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 active psoriatic arthritis NICE Technology appraisal guidance 433 This appraisal was a rapid review of the published NICE technology appraisal guidance on apremilast for treating psoriatic arthritis (TA372). It focused on cost-effectiveness analyses using a patient access scheme agreement, which provides apremilast at a reduced cost.		
Available at	https://www.nice.org.uk/guidance/ta433		
Date of issue	22 February 2017	**Implementation deadline**	22 May 2017

Medicine details[1]

Name, brand name and manufacturer

Apremilast (Otezla)
Celgene

Apremilast is a small-molecule inhibitor of phosphodiesterase 4 (PDE4). It down-regulates the inflammatory response by modulating the expression of inflammatory and anti-inflammatory cytokines and mediators associated with psoriatic arthritis (including tumour necrosis factor [TNF]-alpha and interleukin [IL]-23).

Licensed indication

Otezla, alone or in combination with Disease Modifying Antirheumatic Drugs (DMARDs), is indicated for the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior DMARD therapy.

Formulation

Each film-coated tablet contains 30 mg of apremilast.

Usual dosage

After the initial six day titration, the recommended dose of apremilast is 30 mg twice daily taken orally, morning and evening, approximately 12 hours apart, with no food restrictions.

Table 1: Dose titration schedule

Day 1	Day2		Day 3		Day 4		Day 5		Day 6 & thereafter	
AM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
10 mg	10 mg	10 mg	10 mg	20 mg	20 mg	20 mg	20 mg	30 mg	30 mg	30 mg

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

Brief description of disease[2]

Psoriatic arthritis is a type of arthritis that develops in some people with the skin condition psoriasis. It typically causes affected joints to become inflamed (swollen), stiff and painful.

Like psoriasis, psoriatic arthritis is a long-term condition that can get progressively worse. In severe cases, there's a risk of the joints becoming permanently damaged or deformed, which may require surgical treatment.

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.

Potential patient numbers per 100,000[3]

The population eligible for apremilast is assumed to be people with active psoriatic arthritis who are eligible for TNF inhibitors.

Table 1: Number of people eligible for treatment with apremilast in England.

Population	Proportion of previous row (%)	Number of people
Total adult population		42,724,917
People with psoriatic arthritis[a]	0.65	278,000
People who can have TNF-alpha inhibitors[a]	2.4	6,700
People eligible for apremilast	100	6,700
People estimated to be treated with apremilast each year from 2018/19[b]	10	670

a. Ustekinumab for treating active psoriasis: TA340
b. Expert opinion[3]

Table 2: Potential number of patients eligible for treatment with apremilast at CCG level (using national assumptions as per Table 1):

CCG	Population	Prevalence of psoriatic arthritis	Proportion of patients who can have TNF-alpha inhibitors	Eligible population for apremilast
Crawley	83,931	546	13	13
East Surrey	139,837	909	22	22
Guildford and Waverley	165,066	1073	26	26
Horsham and Mid-Sussex	177,808	1156	28	28
North West Surrey	266,608	1733	42	42
Surrey Downs	222,523	1446	35	35
Surrey Heath	74,455	484	12	12

SUMMARY

Guidance[4]

Recommendations:

1.1 Apremilast, alone or in combination with disease-modifying antirheumatic drugs (DMARDs), is recommended as an option for treating active psoriatic arthritis in adults only if:

- they have peripheral arthritis with 3 or more tender joints and 3 or more swollen joints and
- their disease has not responded to adequate trials of at least 2 standard DMARDs, given either alone or in combination and
- the company provides apremilast with the discount agreed in the patient access scheme.

1.2 Stop apremilast at 16 weeks if the psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis response Criteria (PsARC), defined as an improvement in at least 2 of the 4 PsARC criteria (including joint tenderness or swelling score) with no worsening in any criteria. If the disease has a Psoriasis Area and Severity Index (PASI) 75 response, a dermatologist should decide whether to continue treatment with apremilast after 16 weeks based on skin response.

1.3 When using the PsARC healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate.

1.4 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.

Additional information from NICE TA 433: Committee discussion and summary of appraisal committee's key conclusion.

Section 4.8
The committee concluded that apremilast is not as clinically effective as the TNF-alpha inhibitors for treating psoriatic arthritis.

Section 4.10
The committee concluded that the lack of radiographic evidence and the clinical-effectiveness evidence did not support the use of apremilast before TNF-alpha inhibitors in clinical practice.

Section 4.21
…(that is, when compared with TNF-alpha inhibitors, apremilast cost less but was also the least effective treatment), and also because of the limited evidence presented by the company. The committee agreed that the ICER [incremental cost-effectiveness ratio] for apremilast was not high enough to compensate for the clinical effectiveness that would be lost. It therefore concluded that apremilast could not be recommended as a treatment after TNF-alpha inhibitors. It was unable to make recommendations for its use when people cannot take TNF-alpha inhibitors, because of a lack of evidence for its use in these circumstances.

