The drugs included in this guideline are for use in secondary care only (RED on the Bucks traffic light list).

**NICE Compliance/High Cost Drug Form**
A high cost drug form must be completed and returned to buc-tr.formularyteam@nhs.net before initiating treatment with any of the above. High cost drugs forms can be found on the Buckinghamshire Formulary www.bucksformulary.nhs.uk.

The forms can only be downloaded from the Formulary if the user is linked to the BHNHST server.

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**Box 1: Specific circumstances which may suggest the use of a specific agent**:  
There is a generalised increased risk of infection with the use of biologics

- **Adalimumab**: Psoriasis (TA146)  
  - Crohn’s (TA187)  
  - Ulcerative Colitis (TA329)  
  - Hidradenitis Suppurativa (TA392)

- **Apremilast**: Inability to self-administer or needle-phobia  
  - Less severe disease  
  - Psoriasis (TA368)

- **Certolizumab**: Not licensed for use in psoriasis, only for psoriatic arthritis

- **Etanercept**: Psoriasis (TA103)  
  - Shorter half-life required due to history of TB, infections requiring hospitalisation or other co-morbidity or patient factors (e.g. diabetes, COPD, concurrent corticosteroid use)

- **Golimumab**: Ulcerative colitis (TA329)

- **Infliximab**: Patient or other trained individual unable to administer subcutaneous injections  
  - Non-adherence is suspected after failure of first biologic  
  - Crohn’s (TA187)  
  - Ulcerative Colitis (TA329, TA140)  
  - Psoriasis (TA134)

- **Ustekinumab**: Psoriasis (TA350) – note this would be a cheaper option  
  - Anti-TNF alpha agent contraindicated (TA340)

- **Secukinumab**: Psoriasis (TA350)  
  - Anti-TNF alpha agent contraindicated (TA340)

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**Box 2: Patient factors**
- Device  
- Level of dexterity  
- Frequency route  
- Compliance/ adherence
Psoriatic Arthritis - treatment algorithm

Patient meets NICE criteria for treatment:
- Peripheral arthritis, with 3 or more tender joints and 3 or more swollen joints
- Failure of at least 2 standard DMARDs (administered either individually or in combination)

Decision made based on patient factors, medical circumstances and cost - (see Box 1 & 2)

TNF-α inhibitors not contraindicated

Drugs listed in order of cost, with the least expensive first:
- Secukinumab (TA 445) (see Note 1)
- Apremilast (TA433) or
- Etanercept (TA199) or
- Adalimumab (TA199) or
- Golimumab (TA220) or
- Certolizumab (TA199, TA445) or
- Infliximab (TA199) (see note in dose and administration section below)

TNF-α inhibitors contraindicated

Drugs listed in order of cost, with the least expensive first:
- Secukinumab (TA 445) (see Note 1) or
- Apremilast (TA433) or
- Ustekinumab (TA340) (see note in dose and administration section below)

Is there an adequate response to treatment, defined as:
- Improvement in at least 2 of the 4 PsARC criteria (1 of which has to be the joint tenderness or swelling score) and
- No worsening in any of the 4 criteria?

Response to be first measured at 12 weeks (except 16 weeks for apremilast and secukinumab, 24 weeks for ustekinumab)

Yes - maintain same treatment and monitor patient annually

Does patient have a PASI 75 response?

No

TNF-α inhibitors not contraindicated

Switch to an alternative biologic or apremilast from above list.

Yes

TNF-α inhibitors contraindicated

Switch to an alternative biologic or apremilast from above list.

Adequate response using PsARC criteria as described previously?

No

Yes

Does patient have a PASI 75 response?

No

TNF-α inhibitors not contraindicated

Switch to an alternative biologic or apremilast from above list.

Yes

TNF-α inhibitors contraindicated

Switch to an alternative biologic or apremilast from above list.

Adequate response using PsARC criteria as described previously?

Yes

Does patient have a PASI 75 response?

