**National Institute for Health and Care Excellence**

**Single Technology Appraisal (STA/MTA)**

**Dupilumab for treating adults with severe atopic dermatitis [ID1048]**

**Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)**

**Please note:** Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

**Comment 1: the draft remit**

| Section  | Consultee/ Commentator | Comments [sic] | Action |
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| Appropriateness | **Sanofi** | We believe that it is both timely and appropriate to refer this topic to NICE for appraisal.Atopic dermatitis (AD) is a chronic, immune-mediated disease that can have a substantial and debilitating effect on the lives of patients. AD can significantly impact sleep, quality of life (QoL), and daily functioning, and is often associated with anxiety and depression.Promising Innovative Medicine (PIM) status was granted to dupilumab in December 2015 and EAMS positive scientific opinion was received in March 2017 after granting of preliminary positive opinion in January 2017. The inclusion of dupilumab as the first chronic or dermatological medicine within the EAMS programme by the Medicines and Healthcare products Regulatory Agency (MHRA) recognises both the innovative nature of dupilumab and also that severe AD represents an area of high unmet need, EAMS reflects the priority to ensure access for patients in the UK. In the US, the FDA has recognised the importance of both the disease area and this new medicine and in November 2014, it was granted Breakthrough Therapy Designation (BTD).Moderate to severe AD in adults can be challenging to treat due to the risk/benefit profiles of the available systemic (immunosuppressant) therapies. Only ciclosporin is licensed for limited use for up to 1 year in this setting and is limited by commonly recognised toxicities including hypertension, impaired renal and hepatic function, and potential for increased susceptibility to infections and cancer, particularly skin cancer. There are currently no effective treatments for adult patients with moderate-to-severe AD not controlled by topical medications or systemic immunosuppressants. Hence there is a significant unmet need for safe and effective targeted treatments that do not require laboratory monitoring and are appropriate for long-term disease control. | Comments noted. No changes to the scope required. |
| **BAD****Endorsed by RCP** | YesDupilumab is aimed at patients who resistant to atopic eczema requiring systemic treatment. | Comments noted. No changes to the scope required. |
| **UKCPA** | Yes – it would be very appropriate. Effective, approved treatment for severe atopic eczema is badly needed. Published trials suggest that dupilumab could fill this gap. A decision on dupilumab is expected from the FDA by the end of March 2017 and dupilumab has now been accepted for review by the EMA | Comments noted. No changes to the scope required. |
| **Novartis** | We consider the proposed appraisal appropriate. | Comment noted. |
| Wording | **Sanofi** | The expected marketing authorisation (MA) for dupilumab is:*Dupilumab (Dupixent®) is indicated for treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy. Dupilumab (Dupixent®) can be used with or without topical therapies.*It is likely that within the NHS in England and Wales use of dupilumab in day to day clinical practice would be in a more restricted population than that captured by the draft licence wording above. Our basecase submission will focus on this narrower target population rather than the full licensed population. We request that the following wording is considered as an update to the remit:*To appraise the clinical and cost-effectiveness of dupilumab within its marketing authorisation for treating moderate to severe atopic dermatitis in adults for whom other approved systemic therapies have been inadequately effective, not tolerated or contraindicated.* | Comments noted. Dupilumab will be appraised within its marketing authorisation.  |
| **UKCPA** | Yes. | Comments noted. |
| **Novartis** | We query whether moderate or severe atopic dermatitis have been clearly defined. | Comment noted. Definition of severe atopic dermatitis will be considered during the appraisal. |
