Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

NICE Technology Appraisals: Local implementation

NICE TA Guidance name and number	Ixekizumab for treating axial spondyloarthritis TA718		
Available at	www.nice.org.uk/guidance/ta718		
Date of issue	21 July 2021	**Implementation deadline**	21 October 2021

Medicine details[1]	
Name, brand name and manufacturer	Ixekisumab (Taltz®) Eli Lilly and Company Limited
Mode of action	Ixekizumab is an IgG4 monoclonal antibody that binds with high affinity (< 3 pM) and specificity to interleukin 17A (both IL-17A and IL-17A/F). Elevated concentrations of IL-17A have been implicated in the pathogenesis of psoriasis by promoting keratinocyte proliferation and activation, as well as in the pathogenesis of psoriatic arthritis and axial spondyloarthritis by driving inflammation leading to erosive bone damage and pathological new bone formation. Neutralisation of IL-17A by ixekizumab inhibits these actions.
Licensed indication	Axial spondyloarthritis: *Ankylosing spondylitis (radiographic axial spondyloarthritis r-axSpA)* Taltz® is indicated for the treatment of adult patients with active ankylosing spondylitis who have responded inadequately to conventional therapy. *Non-radiographic axial spondyloarthritis nr-axSpA* Taltz® is indicated for the treatment of adult patients with active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) who have responded inadequately to nonsteroidal anti-inflammatory drugs (NSAIDs).
Formulation	Solution for injection in pre-filled pen and syringes.
Usual dosage	The recommended dose is 160 mg (two 80 mg injections) by subcutaneous injection at week 0, followed by 80 mg every 4 weeks.
Comparison with NICE TA use[2]	This is the same recommended dose and schedule as the NICE TA. *This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the license following NICE publication will need to be considered by the Area Prescribing Committee and **will not be routinely funded** by local commissioners.*

Disease and potential patient group	
Brief description of disease[2,3]	Axial Spondyloarthritis - also known as axSpA or axial SpA - is a painful, chronic arthritis that mainly affects the joints of the spine. It can also affect other joints in the body, as well as tendons and ligaments.

<table>
<tr><td></td><td>Axial Spondyloarthritis may be difficult to diagnose as it cannot always be identified on x-rays or MRI scans of the back. If arthritis of the sacroiliac joints (pelvis) or spine can be seen on x-ray, the term used is radiographic axial Spondyloarthritis (r-axSpA). This condition was previously called Ankylosing Spondylitis (AS) and today, both terms (r-axSpA and AS) are used interchangeably.

If there are no signs of sacroiliitis on x-ray but there is evidence of inflammation in the joints on MRI, the term used is non-radiographic axial Spondyloarthritis (nr-axSpA).

There can be a delay in diagnosis because of non-specific symptoms, an absence of visible structural damage on X-rays, and normal or ambiguous MRI results. They noted that the condition can be mistaken for other conditions such as fibromyalgia.

This delay in diagnosis can result in high functional impairment (difficulties doing day-to-day activities). Almost half of people with non-radiographic axial spondyloarthritis progress to the radiographic version of the disease over a period of 8 to 10 years.

People with axial spondyloarthritis report that it profoundly affects their quality of life and day-to-day activities, such as work.</td></tr>
<tr><td>Potential patient numbers per 100,000[4]</td><td>Table 1: Potential patient numbers per 100,000 adult population for NHS Surrey Heartlands CCG:
<table>
<tr><th></th><th>r-axSpA / AS</th><th>nr-axSpA</th></tr>
<tr><td>Total population, all ages</td><td colspan="2">1,049,170</td></tr>
<tr><td>Adult population</td><td colspan="2">815,884</td></tr>
<tr><td>Prevalence</td><td>1,942</td><td>1,224</td></tr>
<tr><td>Patient numbers per 100,000 adult population</td><td>238</td><td>150</td></tr>
<tr><td>People eligible for treatment with bDMARDs</td><td>777</td><td>465</td></tr>
<tr><td>Patient numbers per 100,000 adult population</td><td>95</td><td>57</td></tr>
<tr><td>People expected to continue treatment</td><td>466</td><td>140</td></tr>
<tr><td>Patient numbers per 100,000 adult population</td><td>57</td><td>17</td></tr>
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SUMMARY

Guidance[2]

1.1 Ixekizumab is recommended as an option for treating active ankylosing spondylitis that is not controlled well enough with conventional therapy, or active non-radiographic axial spondyloarthritis with objective signs of inflammation (shown by elevated C-reactive protein or MRI) that is not controlled well enough with non-steroidal anti-inflammatory drugs (NSAIDs), in adults. It is recommended only if:

- tumour necrosis factor (TNF)-alpha inhibitors are not suitable or do not control the condition well enough, and
- the company provides ixekizumab according to the commercial arrangement.

1.2 Assess response to ixekizumab after 16 to 20 weeks of treatment. Continue treatment only if there is clear evidence of response, defined as:

- reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units and

- a reduction in the spinal pain visual analogue scale (VAS) by 2 cm or more.

1.3 Take into account any communication difficulties, or physical, psychological, sensory or learning disabilities that could affect responses to the BASDAI and spinal pain VAS questionnaires, and make any appropriate adjustments.

1.4 These recommendations are not intended to affect treatment with ixekizumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

When people cannot have TNF-alpha inhibitors or they have not worked well enough the current treatment option is conventional therapy. This includes NSAIDs and physiotherapy. Secukinumab is also an option for treating radiographic disease but there is not enough data to reliably compare it with ixekizumab.

Evidence from clinical trials shows that ixekizumab is effective compared with placebo. The cost-effectiveness estimates for ixekizumab compared with conventional therapy are within what NICE usually considers cost effective. Therefore, ixekizumab is recommended.

