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	Dupilumab for treating moderate to severe atopic dermatitis (NICE TA 534		
Available at	https://www.nice.org.uk/guidance/ta534/resources/dupilumab-for-treating-moderate-to-severe-atopic-dermatitis-pdf-82606900940485		
Date of issue	1st August 2018	**Implementation deadline**	CCGs are required to comply with the recommendations within 3 months. (1st November 2018) However, because dupilumab has been recommended through the early access to medicines process, commissioners have agreed to provide funding to implement this guidance 30 days after publication. (1st September 2018

Medicine details [1,2]	
Name, brand name	Dupilumab (Dupixent)
Manufacturer	Sanofi Genzyme
Licensed indication	www.medicines.org.uk Dupixent is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy.
Formulation	Dupilumab 300 mg solution for injection in pre-filled syringe
Usual dosage	The recommended dose of dupilumab for adult patients is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every other week administered as subcutaneous injection.
NICE recommended dosage/schedule	As above

Disease and potential patient group [2,3]	
Brief description of disease	**www.nhs.uk** Atopic eczema (atopic dermatitis) is the most common form of eczema, a condition that causes the skin to become itchy, red, dry and cracked. Atopic eczema is more common in children, often developing before their first birthday. However, it may also develop for the first time in adults.

<table>
<tr><td></td><td>It's usually a long-term (chronic) condition, although it can improve significantly, or even clear completely, in some children as they get older.</td></tr>
<tr><td>Potential patient numbers per 100,000</td><td>
<u>www.nice.org.uk</u>

Resource impact template at year 5

<table>
<tr><th>Population*</th><th>NICE assumption (%)</th><th>Number of people</th></tr>
<tr><td colspan="2">Adult population per 100,000</td><td>78,672</td></tr>
<tr><td>Prevalence of atopic dermatitis</td><td>2.5%</td><td>1,967</td></tr>
<tr><td>People diagnosed and having treatment</td><td>69%</td><td>1,357</td></tr>
<tr><td>People with moderate to severe atopic dermatitis</td><td>7%</td><td>95</td></tr>
<tr><td>People with moderate to severe atopic dermatitis eligible for systemic therapy</td><td>27%</td><td>26

In line with NICE guidance, where systemic therapy is indicated, patients will be treated with systemic immunosuppressants prior to treatment with dupilumab)</td></tr>
<tr><td>People with moderate or severe atopic dermatitis in whom systemic therapy has failed or is contraindicated</td><td>53%</td><td>14</td></tr>
</table>

Future practice**
<table>
<tr><td>People on best supportive care
Defined by the company as emollients, low to mid potency topical corticosteroids and rescue therapy with higher potency topical or oral corticosteroids or topical calcineurin inhibitors. Phototherapy and psychological support was also included</td><td>40%</td><td>5</td></tr>
<tr><td>People having dupilumab</td><td>60%</td><td>8</td></tr>
</table>

*Company submission
**Clinical opinion
</td></tr>
</table>

SUMMARY

NICE recommendation www.nice.org.uk

1. Recommendations

1.1. Dupilumab is recommended as an option for treating moderate to severe atopic dermatitis in adults, only if:

- the disease has not responded to at least 1 other systemic therapy, such as ciclosporin, methotrexate, azathioprine and mycophenolate mofetil, or these are contraindicated or not tolerated
- the company provides dupilumab according to the commercial arrangement.

1.2. Stop dupilumab at 16 weeks if the atopic dermatitis has not responded adequately. An adequate response is:

- at least a 50% reduction in the Eczema Area and Severity Index score (EASI 50) from when treatment started and
- at least a 4-point reduction in the Dermatology Life Quality Index (DLQI) from when treatment started.

1.3. When using the EASI, healthcare professionals should take into account skin colour and how this could affect the EASI 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 dupilumab 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

Current systemic treatment for moderate to severe atopic dermatitis (eczema) includes ciclosporin, methotrexate, azathioprine and mycophenolate mofetil. Dupilumab would be used after these treatments no longer work, and best supportive care is the only other available option. Dupilumab would likely be offered alongside topical corticosteroids.