| Timing Issues | **Sanofi** | There have been no novel therapies targeted at AD for the last 15 years and for the patient population in the amended remit proposed above, for whom existing treatment strategies have failed, there remains significant unaddressed physical and psychological burden. The burden on the NHS is also high for managing dermatological conditions and skin diseases are some of the most common conditions that primary healthcare professionals manage, accounting for around 13 million GP consultations a year.[1]The EAMS positive scientific opinion means that a significant number of patients are likely to receive dupilumab ahead of marketing authorisation. Under the rules of EAMS these patients are expected to continue on therapy up until the point at which a NICE recommendation is published. Further recognition of the importance of EAMS products is enshrined in the expectation that implementation of such guidance should be within 30 days rather that the more usual 90 day mandate. Moderate to severe AD places a substantial economic burden on patients, caregivers, and payers. Generally healthcare resource utilization is higher in adults with AD than those without AD and resource utilization increases with worsening disease severity.[2]Hence dermatological conditions represent an area of high resource use within the NHS and treatments that effectively address AD are required. As such it is critical to the NHS that guidance is issued quickly. | Comments noted.  |
| **UKCPA** | In view of the imminent approval of the drug in the USA and the possibility of EMA approval later in 2017, this issue is now urgent.  | Comments noted. |
| **Novartis** | No comment. | - |
| Additional comments on the draft remit | No additional comments received. |

Comment 2: the draft scope

| Section  | Consultee/ Commentator | Comments [sic] | Action |
| --- | --- | --- | --- |
| Background information | **Sanofi** | The background information supplied in the draft scope is generally accurate. However we would like to highlight several additional key issues that are important for an understanding of the underlying condition and for the treatment of people with AD. We request that the background description in the draft scope is supplemented with the following information in the appropriate places:**Disease background**• AD is a chronic, immune-mediated disease in which even nonlesional skin is not normal skin, owing to persistent subclinical inflammation throughout the body which leads to skin barrier defects, increased epidermal thickness and ongoing inflammation.[3, 4]• The loss of the protective skin barrier associated with AD leads to water loss, dry skin, and an increased risk for skin infection.[5]• This in turn leads to the ‘itch-scratch cycle’ in which scratching in response to itch (pruritus) exacerbates damaged skin barrier function, leading to penetration of irritants and allergens and further allergic inflammation.[6] This cycle aggravates the condition and makes it more challenging to treat.• The presence (and intensity) of characteristic AD symptoms such as pruritus, skin dryness, and sleep disturbances are significantly correlated with HRQoL and mental health problems such as anxiety or depression. [7-9]• Patients often suffer from other atopic comorbidities, highlighting the underlying systemic nature of the disease.[10]**Assessment of severity** • Disease severity is typically assessed on the basis of evaluation of the disease extent, impact of symptoms on daily functioning and QoL and responsiveness to therapy. • A broadly accepted tool for classifying severity of AD in clinical practice is lacking although objective measures such as Investigators’ Global Assessment (IGA) and composite scoring systems (the Eczema Area and Severity Index [EASI] and the Severity Scoring of Atopic Dermatitis [SCORAD]) are employed.[11]**Current treatment options** • AD is typically managed by a step-wise approach based on level of disease severity and lack of response to lower step treatments [12]• As disease severity increases, broad-spectrum systemic treatments are used to treat AD but these do not specifically target the underlying disease pathophysiology[12-14]• Ciclosporin is the only immunosuppressant drug with an approved indication for severe AD however toxicity limits long-term use of this and other systemic therapies.[13, 14]• There are currently no national guidelines or quality standards in England and Wales on the diagnosis, treatment and management of moderate to severe AD in adults. | Comments noted. The background section of the scope is only intended to provide a brief description of the condition and current treatment options. A detailed description of these aspects will be included in the company’s evidence submission and will be considered during the appraisal.However, in response to your comments, the background section was updated to include the following sentence:*Severe eczema can be physically disabling or incapacitating, and can cause as anxiety or depression.* |