No

Consider alternative management (See note 3)

Key to terms:
DMARD: Disease-modifying anti-rheumatic drug
PASI 75 response: Reduction in psoriasis area severity index (PASI) score of at least 75% from baseline
PsARC: Psoriatic arthritis response criteria
TA: NICE technology appraisal
TNF: Tumour necrosis factor α: Alpha

Note 1: Secukinumab dosing is double in patients with psoriasis or failed TNF-α inhibitors, therefore would be more costly than apremilast.
Note 2: Ustekinumab can be given either with methotrexate or without methotrexate.
Note 3: A maximum trial of 3 biologics AND apremilast is funded, after which an Individual Funding Request is required. Apremilast is not a biologic. Other treatment options need to be considered.
Dosage and administration

Apremilast
Note: This is not a biologic.

The recommended dosage is 30mg twice daily taken orally, approximately 12 hours apart with no food restrictions.

An initial titration schedule is required as shown below in Table 1. No re-titration is required after initial titration.

Table 1: Dose titration schedule

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6 &amp; thereafter</th>
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<tr>
<td>AM 10 mg</td>
<td>AM 10 mg</td>
<td>PM 10 mg</td>
<td>AM 10 mg</td>
<td>PM 20 mg</td>
<td>AM 20 mg</td>
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If patients miss a dose, the next dose should be taken as soon as possible. If it is close to the time for their next dose, the missed dose should not be taken and the next dose should be taken at the regular time.

Certolizumab
400 mg at weeks 0, 2 and 4 then 200 mg every 2 weeks via subcutaneous injection.

Adalimumab
40 mg every other week as a single dose via subcutaneous injection.

Etanercept
Note: ALL prescribing of etanercept must include generic and brand name. Benepali® is first choice etanercept brand. (For further details see formulary entry for etanercept www.bucksformulary.nhs.uk.)

25 mg twice weekly via subcutaneous injection. Alternatively, the SPC^4 allows for a dose of 50 mg once weekly.

Infliximab
ALL prescribing of infliximab must include both the generic and brand name. For new initiations, infliximab biosimilar (e.g. Inflectra®, Remsima®) should be prescribed. Refer to infliximab entry on formulary website www.bucksformulary.nhs.uk for latest cost effective choice.

Infliximab is administered at a dose of 5 mg/kg by intravenous infusion, via an infusion pump, over 2 hours at weeks 0, 2 and 6 and thereafter every 8 weeks.

Refer to Buckinghamshire Healthcare NHS Trust (BHNHST) Injectables Policy and Guide for full details of administration.

Golimumab
50 mg by subcutaneous injection given once a month on the same date each month. In people who weigh more than 100 kg whose rheumatoid arthritis does not show an adequate clinical response after three or four doses, the dosage may be increased to 100 mg once a month.

Golimumab is recommended as a treatment option only if the manufacturer provides the 100 mg dose of golimumab at the same cost as the 50 mg dose.

Ustekinumab
The recommended dose of ustekinumab is 45 mg for people who weigh 100 kg or less and 90 mg for people who weigh over 100 kg. An initial dose of ustekinumab is administered subcutaneously at week 0, followed by another dose at week 4, and then a further dose every 12 weeks.

The manufacturer provides the 90 mg dose (two 45 mg vials) for people who weigh more than 100 kg at the same total cost as for a single 45 mg vial.
Secukinumab

For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNFα inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at 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.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4.

See Guideline 738FM Apremilast, Dimethyl Fumarate and Biologics for the Treatment of Adults with Psoriasis for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis.

Refer to BHNHST Injectables Policy and Guide for full details of administration.

References

3. Summary of Product Characteristic for Cimzia® (USB Pharma Ltd), last updated 23rd June 2015
5. Summary or Product Characteristics for Enbrel® (Pfizer Ltd), last updated March 2015.
6. Summary or Product Characteristics for Remicade® (Schering-Plough Ltd), last updated 23 April 2015.
7. Summary or Product Characteristics for Inflectra® (Hospira UK Ltd), last updated June 2015
8. Summary or Product Characteristics for Remsima® (Napp Pharmaceuticals Ltd), last updated 20 December 2014
10. Summary or Product Characteristics for Stelara® (Janssen-Cilag Interational), last updated 22nd June 2015.

Summary of Product Characteristics found at https://www.medicines.org.uk/emc/.

See also:
Guideline 222 Injectables Policy and Guide – Adults and Paediatrics (BHT users only)
Guideline 280FM Management of Patients on Immunosuppressants admitted with Suspected Infections
Guideline 738FM Apremilast, Dimethyl Fumarate and Biologics for the Treatment of Adults with Psoriasis
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<td><strong>Author/s</strong></td>
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