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Clinical Guideline

Seronegative Spondyloarthropathy Drug Treatment Pathway

Guideline Summary
This clinical guideline outlines the drug treatment pathway for adult patients with Seronegative Spondyloarthropathy.

South East London Area Prescribing Committee: A partnership between NHS organisations in South East London; Bexley/Bromley/Greenwich/Lambeth/Lewisham & Southwark Clinical Commissioning Groups (CCGs) & GSTfT/KCH/SLAM & Oxleas NHS Foundation Trusts & Lewisham & Greenwich NHS Trust.
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Author	**South East London Rheumatology Steering Group:** Acute Trusts: **Kings College Hospital NHS Foundation Trust** Consultant Rheumatologist (Chair) Clinical pharmacy team leader – Post-acute and Planned Medicine Specialist Pharmacist Rheumatology **Guys and St Thomas' NHS Foundation Trust** Principal Pharmacist Immunotherapy (Rheumatology, Dermatology, Allergy) and Clinical Commissioning Highly Specialist Pharmacist Rheumatology Consultant Rheumatologist and Clinical Lead Rheumatology Consultant Rheumatologist Consultant Rheumatologist Advanced Nurse Specialist, Rheumatology **Lewisham and Greenwich NHS Trust** Consultant Rheumatologist Clinical Nurse Specialist, Rheumatology Lead Pharmacist Long term Conditions **Clinical Commissioning Groups** NHS Lambeth CCG (lead CCG), NHS Southwark CCG, NHS Bexley CCG, NHS Bromley CCG, NHS Greenwich CCG, NHS Lewisham CCG
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Change History		
Date	Change details, since approval	Approved by
10.10.16	Secukinumab added to pathway as per NICE TA 407	
10.10.16	Added: free of charges schemes, extended interval dosing and biological withdrawal in remission, biologic choice in women planning pregnancy.	
10.10.16	References updated	
1.11.16	Updated as per NICE TA 383 (removed two BASDAI measurements 12 weeks apart pre-biologic therapy)	
09.12.16	Golimumab 50mg twice monthly dosing statement added to notes box	
27.01.17	7 – added information on administration of vaccinations by early outpatient biologic initiation service	
27.01.17	11 – added information on administration of first dose biologic via outpatient clinic and VAT charge to commissioners	
14.3.17	5.3 – Updated as per NICE TA 433 added apremilast as option pre-biologic therapy	
29.6.17	13.1 – Updated as per NICE TA 445 Added secukinumab as option in Psoriatic Arthritis	
8.10.17	Corrected: Assess response at 24 weeks for ustekinumab	
17.10.17	Added updates to choice of biologic 13.1	

17.10.17	Clarified secukinumab dosing for PsA patients who are inadequate responders to anti-TNF therapy	
22.2.18	5.2 Clarified NSAID treatment prior to biologic initiation (as per NICE)	
22.2.18	5 Updated wording relating to subcutaneous methotrexate use	
22.2.18	13.1 Notes section – updated to include infliximab not commissioned for non-radiographic axial spondyloarthritis	
Review History		
Date	Review details	Approved by
June 2016	Use of sub-cutaneous methotrexate added as an option	
Feb 2018	Updated in line with latest NICE TAGs – see change history	

Contents

1. Scope

This treatment pathway applies to adult patients with a diagnosis of seronegative spondyloarthropathy who are approaching treatment with biologic therapy.

2. Rationale

This treatment pathway provides an evidence based approach for the treatment of seronegative spondyloarthritis whilst maximising cost effectiveness and clinical outcome.

3. Principles

This treatment guideline is based on current available national guidance (National Institute for Health and Care Excellence, NICE, and British Society for Rheumatology, BSR), locally approved guidance and is subject to frequent change as guidance is updated and costs change.

