East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Briefing Paper for Surrey & North West Sussex Area Prescribing Committee (APC) on NICE Technology Appraisals: Local implementation

NICE TA Guidance	Tildrakizumab (Ilumetri) for treating moderate to severe plaque psoriasis (TA 574)		
Available at	https://www.nice.org.uk/guidance/ta575/resources/tildrakizumab-for-treating-moderate-to-severe-plaque-psoriasis-pdf-82607144484805		
Date of issue	17th April 2019	**Implementation deadline**	CCGs are required to comply with the recommendations within 3 months. (17th July 2019)

Medicine details[1,2]	
Name, brand name	Tildrakizumab (Ilumetri) Mechanism of action – Interleukin (IL) 23 protein
Manufacturer	Almirall
Licensed indication	Ilumetri is indicated for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy.
Formulation	Pre-filled syringe contains 100mg/1mL solution for injection
Usual dosage	The recommended dose of Ilumetri is 100 mg by subcutaneous injection at weeks 0, and 4 and every 12 weeks thereafter. In patients with certain characteristics (e.g. high disease burden, body weight ≥ 90 kg) 200 mg may provide greater efficacy. Consideration should be given to discontinuing treatment in patients who have shown no response after 28 weeks of treatment. Some patients with initial partial response may subsequently improve with continued treatment beyond 28 weeks.
NICE recommended dosage/schedule	As above

Disease and potential patient group

<table>
<tr><td>Brief description of disease[3]</td><td>https://patient.info/skin-conditions/psoriasis-leaflet
Psoriasis is a common condition where there is inflammation of the skin. It typically develops as patches (plaques) of red, scaly skin. Once it develops psoriasis it tends to come and go throughout life. A flare-up can occur at any time. The frequency of flare-ups varies. There may be times when psoriasis clears for long spells. However, in some people the flare-ups occur often. Psoriasis is not due to an infection. It cannot be passed on to other people and it does not turn into cancer. The severity of psoriasis varies greatly. In some people it is mild with a few small patches that develop and are barely noticeable. In others, there are many patches of varying size. In many people the severity is somewhere between these two extremes. However, with an early diagnosis and appropriate treatment, it's possible to slow down the progression of the condition and minimise or prevent permanent damage to the joints.</td></tr>
<tr><td>Potential patient numbers per 100,000</td><td>www.nice.org.uk
Resource impact template
<table>
<tr><th>Population</th><th>NICE assumption (%)</th><th>Number of people</th></tr>
<tr><td>Adult population per 100,000</td><td></td><td>78,666</td></tr>
<tr><td>Prevalence of psoriasis</td><td>1.75</td><td>1,377</td></tr>
<tr><td>Proportion with plaque psoriasis</td><td>90</td><td>1,239</td></tr>
<tr><td>People eligible for biologic treatments</td><td>2.55</td><td>32</td></tr>
</table>
Tildrakizumab will be another treatment option for Psoriasis.

Currently there are 3 lines of treatment (after standard systemic treatments) available in the psoriasis pathway in line with national guidance.

Choices are from 10 drugs with 7 different mechanisms of action. Specialists should choose a drug with a different mode of action with each line of treatment.</td></tr>
</table>

SUMMARY

NICE recommendation www.nice.org.uk

1. Recommendations
   1.1. Tildrakizumab is recommended as an option for treating plaque psoriasis in adults, only if:
   - the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and
   - the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these

options are contraindicated or not tolerated
    - and the company provides the drug according to the commercial arrangement.

1.2. Consider stopping tildrakizumab between 12 weeks and 28 weeks if there has not been at least a 50% reduction in the PASI score from when treatment started.

1.3. Stop tildrakizumab at 28 week if the psoriasis has not responded adequately. An adequate response is defined as:
    - a 75% reduction in the PASI score (PASI 75) from when treatment started or
    - a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.

Medicines management team comments:
All treatments within the biologic treatment pathway require a review between 12 & 16 weeks and then are seen again on a 6 monthly basis. See question below for APC to consider in recommendations

1.4. If patients and their clinicians consider tildrakizumab to be one of a range of suitable treatments, the least expensive should be chosen (taking into account administration costs, dosage, price per dose and commercial arrangements).

1.5. When using the PASI, healthcare professionals should take into account skin colour and how this could affect the PASI score, and make the clinical adjustments they consider appropriate.

1.6. When using the DLQI, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DLQI and make any adjustments they consider appropriate.

1.7. These recommendations are not intended to affect treatment with tildrakizumab 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

Treatment for moderate to severe plaque psoriasis includes systemic biological treatments for disease that does not respond to systemic non-biological treatments. Tildrakizumab is proposed as an alternative to other systemic biological treatments already recommended by NICE.