Cost implications* [2,3,4]

Cost:
The list price of ixekizumab is £1,125 for 1 pre-filled syringe containing 80 mg per 1 ml solution (excluding VAT; BNF online, accessed March 2021).

Annual or monthly cost per patient:
The annual cost is £16,875 for 15 injections in year 1 and £14,625 for 13 injections in year 2 (excluding VAT; BNF online, accessed March 2021).

Has dose escalation been considered as part of the NICE costing template?
No.

Costing information per CCG:

1. NICE resource impact statement
No significant resource impact is anticipated.

'We do not expect this guidance to have a significant impact on resources; that is, the resource impact of implementing the recommendations in England will be less than £5 million per year in England (or £9,000 per 100,000 population).

This is because the technology is a further treatment option, the overall cost of treatment will be similar and we do not think practice will change substantially as a result of this guidance'.

Availability of PAS and details (if appropriate):
Yes - the PAS price will be given to trusts which would reduce the cost price stated above.

Availability of homecare service (if appropriate): Yes

*NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the APC may reconsider the commissioning status.

2. NICE resource impact template

On an adult population base for NHS Surrey Heartlands CCG of 815,884 and the use of *both* secukinumab and ixekizumab (same resource template), the resource impact in 5 years is:

Indication	Cost	Cost/100,000 per adult CCG population
r-axSpA	£577,825	£70,821
nr-axSpA	£110,748	£13,573
axSpA	£688,573	£84,396

Please note:

- *Use of secukinumab in r-axSpA is already commissioned.*

Alternative treatments and cost per patient per year

Other NICE recommended products:

Table 1: Differences in licensing and relevant NICE TAs

Technology	r-axSpA (ankylosing spondylitis [AS])		nr-axSpA	
	License	NICE TA*	License	NICE TA*
Adalimumab	✓	TA383	✓	TA383
Certolizumab	✓	TA383	✓	TA383
Etanercept	✓	TA383	✓	TA383
Golimumab	✓	TA383	✓	TA497
Infliximab	✓	TA383	×	×
Secukinumab	✓	TA407	✓	TA719

*NICE Technology appraisal guidance:

NICE TA	Technology	Publication date
TA383	TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis	February 2016
TA718	Ixekisumab for treating axial spondyloarthritis	July 2021
TA407	Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors.	September 2016
TA497	Golimumab for treating non-radiographic axial spondyloarthritis	January 2018
TA719	Secukinumab for treating non-radiographic axial spondyloarthritis	July 2021

NICE TA guidance for tofacitinib and upadacitinib expected.

Please note:

- *Biosimilar adalimumab is the most cost-effective choice.*

Options not reviewed by NICE but used in standard practice:

The first treatment is with non-steroidal anti-inflammatory drugs (NSAIDs). The current pathway states that patient has to have had adequate therapeutic trials of at least 2 NSAIDs before bDMARDs.

Impact to patients

- An additional treatment option with a different mechanism of action would be valued by patients.
- This medicine is available under a homecare service so will be delivered directly to the patient.

Impact to primary care prescribers

- This is a National Tariff excluded high-cost drug (NTexHCD) and is commissioned by CCGs for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving this medicine and ensure that this is recorded in the patient's notes in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will also ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.

Impact to secondary care

- The initiation, administration and on-going treatment is managed by secondary care.
- Homecare arrangements will be managed by the trust.
- This medicine is available on homecare.
- An additional treatment option with a different mechanism of action would be valued by clinicians.

Impact to CCGs

- The technology is commissioned by clinical commissioning groups (CCGs), and they are required to comply with the recommendations in a NICE TA within 3 months of its date of publication.
- Providers are NHS hospital trusts.
- Potential savings for out-patient appointments as this medicine is available on homecare.

Implementation

- NICE TA implementation must be within 90 days of publication
- Blueteq forms to be developed
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare.
- Pathway to be discussed at Rheumatology Network. Points to consider:
  - Revisions to the pathway:
    - Golimumab now has a NICE TA for treating nr-axSpA.
  - Choice of therapy:
    - Place of ixekizumab in the pathway as it is be used when TNF-alpha inhibitors are contraindicated or otherwise not suitable, after primary non-response to a TNF-alpha inhibitor or after a poor response or loss of response to TNF-alpha therapy (second or subsequent lines after TNF-alpha inhibitors).
    - There is insufficient evidence to compare the effectiveness of ixekizumab and secukinumab

Recommendation to PCN

National Tariff excluded high-cost drug (NTexHCD): Yes

Recommended traffic light status: Red

References:

1 Ixekizumab. Specification of Product Characteristics. emc. Available at: https://www.medicines.org.uk/emc/product/8199/smpc Accessed <3.8.21>

2 NICE Technology Appraisal Guidance: Ixekizumab for treating axial spondyloarthritis. Available at: www.nice.org.uk/guidance/ta719 Accessed <2.8.21>

3 Axial Spondyloarthritis. The Leeds Teaching Hospitals NHS Trust. Chapel Allerton Hospital. Available at: https://www.leedsth.nhs.uk/a-z-of-services/rheumatology/specialist-spondyloarthritis-service/axial-spondyloarthritis/ Accessed <2.8.21>

4 NICE Resource impact report. Available at: https://www.nice.org.uk/guidance/ta718/resources Accessed <3.8.21

	Name	Role	Date	Declaration of interests (please give details below table)
Prepared by	Tejinder Bahra	Lead Commissioning Pharmacist	3.8.21	None
Reviewed by:				

Explanation of declaration of interest:
None.