| **UKCPA** | The wording of the background should be expanded to include reference to the wide variations in the severity of eczema and its impact on quality of life. This would help to provide a more accurate reflection of the scale and impact of severe eczema and provide a logical rationale for the use of a high-cost drug. Although the current first paragraph mentions the possibility of hospitalisation it does not give the full picture. It should be added that for some people severe eczema can be physically disabling or incapacitating. In addition, it can be linked with severe anxiety, depression and suicidal ideation.In the third paragraph of the background azathioprine, ciclosporin and mycophenolate mofetil are all described as immunosuppressants but methotrexate is described as a disease-modifying anti-rheumatic drug. Presumably this was done because they appear under these headings in the BNF. They are all used in a number of conditions and the way that they are currently described in the document is a bit misleading. It is my understanding that all of these drugs are used as immune-modulators in eczema (although they act at different points in the immune/inflammatory process). They are used in smaller doses than when used for their immunosuppressant action.  | Comments noted. The background section of the scope is only intended to provide a brief description of the condition and current treatment options. A detailed description of these aspects will be included in the company’s evidence submission and will be considered during the appraisal.However, in response to your comments, the third paragraph of the background section was corrected, and the following sentence was added:*Severe eczema can be physically disabling or incapacitating, and can cause anxiety or depression.* |
| **Novartis** | We query why methotrexate has been classified as a “disease-modifying anti-rheumatic drug” since rheumatology terminology will not be relevant to this dermatology appraisal. We consider that in the context of this appraisal, it would be more appropriate to classify methotrexate as a systemic immunosuppressant, alongside azathioprine, ciclosporin and mycophenolate mofetil. | Comment noted. In response to your comment, the relevant paragraph of the background section was corrected. |
| The technology/ intervention | **Sanofi** | The brand name for dupilumab is Dupixent®. The brief description of the mode of action of the technology is accurate in the draft scope however there are several key features of the disease and treatment that are also important to note. We request the following additions to the scope:**AD is a Th2 mediated disease**. The Th2 cytokines interleukin-4 (IL4) and interleukin-13 (IL13) are key mediators of AD and other atopic conditions. IL-4 and IL-13 signalling leads to increased expression of other type 2 (including Th2) cytokines and chemokines and activation of additional inflammatory cell types (B cells, T cells, monocytes, eosinophils) and affects epidermal barrier function.[15]**Dupilumab blocks this part of the Th2 pathway**. Dupilumab is a human monoclonal antibody that binds specifically to the receptor subnunit IL-4Rα and inhibits signalling of both IL-4 and IL-13.Thus dupilumab treatment results in suppression of aberrant inflammation and a partial normalisation of the skin gene expression profile of AD. [16] **Skin barrier function.** Dupilumab improves the skin barrier due to the upregulation of genes encoding proteins involved in epidermal structure (and potentially due to reduction in itch (itch-scratch cycle)). Correspondingly, skin infections are also reduced. [17] | Comments noted. Dupilumab brand name was added to the scope. However, the scope is only intended to provide a brief description of the technology. No changes to the scope required. |
| **UKCPA** | I believe that the brand name Dupixent has been conditionally accepted by both the FDA and the EMA | Comments noted. Dupilumab brand name was added to the scope. |
| **Novartis** | No comment. | No comments received. |
| Population | **Sanofi** | AD is a disease that waxes and wanes in its presentation whilst remaining active below the skin and the objective clinical endpoints to measure disease severity such as EASI or SCORAD are therefore only a snapshot in time. Clinicians will also consider more generally how the disease affects the patient. This is because the clinical endpoints primarily focus on the signs and symptoms of the disease but not the impact of the disease on daily functioning, QoL and responsiveness to treatment. Hence patients who are moderate by score can be judged severe in nature. It is therefore important to include both moderate and severe patients as assessed by these clinical endpoints in the target population.The evidence base for dupilumab directly supports this positioning. As part of the LIBERTY AD trial program the CAFÉ study is a Phase III randomised controlled trial that examines the safety and efficacy of dupilumab in a population of patients with moderate to severe AD who are not adequately controlled with or are intolerant to oral ciclosporin, or when this treatment is not medically advisable. Similarly in the larger CHRONOS Phase III study ~30% of patients had previous exposure to ciclosporin and the most common reason for its discontinuation was inadequate efficacy. Both studies include background topical corticosteroid (TCS) use as would be expected in real world clinical practice.Hence the target population for the base case is uncontrolled moderate to severe patients with background TCS use for whom systemic immunosuppressants have failed or who are contraindicated or intolerant to them. Patients included in the EAMS program will be more severe reflecting the population with greatest need. | Comments noted. Dupilumab will be appraised within its marketing authorisation.  |