4. Definitions

4.1 Adequate response

- Psoriatic Arthritis
  - An improvement in at least 2 of the 4 Psoriatic Arthritis Response Criteria (PsARC) at 12 weeks*, one of which has to be *tender or swollen joint count* with no worsening in any of the 4 criteria.
  - A Psoriasis Area and Severity Index (PASI) 75 response at 12 weeks*, but a PsARC which does not justify continuation of treatment; with review by a dermatologist where skin improvement justifies continuation of treatment.
- Ankylosing Spondylitis
  - Reduction of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units AND reduction of the spinal visual analogue scale (VAS) by 2cm or more.

4.2 Inadequate response

- Psoriatic Arthritis
  - Improvement in less than 2 of the 4 Psoriatic Arthritis Response Criteria (PsARC) at 12 weeks* or worsening in any of the 4 criteria
  - Not achieving a PASI 75 response at 12 weeks*
- Ankylosing Spondylitis
  - Less than 50% reduction in the BASDAI score of the pre-treatment value or by less than 2 units OR a less than 2cm reduction in the spinal VAS at 12 weeks*.

4.3 Primary failure – patient does not achieve an adequate response after 12 weeks treatment*

4.4 Secondary failure – patient initially achieves an adequate response after 12 weeks* but this is not sustained, resulting in an inadequate response.

4.5 Oligoarthritis

- Persistent pain and swelling of less than 3 joints with failure of 2 Disease Modifying Anti-Rheumatic Drugs (DMARDs), and short-lived or no response to intra-articular corticosteroid.

*Apremilast and secukinumab – 16 weeks and ustekinumab – 24 weeks

5. Pre-biologic therapy [Non-steroidal anti-inflammatory drugs (NSAIDs), steroids, DMARDs and Apremilast]

5.1. Psoriatic Arthritis (PsA)

NSAIDs and/or local intra-articular steroids

Active and Progressive Psoriatic Arthritis	severe persistent oligoarthritis	Active and Progressive Psoriatic Arthritis
peripheral arthritis +		(≥5 swollen joints AND elevated C-reactive protein (CRP) for
≥ 3 tender joints and ≥3 swollen joints	**AND**	≥ 3 months or structural joint damage due to disease)
AND		**AND**
Failure of at least 2 DMARDs	Failure of at least 2 DMARDs	Failure of at least 1 DMARD
(Sequentially or in combination)	(Sequentially or in combination)	

(DMARDs used for 12 weeks at standard dosage unless dose or duration limited by toxicity)

5.2. Axial Spondyloarthritis (including ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis)

2 or more NSAIDs taken sequentially at maximum tolerated or recommended doses for 4 weeks
UNLESS contraindicated, failure to respond or patient demonstrates intolerance

↓

Patient's disease satisfies the modified New York criteria for diagnosis of ankylosing spondylitis
AND/OR
satisfies the ASAS (Assessment of SpondyloArthritis International Society) classification criteria for axial spondyloarthritis

AND

There is confirmation of sustained active spinal disease demonstrated by:
a BASDAI of at least 4 units
AND
a VAS of at least 4cm

Strategies for maximising the use of DMARDs prior to apremilast and biologic therapy:

- Adjusting folic acid dose/frequency/formulation to improve tolerance to oral methotrexate (e.g. folic acid liquid 1mg daily except day methotrexate is taken)
- Subcutaneous methotrexate where clinically appropriate (e.g. gastrointestinal adverse effects with oral methotrexate or poor compliance). When used in this situation, subcutaneous methotrexate is billable to CCGs for approved indications in line with the CCG high cost drugs policy and CCG commissioned drug list. Whilst the majority of dispensing will be via homecare, commissioners have agreed that there may be exceptional circumstances where homecare may not be possible (e.g. due to patient circumstances or to cover initiation doses) and these can be billed.
- Where appropriate, maximum intensification of combination therapy using maximum tolerated doses.

5.3 Apremilast in Psoriatic Arthritis

Apremilast, alone or in combination with DMARDs, is recommended as an option for treating active psoriatic arthritis if:

- Peripheral arthritis with ≥ 3 tender joints and ≥3 swollen joints
  AND
- Their disease has not responded to adequate trials of at least 2 DMARDs given either alone or in combination

Assess response at 16 weeks

Psoriatic Arthritis
PsARC measured at 16 weeks – Response in 2 out of 4 PsARC criteria with no worsening of any of the 4 criteria OR PASI 75 response at 16 weeks + dermatologist review of skin response if indicated.

