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 Prescribing Clinical Network on NICE Technology Appraisals: Local implementation

NICE TA Guidance	Apremilast for treating moderate to severe plaque psoriasis Technology appraisal guidance 419		
Available at	**https://www.nice.org.uk/guidance/ta419/resources/apremilast-for-treating-moderate-to-severe-plaque-psoriasis-82604611623877**		
Date of issue	23 November 2016	**Implementation deadline**	23 February 2017

Medicine details[1]	
Name, brand name and manufacturer	Apremilast (Otezla) Celgene **Mode of action:** Inhibits the activity of Phosphodiesterase Type-4 Inhibitor (PDE4) which results in suppression of pro-inflammatory mediator synthesis and promotes anti-inflammatory mediators[1].
Licensed indication	**www.medicines.org.uk** **Psoriasis** Otezla is indicated for the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or psoralen and ultraviolet-A light (PUVA).
Formulation	Film coated tablet
Usual dosage	The recommended dosage is 30 mg twice daily after an initial titration schedule. A single 10 mg dose is given on the first day of treatment; this is titrated to 30 mg twice daily over 5 days (see the summary of product characteristics for the dose titration schedule at **www.medicines.org.uk** This is the current dose considered by NICE as part of the NICE evaluation. Subsequent changes in the license following NICE publication will need to be considered by the Prescribing Clinical Network and will not be routinely funded by local commissioners

Disease and potential patient group[2]	
Brief description of disease	**www.patient.co.uk** What is psoriasis? Psoriasis is a common condition where there is inflammation of the skin. It typically develops as patches (plaques) of red, scaly skin. Once you develop 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. You cannot pass it 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.
Potential patient numbers per 100,000	**www.nice.org.uk** **CG153 Psoriasis – Diagnosis and Management (2012)** In the costing template for this guideline the estimated prevalence of Psoriasis per 100,000 population is 1750 Apremilast is not a biologic treatment but NICE anticipate that Apremilast will be a treatment option alongside the biologic treatments The Resource impact statement for NICE TA419 states[2]: No resource impact is anticipated We do not expect this guidance to have an impact on resources. This is because the technology is a further option alongside current standard treatment options, and we are not expecting a significant change to current practice because of this guidance.

SUMMARY

Guidance

1. Recommendations:

1.1. Apremilast is recommended as an option for treating chronic plaque psoriasis in adults whose disease has not responded to other systemic therapies, including ciclosporin, methotrexate and PUVA (psoralen and ultraviolet-A light), or when these treatments are contraindicated or not tolerated, only if:

- the disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10
- treatment is stopped if the psoriasis has not responded adequately at 16 weeks; 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 start of treatment
- the company provides apremilast with the discount agreed in the patient access scheme.

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

1.3. This guidance is not intended to affect the position of patients whose treatment with apremilast was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

Cost implications

Cost:

The price of apremilast is £550.00 for a 28-day pack (56×30 mg tablets) (excluding VAT; British National Formulary online, accessed July 2016).

Titration pack £265.18 (Current available MIMS price **www.mims.co.uk/drugs**)

Annual cost per patient:
The recommended dose of Otezla is 30 mg twice daily taken orally, morning and evening, approximately 12 hours apart, with no food restrictions. An initial titration schedule is required. No re-titration is required after initial titration.

Availability of PAS and details (if appropriate):
The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of apremilast, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

Availability of homecare service (if appropriate):
Not appropriate.

Alternative treatments and cost per patient per year

Other NICE recommended products:
Based on the list price:

1st year (including loading dose) (All via homecare so no VAT except infliximab which is given by intravenous infusion in hospital and a day care tariff will be applied)

TNF-alpha inhibitors
Adalimumab (Humira) - **£9,115**
Etanercept (Enbrel) - **£9,295** (there has been a recent discount applied to this product)
Etanercept (Benepali – Biosimilar) – **£8,528**
Infliximab (Remicade, Inflectra, Remsima) (weight based dosing average adult weight 76kg) – **(£14.5k - £20k inclusive of VAT)**

Interleukin inhibitors
Secukinumab (Cosentyx -IL17a) - **£9,750**
Ustekinumab (Stelara – IL23a) - **£10,735**

Impact to patients

- Apremilast is an oral treatment, so this may be patient preference over the subcutaneous or intravenous infusions of the biologic treatments.

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 apremilast in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care.

Impact to secondary care

- The initiation, administration and on-going treatment is managed by secondary care.
- Patients should be reviewed by a specialist every 6 months for monitoring purposes (potential adverse effects, patient compliance & NICE compliance (response to treatment)
- Prescribers would welcome additional options to treat moderate to severe plaque psoriasis
- There is advantage over biological agents is that it is not contraindicated in people with tuberculosis[2].
- Apremilast has a different mode of action to the current treatment options

Impact to CCGs

- The technology is commissioned by clinical commissioning groups (CCGs).

