-Blind, Randomized Controlled Study of Etanercept and Methotrexate in Combination or as Monotherapy in Subjects With Psoriatic Arthritis Phase 3 NCT02376790	Enrolment: 840 Start date: March 2015 Estimated completion: May 2018
Single-arm, Multicenter Study to Evaluate the Ability of Subjects With Rheumatoid Arthritis or Psoriatic Arthritis to Effectively Use a Reusable Electromechanical Autoinjector to Self-inject Etanercept Phase 3 NCT01901185	Enrolment: 77 Start date: June 2013 Estimated completion: December 2013 Results available
Investigation of Factors Influencing Psoriatic Arthritis and Psoriasis Response to Therapy with Biologic Drugs OUTPASS UKCRN 13910	Purpose: to study patients with psoriasis and psoriatic arthritis to assess whether antibodies affect how drugs work Enrolment: 300 Closure date: April 2016
Golimumab Safety and Surveillance Program Using the Ingenix NHI Database Phase 4 NCT01081717	Prospective, observational cohort using the US Health Insurance claims database to estimate the incidence of serious outcomes in patients with rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis treated with golimumab and other types of biological and systemic non biological treatments Enrolment: 1000 Start date: April 2009 Estimated completion: September 2017
Effects of Biological Treatment on Blood Pressure and Endothelial Function in Patients With Rheumatoid Arthritis, Psoriatic Arthritis and Ankylosing Spondylitis Phase 4	Enrolment: 100 Start date: June 2013 Estimated completion: July 2014

Trial name and registration number	Details
A Post-Marketing Surveillance For Safety And Adherence To Treatment Of Enbrel In Adults With Psoriatic Arthritis In Belgium PROVE NCT00938015	Enrolment: 303 Start date: October 2004 Completion: April 2012 Results available
Biologic Treatment Registry Across Canada) Rheumatology (Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis BioTRAC NCT00741793	Enrolment: 3000 Start date: October 2010 Estimated completion: April 2018

Additional information

All Wales Medicines Strategy Group (2014) Final Appraisal Recommendation – 4214: Infliximab (Inflectra) 100 mg powder for concentrate for solution for infusion.

All Wales Medicines Strategy Group (2014) Final Appraisal Recommendation – 4314: infliximab (Remsima) 100 mg powder for concentrate for solution for infusion.

British Society for Rheumatology (2012) Guidelines for the treatment of psoriatic arthritis with biologics. Review date: 2016.

European League Against Rheumatism (2012) European League Against Rheumatism recommendations for the management of psoriatic arthritis with pharmacological therapies.

Scottish Medicines Consortium (2015) Infliximab, 100mg, powder for concentrate for solution for infusion (Inflectra) SMC No. (1007/14).

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