Clinical trial results show that tildrakizumab improves severe plaque psoriasis compared with placebo or etanercept. More improvement is usually seen at 28 weeks compared with 12 weeks of treatment. When compared indirectly, tildrakizumab appears to be as effective as adalimumab and ustekinumab but not as

effective as other biological treatments.

The most plausible cost-effectiveness estimates for tildrakizumab compared with most other available biological treatments show that it is generally cost effective. Therefore, tildrakizumab is recommended as an option for use in the NHS for severe psoriasis that has not responded to systemic non-biological treatments, or if these are contraindicated or not tolerated.

Medicines management team comments:

PASI: The Psoriasis Area Severity Index (PASI) is an index used to express the severity of psoriasis.
It combines the severity (erythema, induration and desquamation) and percentage of affected area.

DLQI: The Dermatology life Quality Index (DLQI) is a ten-question questionnaire used to measure the impact of skin disease on the quality of life of an affected person.

Cost implications*

Cost of product:
£3241 per 100 mg/200mg (pack size) pre-filled syringe (excluding VAT, British national formulary online; accessed April 2019). The company has a **commercial arrangement.**

Annual cost per patient:
Year 1:
Injections (100mg) at 0 & 4 weeks (induction) and then every 12 weeks thereafter (5 injections) = £16,205 (if provided via homecare then VAT not applicable

Year 2:
12 weekly injections (total 4 injections) = £12,964

Patients with high disease burden or body weight over 90kg will be considered for the 200mg dose but the company provide that at the same cost as the 100mg dose

Treatment schedule	Cumulative cost over time
4 weeks (induction)	**£ 6,482**
12 weeks (induction only received at this point)	**£ 6,482**
16 weeks (induction plus 1st , 12 weekly dose)	**£ 9,723**
28 weeks (induction plus 1st & 2nd , 12 weekly dose)	**£12,964**

Availability of PAS and details (if appropriate): www.nice.org.uk
The company has a commercial arrangement. This makes tildrakizumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the

discount.

Availability of homecare service (if appropriate):
Home care service is available

**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.*

Alternative treatments available with the psoriasis pathway

TNF-Alpha inhibitors
- adalimumab, etanercept & infliximab **(& certolizumab)**

Fumaric Acid Ester
- dimethyl fumarate

Phosphodiesterase (PDE4) inhibitor
- apremilast

Interleukin 17RA inhibitor
- brodalumab

Interleukin 17 inhibitor
- secukinumab & izekizumab

Interleukin (IL)23 protein
- guselkumab (**& tildrakizumab)**

Interleukin (IL)12/23 inhibitor
- ustekinumab

Clinical effectiveness: **www.nice.org.uk**
NICE concluded that tildrakizumab was more clinically effective than placebo and etanercept.

Impact to patients

- An additional treatment option for plaque psoriasis would be valued by patients.

Impact to primary care prescribers

- This is a PbRe drug 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 tildrakizumab 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 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.
- An additional treatment option for plaque psoriasis would be valued by clinicians.
- Blueteq forms for initiation and continuation will need to be completed by dermatology specialists.

Impact to CCGs

- The technology is commissioned by clinical commissioning groups (CCGs).
- Providers are NHS hospital trusts.
- Tildrakizumab is PbRe and if a patient meets NICE criteria, treatment can be

initiated and invoiced to the commissioner (if Blueteq forms have been completed).
- Revision of the psoriasis pathway discussed with dermatology specialist teams prior to APC discussion

Implementation

- NICE TA implementation must be within 90 days of publication – 17th July 2019
- Blueteq forms to be developed

Recommendation to PCN

APC to consider

- **RED TRAFFIC LIGHT STATUS –** Blueteq forms for initiation and continuation will be developed for specialists to complete.

APC/Dermatology clinical network has two questions to consider

- Patients have a clinical review (face to face) between weeks 12 - 28 to check PASI has dropped in line with NICE thresholds and then again at week 28 to check NICE thresholds continue to be met, then 6 monthly thereafter OR
- Continue to treat a patient until week 28 (6.5 months) , when there will be a face to face clinical review, but the patients treatment may not have met NICE thresholds and the patient could have continued to be treated without full benefit.

References:

1. www.medicines.org
2. NICE www.nice.org.uk
3. What is psoriasis? Patient Platform Ltd. Available at: https://patient.info/health/psoriasis-leaflet
4. Resource impact statement & template www.nice.org.uk
5. NHS choices www.nhs.uk

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Declaration of Interest:

None

Date: 16/07/2018

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
v.1		*Clare Johns*	*Draft*	*For peer review prior to consultation with specialist teams and APC*