| **UKCPA** | Yes – I presume the definition means people refractory to treatment with TOPICAL corticosteroids and TOPICAL calcineurin inhibitorsI wonder if people with severe hand eczema should be considered separately? | Comments noted. Dupilumab will be appraised within its marketing authorisation. The population has been updated to: *Adults with moderate to severe atopic dermatitis who are candidates for systemic therapy.* A subgroup *of people with atopic dermatitis affecting the hands*, was added to the scope for consideration. |
| **Novartis** | We query whether moderate or severe atopic dermatitis have been clearly defined. | Comment noted. Definition of severe atopic dermatitis will be considered during the appraisal. |
| Comparators | **Sanofi** | The use of dupilumab within real world clinical practice in the UK is predicted to be following failure (or contraindication) of topical therapies and systemic immunosuppressant agents. This is in line with clinical opinion for a new biologic medicine in an area where there are no other biologics. At this point in the patient journey there are currently no long-term safe and effective treatments beyond best supportive care (BSC) which deals with active symptom control. BSC can be defined as a combination of emollients, low to mid potency topical corticosteroids (TCS) and rescue therapy (such as higher potency topical or oral corticosteroids or topical calcineurin inhibitors (TCIs)).BSC is defined within the LIBERTY AD trial program in the CHRONOS (~30% ciclosporin experienced patients) and CAFÉ (all with (or contraindicated to) ciclosporin experience) studies as emollients, topical corticosteroids and protectives. A proportion of patients also received ‘rescue therapies’ which included higher dose topical steroids and a very small proportion took TCIs.These treatments are routinely used in clinical practice in the UK for the target group of patients and so should be considered as a relevant comparator set (BSC). Thus, in the clinical trial setting for the patients described in the suggested update to the remit, dupilumab has been compared to BSC.xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx. This is in line with anticipated use in clinical practice for patients with the highest unmet need and disease burden. This is the population with the greatest potential to benefit. | Comments noted. Dupilumab will be appraised within its marketing authorisation. Comparators currently listed in the draft scope (including BSC) are relevant comparators in this population and the types of treatment used as part of BSC has been defined. |
| **BAD****Endorsed by RCP** | • PUVA has limited place in management of atopic dermatitis. We agree with the other suggested comparators but many of them have limitation. • Ciclosporin is not a long term option due to potential side effects. • Azathioprine can be effective but carries unacceptable long term side effects. • Methotrexate is increasingly used in patients with atopic dermatitis unresponsive to topical treatment. • Alitretinoin can be considered as a comparator for dupilumab in people with atopic dermatitis affecting the hands. | Comments noted. In response to consultees’ comments, the list of comparators was updated:* Phototherapy including with ultraviolet (UVB) radiation or psoralen-ultraviolet A (PUVA)
* Immunosuppressive therapies (azathioprine, ciclosporin, and methotrexate)
* Oral steroids
* Best supportive care (combination of emollients, low to mid potency topical corticosteroids, and rescue therapy including higher potency topical or oral corticosteroids or topical calcineurin inhibitors)
* Alitretinoin (in people with atopic dermatitis affecting the hands)
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| **UKCPA** | Yes, the first three are the standard treatments that are used in the NHS. I do not understand what is meant by ‘best supportive care’. The most logical comparators would be the agents used as immunomodulators – azathioprine and ciclosporin. In the case of severe hand eczema allitretinoin (full dose) would be a suitable comparator. | Comments noted. In response to consultees’ comments, the list of comparators was updated:* Phototherapy including with ultraviolet (UVB) radiation or psoralen-ultraviolet A (PUVA)
* Immunosuppressive therapies (azathioprine, ciclosporin, and methotrexate)
* Oral steroids