Continue to reassess response every 6 – 12 months

If minor adverse effects develop at any time or initial response is not sustained (secondary failure) go to section 13.1.

6. Pre-biologic Infection screen

- Tuberculosis (T spot or quantiferon and chest x-ray)
- Viral serology: hepatitis B, C and Human Immunodeficiency Virus (HIV) as clinically appropriate

7. Vaccinations (click for Department of Health Green Book)

Patients should be counselled on the need to avoid live vaccines and the implication that may have for travelling.

Patients aged 70 years and over are now routinely offered vaccination against varicella zoster virus in primary care. This is a live vaccination and patients should not be given the vaccine if they are receiving biologic treatments. For patients aged over 60 and not receiving biologic treatment, the Consultant Rheumatologist may consider recommending the vaccine after careful assessment of the degree of current

immunosuppression from DMARDs and glucocorticoids. To avoid inadvertent administration of this live vaccine, on receipt of clinic letters, GPs should update practice records to indicate which patients are currently receiving biologic treatment.

Patients should receive annual influenza vaccine and pandemic influenza vaccine when recommended and pneumococcal vaccination prior to biologic therapy. This can be prescribed and administered in the community or by the hospital as part of an outpatient biologic initiation service. GP's must be informed if the hospital administer to outpatients.

8. Recruitment into clinical trials

Where possible patients should be invited to participate in clinical trials currently recruiting within local rheumatology departments. Where a clinical trial does not meet the requirements of the pathway, approval should be obtained from commissioners prior to initiation.

9. Free of charge schemes

New biologics and DMARDS are often licensed and made commercially available many months before NICE are due to issue their NICE Technology Appraisal Guidance. Where this situation exists, individual rheumatology departments may enter discussions with the pharmaceutical company to determine if a 'free of charge' (FOC) early access scheme is feasible.

When a FOC is proposed it must satisfy the following criteria:

- Fund the treatment at zero cost to the NHS up to and for 90 days after the positive NICE Technology Appraisal Guidance is issued and formally commissioned
- Continue to fund treatment in the event of a negative NICE Technology Appraisal Guidance until
    - 90 days after a future positive NICE Technology Appraisal Guidance
    - Until the rheumatologist considers it no longer clinically appropriate to continue the drug
- All schemes require sign off in each NHS Trust and this usually requires the Chief Pharmacist, the Pharmacy Procurement Lead and Director of Finance to authorise the scheme.

10. Extended interval dosing ('off-label' indication) and biologic withdrawal in remission

After discussion with the patient a Consultant may decide to extend the dosage interval or withdraw biologic therapy completely as appropriate for the clinical situation. This may require the use of ultrasound to confirm if the patient is in remission. If patients flare following the extension in dose interval or withdrawal; re-initiation of the previous biologic at the same dosage regimen is acceptable but consider using an alternative agent due to immunogenicity. Whilst a patient maintains remission or low disease activity on an extended dose interval, the Trust can recover a share of the savings from the commissioner. This is subject to local discussion and contractual agreement.

11. Method of medication supply

Subject to local arrangements patients may be offered a choice of method of supply. This may include a traditional homecare service or enhanced outpatient pharmacy service via outsourced outpatient pharmacies on main hospital sites. Where there is agreement with pharmaceutical companies, unbundling of homecare and direct procurement via outsourced pharmacies may result in a reduction in the drug acquisition cost. This may further influence the biologic choice at local Trust level.

In order to reduce the time to biologic initiation, the first biologic doses (2 – 4 weeks supply) may be given in clinic as part of an outpatient biologic initiation service. This provides sufficient supply, improved patient training and assessment in clinic prior to initiation on homecare. As the first dose(s) are administered in the outpatient clinic, the cost will incur VAT and this will be passed onto commissioners.

