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	Brodalumab for treating moderate to severe plaque psoriasis (TA 511)		
Available at	https://www.nice.org.uk/guidance/ta511/resources/brodalumab-for-treating-moderate-to-severe-plaque-psoriasis-pdf-82606774969285		
Date of issue	21 March 2018	**Implementation deadline**	21 June 2018

Medicine details[1,2]	
Name, brand name	Brodalumab (Kyntheum®) Mechanism of action www.medicines.org.uk Brodalumab is a recombinant fully human monoclonal immunoglobulin IgG2 antibody that binds with high affinity to human IL-17RA and blocks the biological activities of the pro-inflammatory cytokines IL-17A, IL-17F, IL-17A/F heterodimer and IL-25, resulting in inhibition of the inflammation and clinical symptoms associated with psoriasis. IL-17RA is a protein expressed on the cell surface and is a required component of receptor complexes utilized by multiple IL-17 family cytokines. IL-17 family cytokine concentrations have been reported to be increased in psoriasis. Blocking IL-17RA inhibits IL-17 cytokine-induced responses resulting in normalization of inflammation in the skin. www.nice.org.uk The committee understood that brodalumab targets the same pathway as, but has a different mechanism of action from, other interleukin-17 inhibitors; it targets a different part of the pathway. However, the committee concluded that, without evidence on the benefit of targeting a specific part of the pathway, there were no additional gains in health-related quality of life over those already included in the QALY calculations.
Manufacturer	Leo Pharma
Licensed indication	Brodalumab (Kyntheum®) is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy
Formulation	Pre-filled syringe contains 210 mg brodalumab in 1.5 ml solution
Usual dosage	The recommended dose is 210 mg (1.5ml) administered by subcutaneous injection at weeks 0, 1, and 2 followed by 210 mg every 2 weeks. Consideration should be given to discontinuing treatment in patients

	who have shown no response after 12-16 weeks of treatment. Some patients with initial partial response may subsequently improve with continued treatment beyond 16 weeks.
NICE recommended dosage/schedule	As above

Disease and potential patient group

Brief description of disease[3]

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.

Potential patient numbers per 100,000

www.nice.org.uk Resource impact template

Population	NICE assumption(%)	Number of people
Adult population per 100,000		78,674
Prevalence of psoriasis	1.75	1,377
Proportion with plaque psoriasis	90	1,239
People eligible for biologic treatments	2.55	32
People estimated to be treated with brodalumab over time (5 years)	9	3

SUMMARY

NICE recommendation www.nice.org.uk

1. Recommendations

1.1. Brodalumab 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 therapies, including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet A radiation), or these options are contraindicated or not tolerated and
- the company provides the drug with the discount agreed in the patient access scheme.

1.2. Stop brodalumab at 12 weeks if the psoriasis has not responded adequately, 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.

1.3. 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.

1.4. 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.

1.5. These recommendations are not intended to affect treatment with brodalumab 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.

Committee discussion:
Position of brodalumab in the treatment pathway
Brodalumab is most likely to be used fourth line as an alternative to systemic biologic therapies apremilast and dimethyl fumarate.

The marketing authorisation for brodalumab is for 'adults who are candidates for systemic therapy'. However, the company positioned brodalumab fourth line, as an alternative to biological therapies, apremilast and dimethyl fumarate. One clinical expert confirmed that this is the stage in therapy at which NHS clinicians would most likely use brodalumab. **The committee concluded that it would appraise brodalumab as a fourth-line therapy, which is when other biological therapies, apremilast and dimethyl fumarate are current treatment options.**

Medicines Management team clarification: Fourth line denotes treatment as follows (taken from NICE guidance:

- **1st line: Topical therapies**
- **2nd line: phototherapy**
- **3rd line: systemic conventional non-biologic therapies (such as methotrexate, ciclosporin or acitretin)**
- **4th line: to include systemic biological therapies (such as adalimumab, etanercept, ixekizumab, infliximab, secukinumab or ustekinumab), apremilast or dimethyl fumarate**

Cost implications*

Cost of product:
£1,280 per pack of 2 syringes of 210mg/1.5ml solution (excluding VAT, British National Formulary (BNF) online (accessed January 2018)

Annual cost per patient:
The estimated annual cost of treatment in the year 1 (with induction) is £17,920 (via homecare so no VAT and without PAS).

Year 2 onwards estimated cost of treatment will be £7,680 (210mg x 12 injections)

Availability of PAS and details (if appropriate): www.nice.org.uk
The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of brodalumab, 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
Leo pharma have nominated HealthNet & Lloyds Homecare)

**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 PCN may reconsider the commissioning status.*

Alternative treatments and cost per patient (per year / per month as appropriate)

Other NICE recommended products:
Based on the list price:

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

Prices below are before PAS prices have been applied. The prices of all the biosimilars have further reduced recently but these prices are commercially confidential

Drug cost	**Purchase quantity (taken from BNF)**	**Cost taken from BNF.**	**Cost per dose** (after induction)	**Quantity per dose**	**Annual Cost in year 1**
Adalimumab (Humira)	2 pre filled packages : 50 mg/1ml	£704.28	£352.14	50 mg BI weekly	£9,156
Etanercept (biosimilar cost)	4 pre filled packages : 50 mg/1ml	£656.00	£164.00	50 mg once weekly	£5,300
Infliximab (biosimilar cost)	100 mg/1ml	£377.00	£377.00	4 Vials every 8 weeks	£9,802
Ustekinumab (Stelara)	1 pre-filled syringe: 90mg/ml	£2147.00	£2147.00	45mg-90mg every 12 weeks (weight based dosing)	£8,588
Ixekizumab (Taltz)	1 pre filled pen/syringe 80mg/ml	£1125.00	£1125.00	80mg every 4 weeks	£14,625
Apremilast	56x 30mg tablets	£550.00	£9.82	30 mg twice daily	£7,150
Dimethyl Fumarate	90 x 120mg tablets	£190.80	Average maintenance dose up to 480mg/day £8.48	Average maintenance dose up to 480mg (4 tablets per day	£3,086.72

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 brodalumab 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. • Leo Laboratories have nominated 2 homecare providers (HealthNet and Lloyds Homecare) • 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. • Caution should be exercised when prescribing brodalumab to patients with a history of Crohn's disease. Patients with a history of Crohn's disease should be followed for signs and symptoms of active Crohn's disease. If patients develop active Crohn's disease, treatment should be discontinued permanently.
Impact to CCGs
• The technology is commissioned by clinical commissioning groups (CCGs). • Providers are NHS hospital trusts. • Brodalumab 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 PCN discussion
Implementation
• NICE TA implementation must be within 90 days of publication – 21 June 2018 • Blueteq forms to be developed
Recommendation to PCN
PbRe: Y **Recommended traffic light status** • **RED –** Blueteq forms for initiation and continuation will be developed for specialists to complete.

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: 24/04/2018

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Declaration of Interest: None

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VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
v.1	*17/04/2018*	*Clare Johns*	*Draft*	*For peer review prior to consultation with specialist teams and PCN*
2	*26.4.18*	*Tejinder Bahra*	*Draft*	*Peer review:* *Minor amendments and format changes* *Guidance on referencing*