* Best supportive care (combination of emollients, low to mid potency topical corticosteroids, and rescue therapy including higher potency topical or oral corticosteroids or topical calcineurin inhibitors)
* Alitretinoin (in people with atopic dermatitis affecting the hands)

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| **Novartis** | We agree that ciclosporin, as a licensed treatment option in atopic dermatitis, may be a relevant comparator, depending on usage within UK clinical practice. We note that azathioprine, mycophenolate mofetil and methotrexate would be off-label comparators.We query whether phototherapy with UVB radiation should also be included as a potential comparator e.g. “Phototherapy, including with ultraviolet (UVB) radiation or psoralen-ultraviolet A (PUVA)”.We raise a query regarding the definition of best supportive care and comment that this will need to be clearly defined i.e. what constitutes best supportive care, and the precise populations in whom best supportive care is currently used in UK clinical practice (e.g. after non-response to which specific interventions). | Comments noted. In response to consultees’ comments, the list of comparators was updated:* Phototherapy including with ultraviolet (UVB) radiation or psoralen-ultraviolet A (PUVA)
* Immunosuppressive therapies (azathioprine, ciclosporin, and methotrexate)
* Oral steroids
* Best supportive care (combination of emollients, low to mid potency topical corticosteroids, and rescue therapy including higher potency topical or oral corticosteroids or topical calcineurin inhibitors)
* Alitretinoin (in people with atopic dermatitis affecting the hands)
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| Outcomes | **Sanofi** | The outcomes presented in the draft scope are appropriate. | Comment noted. No changes to the scope required. |
| **BAD****Endorsed by RCP** | Additional outcomes that should be considered includes:• Time of work • Infections• Hospital admissions• Impact on family members/carers• Impact on associated atopic disease (asthma)Be aware of skin type iv- vi - disease severity scores may underestimate disease severity (not picking up erythema) – consider stratifying for ethnicity/skin type. | Comments noted. Standard outcomes are included in the scope**.** If evidence is available the effectiveness of treatment by skin colour will be considered |
| **UKCPA** | Yes – but I would emphasise the importance of patients’ assessments of treatment and outcomes wherever these are reported (in addition to investigator assessments) and health-related QoL measures. | Comment noted. No changes to the scope required. |
| **Novartis** | No comment. | - |
| Economic analysis | **Sanofi** | The economic analysis will be carried out in line with the NICE reference case and for the population of patients xxxxxxxxxxxxxxxxxxxxxxxxxxA lifetime time horizon will be implemented and the perspective will be from the NHS and PSSRU point of view. A confidential patient access scheme (PAS) is expected for dupilumab. | Comment noted.  |
| **UKCPA** | An economic analysis would need to evaluate the impact of treatment over a one year period.It might be useful for the QALY calculation to take into account the considerable reduction in anxiety and depression that can result from dupilumab treatment | Comment noted.  |
| **Novartis** | No comment. | - |
| Equality and Diversity | **Sanofi** | We have not identified any equity or equality issues within the draft scope. | Comment noted.  |
| **UKCPA** | I am not aware of any. | Comment noted. |
| **Novartis** | No comment. | - |
| Other considerations  | **Sanofi** | None. | - |
| **UKCPA** | none | - |
| **Novartis** | No comment. | - |
| Innovation | **Sanofi** | Moderate-to-severe AD is a serious, chronic, debilitating disease with substantial impact on daily functioning and well­being of affected patients. There is significant unmet medical need for a treatment that is safe and effective for long-term use for many people suffering with moderate to severe AD.For some people the currently available treatments have important limitations including unsatisfactory effectiveness and significant risks and side effects. These limitations result in a number of patients with moderate-to-severe AD whose disease cannot be safely controlled by the existing therapies. There have been no substantive new treatments for any form of AD for the last 15 years unlike the recent developments in psoriasis. Dupilumab is the first biologic to be available in this area. It has a targeted mode of action and this is in contrast to the existing non-speciﬁc immunosuppressant treatments which have poor side effect profiles limiting their use.The LIBERTY AD clinical trial program has demonstrated that dupilumab provides significant and sustained benefits in symptom control and QoL. The side effect profile of dupilumab has been shown to be comparable to placebo in the studies. There is considerable anecdotal evidence to suggest that for many patients treated within the program, dupilumab has been a life changing medicine and can be considered a step-change in the management of the condition.This, and the extent of the unmet need in this area, has contributed to the recognition by the FDA and MHRA of the innovative nature of the medicine within their accelerated access programs. | Comments noted. Consultees are encouraged to describe the innovative nature of the technology in their evidence submissions. The Committee will consider this information during the appraisal process. |