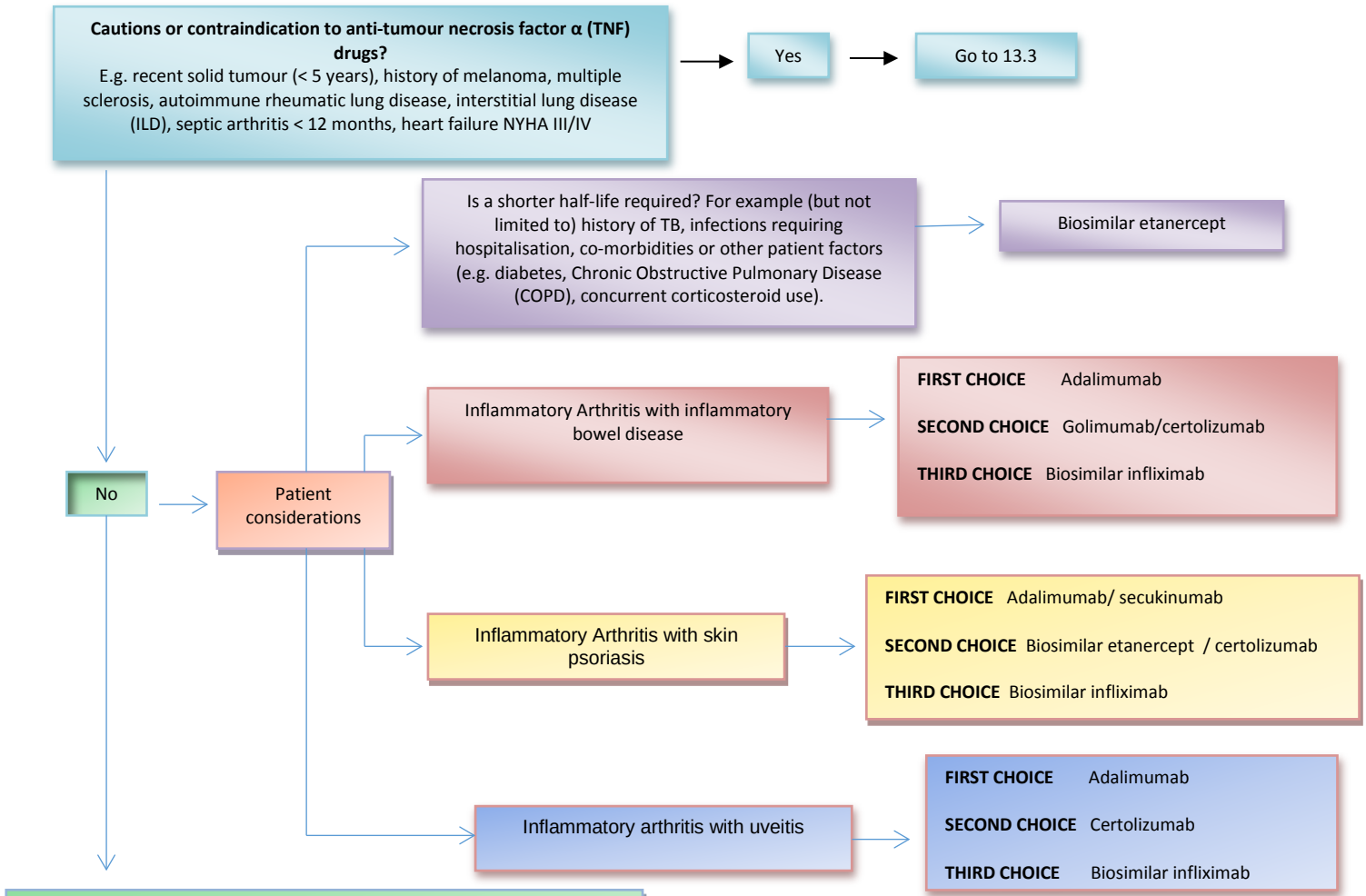
12. Biologic choice in women planning pregnancy