Section 4.30
The committee agreed that some patients may be willing to accept a certain level of reduced

effectiveness because apremilast, unlike the TNF-alpha inhibitors and ustekinumab, is taken orally. The committee therefore agreed that apremilast could improve patient choice while also offering the opportunity of cost savings for the NHS (with cost savings at a more acceptable level given the QALY gain that would be lost). It concluded that apremilast could be recommended as a cost-effective use of NHS resources.

Cost implications[3,4,5]

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

Annual cost per patient:
The annual cost of treatment is £550.00 x 12 = £6,600 (excluding VAT and without PAS).

Table 3: Resource impact for uptake of apremilast per CCG for 2020/21 (excluding VAT and without PAS).[5]

CCG	Current practice	No of patients on apremilast	Future practice	Resource impact
Crawley	£ 119,941	1	£ 117,308	-£ 2,633
East Surrey	£ 199,832	2	£ 195,447	-£ 4,385
Guildford and Waverley	£ 235,886	3	£ 230,709	-£ 5,177
Horsham and Mid-Sussex	£ 254,094	3	£ 248,518	-£ 5,576
North West Surrey	£ 380,993	4	£ 372,631	-£ 8,362
Surrey Downs	£ 317,994	3	£ 311,015	-£ 6,979
Surrey Heath	£ 106,399	1	£ 104,064	-£ 2,335

Current practice is defined as the drug costs for patients having adalimumab, etanercept, infliximab and golimumab plus the administration costs for patients having infliximab (with 0 patients on apremilast).[5]

Future practice is defined as the drug costs for patients having adalimumab, etanercept, infliximab and golimumab plus the administration costs for patients having infliximab plus patients having apremilast.[5]

Using the list price of apremilast, the drug is cost saving for the NHS. The potential cost saving to the CCGs listed is £35,447.

Availability of PAS and details (if appropriate):
Yes. 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):
Yes

Alternative treatments and cost per patient per year[5]

Other NICE recommended products:

Drug cost	Purchase quantity (taken from BNF)	Cost taken from BNF.	Cost per dose	Quantity per dose	Weekly cost	Annual Cost
Adalimumab	2 pre filled packages : 50 mg/1ml	£704.28	£352.14	50 mg BI weekly	£176.07	£9,156
Etanercept	4 pre filled packages : 50 mg/1ml	£656.00	£164.00	50 mg once weekly	£164.00	£8,528
Infliximab	100 mg/1ml	£377.00	£377.00	4 Vials every 8 weeks	£188.50	£9,802
Golimumab	50 mg/1ml	£762.97	£762.97	50 mg once monthly	£176.07	£9,156
Apremilast	56, 30mg tablets	£550.00	£9.82	30 mg twice daily	£137.50	£7,150

Options not reviewed by NICE but used in standard practice:
N/A

Impact to patients

- An additional treatment option for psoriatic arthritis would be valued by patients.
- Apremilast is available under a homecare service so will be delivered directly to the patient. This reduces the number of hospital appointments to those required for review and/or monitoring.
- Apremilast is a tablet taken orally twice daily – unlike the TNF-alpha inhibitors and ustekinumab.
- Some patients may be willing to accept a certain level of reduced effectiveness because apremilast is taken orally.

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.
- Homecare arrangements will be managed by the trust.
- Apremilast is available on homecare and patients will only require appointments for review and/or monitoring.
- An additional treatment option for psoriatic arthritis would be valued by clinicians.

Impact to CCGs

- The technology is commissioned by clinical commissioning groups (CCGs).
- Providers are NHS hospital trusts.
- Potential savings for out-patient appointments as apremilast is available on homecare.

Implementation

- NICE TA implementation must be within 90 days of publication – 22 May 2017
- Blueteq forms to be developed
- Trusts to initiate homecare
- Revision to psoriatic arthritis pathway discussed at Rheumatology Network meeting in March 2017 and amendments made to the pathway. Following another consultation period, the pathway has been agreed by the members of the network.

Recommendation to PCN
PbRe: Y **Recommended traffic light status:** RED **Additional comments:**

References:

1 Specification of Product Characteristics. Otezla 30mg tablets. Available at: https://www.medicines.org.uk/emc/medicine/29792 Accessed <23.2.17>

2 NHS Choices. Psoriatic arthritis. Available at: http://www.nhs.uk/conditions/psoriatic-arthritis/Pages/Introduction.aspx Accessed <23.2.17>

3 NICE Resource impact report: Apremilast for treating active psoriatic arthritis (TA433). Published 22 February 2017. Available at: https://www.nice.org.uk/guidance/ta433/resources/resource-impact-report-4367148013 Accessed <23.2.17>

4 NICE Technology appraisal 433: Apremilast for treating active psoriatic arthritis. Published 22 February 2017. Available at: https://www.nice.org.uk/guidance/ta433 Accessed <23.2.17>

5 NICE Resource impact template: Apremilast for treating active psoriatic arthritis (TA433). Published 22 February 2017. Available at: https://www.nice.org.uk/guidance/ta433/resources Accessed <23.2.17>

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Declaration of Interest:

None.

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Reviewed by:

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VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
1	28.2.17	T. Bahra	Draft	Ready for review.
2	6.3.17	T. Bahra	Draft	Incorporate comments (SW)
3	25.4.17	T. Bahra	FINAL	Incorporate final comments