The clinical evidence shows that dupilumab is very effective when used in this way. The most plausible cost-effectiveness estimates for dupilumab plus topical corticosteroids compared with best supportive care are within the range that NICE normally considers an acceptable use of NHS resources.

Cost implications*

CCGs have a responsibility to provide the funding to enable this guidance (NICE TA534) to be applied. Funding is mandatory within 90 days but CCGs are being asked to fund after 30 days due to the demonstrated innovative value of this medicine- the latter optional. The following costs are for information only. Please note that there is a commercial arrangement (a simple discount patient access scheme for dupilumab) in place, which means that the actual costs will be less than noted.

Cost of product: £1,264.89 per pack 2 x 2ml syringes of 150mg/1ml solution (excluding VAT; British National Formulary online accessed 6th August 2018

Annual cost per patient:

Induction – 600mg (2 x 300mg injections) - £1,264.89

Maintenance – 300mg every other week - £632.44/dose (25 further doses) =£15,811
1st year cost (with induction) - £17,075.89
2nd year cost - £16,443.44

Cost per 100,000 population for each CCG based on assumptions made by NICE above

Cost pressure for local commissioners (before Patient Access Scheme is applied)

CCG	***CCG population (www.nice.org.uk)***	***Expected Number of patients per CCG in year 1 (18/19)***	***Expected Number of patients per CCG by (22/23)***	***Cost CCG population (1st year- includes induction)***	***Maintenance (2nd year onwards)***
Surrey Downs	*288,199*	2	*23*	*£394,965*	*£380,336*
Surrey Heath	*96,685*	1	*8*	*£131,996*	*£127,107*
Guildford & Waverley	*207,782*	1	*17*	*£283,801*	*£273,289*
East Surrey	*183,664*	1	*15*	*£250,844*	*£241,554*
North West Surrey	*344,601*	2	*28*	*£470,611*	*£453,181*
Crawley	*111,375*	1	*9*	*£152,146*	*£146,511*
Horsham & Mid Sussex	*233,525*	2	*19*	*£318,977*	*£307,163*

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

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

Availability of homecare service (if appropriate): Yes (NICE have assumed that dupilumab will be dispensed in secondary care for the first 13 weeks of the initial treatment.
Thereafter dupilumab will be delivered through homecare services and will not include VAT.

**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) www.nice.org.uk

Atopic dermatitis can be treated with topical therapies, phototherapy and systemic immunosuppressant therapies

Although clinicians individualise therapy for patients, a typical treatment pathway involves:

- emollients and topical corticosteroids (first line),
- topical calcineurin inhibitors (second line),
- phototherapy (third line) – Information from specialist notes that eczema patients don't tend to respond as well to phototherapy as psoriasis patients and also a significant proportion of eczema patients will have photo exacerbated eczema whereby their eczema is made worse of UV light.
- systemic immunosuppressant therapies (fourth line) including ciclosporin (the only licensed drug), methotrexate, azathioprine and mycophenolate mofetil.

For people whose disease does not respond to multiple systemic therapies, the only remaining treatment option is best supportive care, which may include education, psychological support, emollients, topical corticosteroids, bandages and hospitalisation.

Managing exacerbations (flares) in atopic dermatitis includes using short-term potent topical corticosteroids, oral corticosteroids and systemic therapy.

Positioning of dupilumab in the treatment pathway
Dupilumab would be used after existing systemic therapies

www.nice.org.uk
'The marketing authorisation for dupilumab is for 'moderate to severe atopic dermatitis in adults who are candidates for systemic therapy'. The company only submitted evidence for dupilumab **as a fifth-line treatment, after systemic immunosuppressant therapies, as an alternative to best supportive care.** The clinical experts explained that people are likely to have had at least 1 systemic therapy before dupilumab in clinical practice. The committee concluded that it would appraise dupilumab for moderate to severe atopic dermatitis, compared with best supportive care'. (after failure of systemic immunosuppressants)

Impact to patients

- This is the first monoclonal antibody available where other treatment options (above) have failed and atopic dermatitis continues to flare.
- This additional treatment option will be valued by patients with atopic dermatitis.
- Treatment will be available via homecare.
- Patients will need to be trained to use the pre-filled pen device. (Service usually provided by homecare company)