Certolizumab pegol is compatible with all three trimesters of pregnancy and has reduced placental transfer when compared with other tumour necrosis factor α (TNF) inhibitors. For these reasons it is the biologic of choice before, during and after pregnancy (whilst breast feeding). Patients may require to be switched from their current biologic to certolizumab pegol in advance of conception. This should not count as a routine biologic switch. For further recommendations on biologic or DMARD choice in pregnancy or breast feeding, refer to the British Society for Rheumatology (BSR) / British Health Professionals in Rheumatology (BHPR) guideline.

http://www.rheumatology.org.uk/resources/guidelines/default.aspx

Biologic Treatment Pathways

13.1 Initiation of first Biologic



NOTES

1. Consider assessing infection risk with online assessment tool e.g. RABBIT- Risk Score
2. If unable to administer subcutaneous injection or history of poor compliance use intravenous biosimilar infliximab
3. Consider golimumab as first line anti-TNF in patients weighing > 100kg. Golimumab initiated at 50mg once a month may be escalated to 100mg once monthly. Anecdotally, in a small proportion of patients on golimumab 100mg once monthly who experience a subjective loss of efficacy near injection time, golimumab may be administered as 50mg twice monthly. It should be noted that this dosing frequency is an off-label use of golimumab. The 50mg twice monthly dosing regimen is provided at no additional cost to the NHS.
4. Certolizumab pegol first line in pregnancy (monotherapy), see section 12.
5. Infliximab is not commissioned for use in non-radiographic axial spondyloarthritis.

Assess response at 12 weeks*

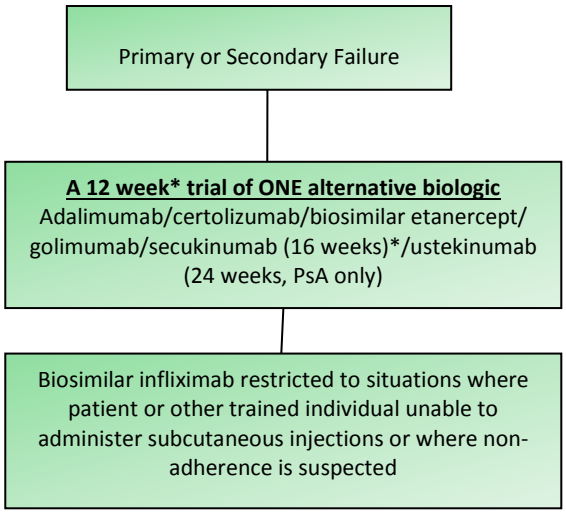
Psoriatic Arthritis
PsARC measured at 12 weeks (*secukinumab – 16 weeks) – Response in 2 out of 4 PsARC criteria with no worsening of any of the 4 criteria OR PASI 75 response at 12 weeks* + dermatologist review of skin response if indicated.

Ankylosing Spondylitis
BASDAI measured at 12 weeks (*secukinumab - 16 weeks) - Reduction of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units AND reduction of the spinal visual analogue scale (VAS) by 2cm or more.

Continue to reassess response every 6 – 12 months if adequate response achieved and consider dose optimisation /withdrawal (see section 10)

If minor adverse effects (e.g. injection site reactions) develop at any time or initial response is not sustained (secondary failure) go to section 13.2.

13.2 Primary or Secondary Failure (loss of efficacy) or minor adverse effects (e.g. injection site reactions) with first anti-TNF



Assess response at 12 weeks*

Psoriatic Arthritis
PsARC measured at 12 weeks (*s**ecukinumab – 16 weeks / ustekinumab – 24 weeks**) – Response in 2 out of 4 PsARC criteria with no worsening of any of the 4 criteria OR PASI 75 response at 12 weeks + dermatologist review of skin response if indicated.

Ankylosing Spondylitis
BASDAI measured at 12 weeks (*secukinumab – 16 weeks) - Reduction of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units AND reduction of the spinal visual analogue scale (VAS) by 2cm or more.