• Providers are NHS hospital trusts.
Implementation
• NICE TA implementation must be within 90 days of publication – 23 February 2017 • Blueteq forms to be developed • Pathway to be discussed with Dermatologists for agreement on place in therapy. • The NICE committee recognised that apremilast was less effective than biological therapies, but that patient preference (mainly relating to method of administration) would influence whether it would be an appropriate treatment option. • The marketing authorisation for apremilast allows it to be positioned before, instead of, and after biological therapies. However, clinical experts did not consider that apremilast would displace a biological therapy in the treatment pathway, and agreed that the positioning of apremilast (either before or after biological therapy) would be largely driven by patient choice and intolerance or contraindications to biological therapy
Recommendation to PCN
PbRe: Yes **Recommended traffic light status:** **Red** **Additional comments:** Treatment option in line with Psoriasis treatment pathway.

References:

1. British National Formulary No:72 September 2016 – March 2017
2. **www.nice.org.uk** Apremilast for treating moderate to severe plaque psoriasis (NICE TA 419)

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
V1	16/12/2016	Clare Johns	Draft	Circulation (with proposed treatment pathway) to the local dermatologists and PCN network members for consideration of place in therapy.

Email to PCN members and specialists on 28th December 2016

Dear All

Please find attached a briefing paper and proposed Psoriasis treatment pathway following the publication of NICE TA419 recently. These have been produced for consideration at the Prescribing Clinical Network (PCN) on 1st February 2017.

Please include any comments to me by Friday 20th January 2017. If there are any other colleagues that you feel we need to engage with please also let us know their names and where/how they can be contacted.

Please note that for anyone commenting on the documents, Declarations of Interest will be required to be submitted for each person (using the declaration form attached) or your comments will not be able to be taken into consideration by the PCN.

Any comments and additional information received from you will be incorporated into the papers and circulated to the PCN member for consideration at the meeting.

It is important that we receive your input and we value your comments. Decisions made at the PCN will affect the treatment of your patients. Please note that if you do not use this opportunity to give your feedback, it will be assumed that you do not disagree with its contents.

The PCN values clinician input and welcomes their attendance at the meeting and if you like to attend to support the review you are most welcome, however, due to limited meeting room capacity, we would recommend the nomination of one clinician to represent the group, please contact me if you like to attend.

Thank you for your time and for assisting the PCN in making cost-effective, evidence-based recommendations for the treatment of our patients.

We look forward to hearing from you. If you have any questions, please let us know.

Comments received:

Comment from Dr Colin Holden Dermatologist from Epsom & St Helier University Hospitals NHS Trust

The documents seem ok

Why do we have to reapply every 6 months? I think annually should be appropriate. Does this mean we don't have to refer to a centre of excellence before using a third drug? I have no links with any companies.

Regards

Colin Holden

……

Comments to Dr Holden from the lead author

Hi Dr Holden

Many thanks for your comments much appreciated. The 6 monthly clinical review is historical, but in Rheumatoid Arthritis NICE requires review at least every 6 months and as the same class of drugs are being used for Rheumatology & Dermatology it made sense for clinical review every 6 months for other specialities.

You mention that you believe that 12 monthly clinical reviews would be appropriate and in order to consider changing the clinical review from 6 monthly to 12 monthly the commissioners would probably want some information from the specialists to assure that by doing so the patients would not be under any increased risk by moving from 6 monthly to 12 monthly clinical reviews. More than

happy to ask the commissioners but will need help from you and your colleagues as I would need to take a recommendation to a future Prescribing Clinical Network.

How often do patients come to clinic currently and what measurements are made to access their disease control?

With regards your other question, 3rd line treatment does not require you to refer to a centre of excellence, the forms are available on blueteq if 3rd line treatment is clinically appropriate. I did a piece of work last year and it was highlighted that all local specialists were referring patients up to tertiary centres (usually Guys) for initiation of a 3rd line biologic. We have the specialists locally and it made sense to commission initiation of 3rd line biologics at local centres. This was approved by the commissioners in the summer last year and was noted at the New Drugs and Interface Group in the trust.

We have clinical networks for Rheumatology, Gastroenterology & Ophthalmology, where local consultants in each of these areas meet to discuss service developments, pathways and new treatments, what do you think the appetite would be for the Surrey dermatologists to meet? Do you meet altogether anywhere, currently?

Thanks again for your comments

……

Comment from Dr Colin Holden Dermatologist from Epsom & St Helier University Hospitals NHS Trust

We review our patients at least 6 monthly and more frequently if required to give them appropriate clinical care. What I am querying is why we have to apply for continuation of funding every time we review them. If the drug is failing clearly we will apply for a change. Other areas of the country don't require 6 monthly updates for funding. It is creating a huge amount of excessive administration for us and you. I dont see why we can't apply for continuation of funding on an annual basis.
Regards
Colin Holden

……

Comments from Elizabeth Wong MD, FRCP, Consultant Dermatologist, Concordia Community Outpatients

It would be useful to have this oral medication, the only one available that is not a cytotoxic for our severe psoriasis cases who fail other systemics; I have personally know 4 successfully treated patients out of 7 tried; one of them only needed 30 mg once a week as recommended dose caused side effects.
However it should be a hospital prescribed drug only due to severe side effects reported!

……

Comments from Dr Imran consultant dermatologist ASPH

It would be useful to have apremilast as systemic treatment in those cases where other systemics are contraindicated .I recently have one patient with severe psoriasis was on methotrexate .He now has melanoma excised so immunosuppresive and anti TNF contraindicated so it would be great to have this as a sytemic agent .

Regards