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.
- **www.medicines.org.uk** Comorbid asthma Safety and efficacy of Dupixent have not been established in the treatment of asthma. Patients with comorbid asthma should not adjust or stop their asthma treatments without consultation with their physicians. Patients with comorbid asthma should be monitored carefully following discontinuation of Dupixent.
- Primary care prescribers should be aware that their patient is receiving dupilumab 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.
- NICE have assumed that dupilumab will be dispensed in secondary care for the first 13 weeks of the initial treatment. Thereafter dupilumab will be delivered through homecare services and will not include VAT.
- An additional treatment option for atopic dermatitis would be valued by clinicians.

- Blueteq forms for initiation and continuation will need to be completed by dermatology specialists.

Impact to CCGs

- This is a new treatment option available for this cohort of patients and this will be a cost pressure to CCGs
- Dupilumab is PbRe and if a patient meets NICE criteria, treatment can be initiated and invoiced to the commissioner (if Blueteq forms have been completed
- Clinical Commissioning Groups are the responsible commissioner for this new treatment
- Providers are NHS hospital trusts.
- A treatment pathway for the treatment of Atopic Dermatitis will be required, this pathway will be developed in collaboration with the local dermatology specialists

Implementation

- CCGs are required to comply with the recommendations within 3 months. (1st November 2018) However, because dupilumab has been recommended through the early access to medicines process, commissioners have agreed to provide funding to implement this guidance 30 days after publication. (1st September 2018)
- Blueteq forms to be developed
- Liaison with specialists about treatment pathway prior to dupilumab use

Recommendation to PCN

20180323 Colour classification guideline

PbRe: Y

Recommended traffic light status (see attached guidelines):

RED –

- Dupilumab is a Payment by Results excluded drug
- Treatment should be initiated and continued by dermatology specialists in secondary or tertiary care.
- Blueteq forms for initiation and continuation will be developed for specialists to complete

Recommendations for tick box proformas & proposed pathway below

- Dupilumab use in conjunction with TOPICAL corticosteroids
- The disease has not responded to the following (or these are not tolerated or CLINICALLY contraindicated)
    - Topical corticosteroids monotherapy
    - Topical tacrolimus (NICE TA82)
    - At least 1 systemic immunosuppressant (ciclosporin, methotrexate, azathioprine or mycophenolate)
    - If patient has trialled phototherapy this can be indicated on the form, although this is not a pre-requisite to treatment.
- EASI score ≥ 16 (indicates moderate disease) & DLQI ≥10 (indicates moderate impact on patients life)

DRAFT TREATMENT PATHWAY IN LINE WITH NICE Clinical Knowledge Summaries (CKS) for Eczema – atopic www.nice.org.uk

Emollients

⇩

1ST LINE: Topical corticosteroids (maintenance regimen to control skin prone to flares)
Consider 'step down' approach or intermittent treatment

⇩

CONSIDER REFERRAL or GP with specialist interest (GPSI) to consider

2ND LINE: Calcineurin inhibitors (Tacrolimus) NICE TA82

⇩

3rd line (if used): Phototherapy may be considered here although this is not a pre-requisite to treatment with dupilumab

⇩

3rd or 4th line: Oral systemic immunosuppression (secondary care specialists)

⇩

4th or 5th line: DUPILUMAB INITIATION (in line with NICE TA 534)

References:

1. www.medicines.org.uk
2. www.nice.org.uk **(NICE)**
3. www.nhs.uk

Prepared by:

Clare Johns (Lead Commissioning Technician – Hosted Medicines Management Service)

Declaration of Interest:

None

Date: 6th August 2018

Reviewed by:

Sarah Watkin (Associate Director of Pharmaceutical Commissioning)

Declaration of Interest:

None

Date: 7th August 2018

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
v.1	*07/08/2018*	*Clare Johns*	*DRAFT*	*Peer Review*
v.2	*07/08/2018*	*Clare Johns*	*Draft*	*Out for consultation*
v.3				