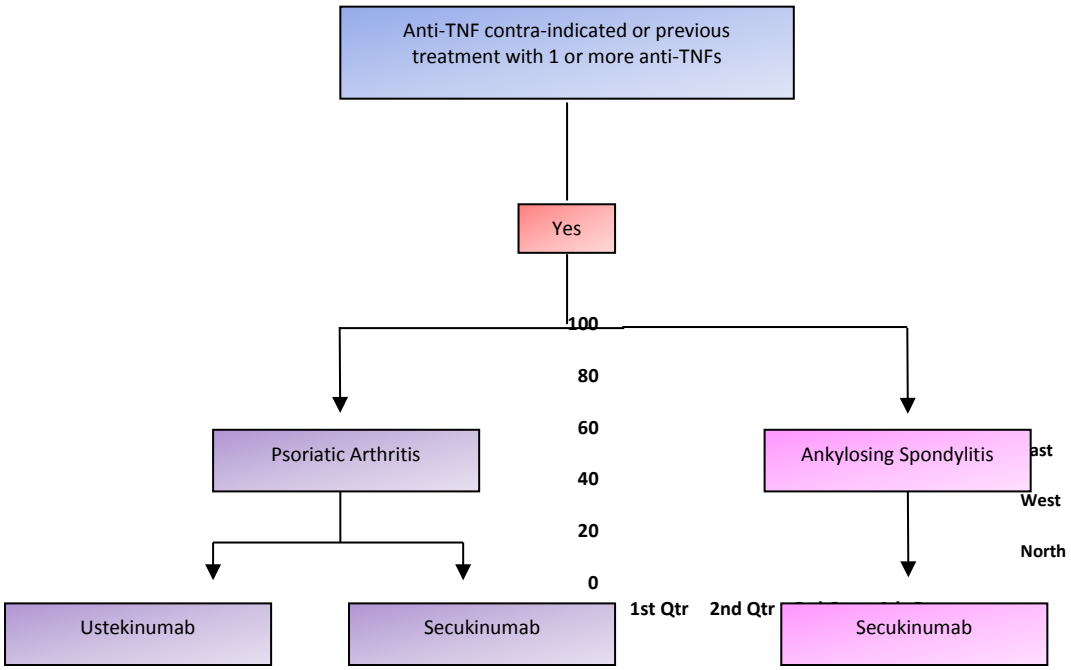
Continue to reassess response every 6 – 12 months if adequate response achieved and consider dose optimisation /withdrawal (see section 10)

If minor adverse effects (e.g. injection site reactions) develop at any time or initial response is not sustained (secondary failure) go to section 13.2 or 13.3.

NOTES

***Psoriatic Arthritis**
For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNFα inadequate responders, the recommended dose of secukinumab is 300 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing

13.3 Initiation of first biologic (anti-TNF contraindicated) OR previous treatment with 1 or more anti-TNFs



Assess response at 12 weeks*

Psoriatic Arthritis
PsARC measured at 12 weeks **(Secukinumab – 16 weeks/Ustekinumab – 24 weeks)*** – Response in 2 out of 4 PsARC criteria with no worsening of any of the 4 criteria OR PASI 75 response at 12 weeks + dermatologist review of skin response if indicated.

Ankylosing Spondylitis
BASDAI measured at 12 weeks (Secukinumab – 16 weeks) - Reduction of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units AND reduction of the spinal visual analogue scale (VAS) by 2cm or more.

Continue to reassess response every 6 – 12 months if adequate response achieved.

NOTES

Psoriatic Arthritis

For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNFα inadequate responders, the recommended dose of secukinumab is 300 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing

14. Monitoring adherence with the guideline

Adherence to this pathway will be reviewed using the South East London Rheumatology Pathways, Outcomes and Monitoring Framework which includes Key Performance Indicators agreed by South East London Area Prescribing Committee. See http://www.lambethccg.nhs.uk for further details. The Rheumatology and Pharmacy Departments may undertake separate clinical audits as part of their annual clinical audit plan.

15. Supporting documents

- See relevant local guidelines

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Consultation Process –current version

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SEL Medicines and Pathways Review Group (MPRG): April 2018