| **BAD****Endorsed by RCP** | YesIt offers potential significant and substantial health-related benefits. The NICE QALY calculation should pick up the wider benefits of dupilumab.  | Comments noted. Consultees are encouraged to describe the innovative nature of the technology in their evidence submissions. The Committee will consider this information during the appraisal process. |
| **UKCPA** | Yes- dupilumab does represent a step change in the way that atopic eczema is treated. | Comments noted. Consultees are encouraged to describe the innovative nature of the technology in their evidence submissions. The Committee will consider this information during the appraisal process. |
| **Novartis** | No comment. | - |
| Questions for consultation | **Sanofi** | None. | - |
| **BAD****Endorsed by RCP** | • Are there any subgroups of people in whom dupilumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? 1. Possibly eczema at different sites eg photoaggravated eczema, hand eczema. 2. Severe eczema being controlled with interventions that are causing significant side effects/sequelae (eg steroids and osteoporosis; ciclosporin and nephropathy etc).3. Those with other atopic disease (eg asthma) where dupilumab also has efficacy. • Where do you consider dupilumab will fit into the existing NICE pathway, treating eczema in people over 12? Dupilumab is aimed at patients whose eczema is not controlled with standard therapy; after topical steroids, topical tacrolimus, and phototherapy. | Comments noted. In response to consultees’ comments, the following subgroups were included in the scope:* people with atopic dermatitis affecting the hands;
* people for whom therapies have been inadequately effective, not tolerated or contraindicated, and
* skin colour subgroups.
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| **UKCPA** | none | - |
| **Novartis** | Have all relevant comparators for dupilumab been included in the scope?*Novartis: See comments above on “Comparators”*• Should both phototherapy and/or PUVA be included as a comparator for dupilumab?*Novartis: Potentially, depending on proposed positioning of dupilumab within the UK treatment pathway.*• What immunosuppressive therapies should be considered as a comparator for dupilumab: azathioprine, ciclosporin, and mycophenolate mofetil?*Novartis: See earlier comments under “Comparators”*• Should methotrexate be considered as a comparator for dupilumab?*Novartis: See earlier comments under “Comparators”*• Should alitretinoin be considered as a comparator for dupilumab in people with atopic dermatitis affecting the hand?*Novartis: Alitretinoin may be an appropriate comparator for the sub-group of patients with severe chronic hand dermatitis that has not responded to potent topical corticosteroids and in whom the disease is severe, as defined by the physician's global assessment (PGA) and a dermatology life quality index (DLQI) score of 15 or more.1*• Is best supportive care a relevant comparator for dupilumab? And if yes, how it should be defined?*Novartis: Best supportive care may be an appropriate comparator for a sub-group of patients who are currently receiving such care in UK clinical practice. We have no comments regarding the appropriate definition of best supportive care.* Are the outcomes listed appropriate?*Novartis: No comment.*Are there any subgroups of people in whom dupilumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? *Novartis: No comment.*Where do you consider dupilumab will fit into the existing NICE pathway, Treating eczema in people over 12?*Novartis: We would anticipate that dupilumab will fit in the pathway as a treatment option for patients aged 18 or over with moderate to severe atopic dermatitis that is refractory to adequate use of topical therapies, potentially as an alternative to immunosuppressive therapies, depending on clinical- and cost-effectiveness*.NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. *Novartis: No comment*.Do you consider dupilumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a ‘step-change’ in the management of the condition)?*Novartis: No comment.*Do you consider that the use of dupilumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? *Novartis: No comment.* | Comments noted. In response to consultees’ comments, the list of comparators was updated:* Phototherapy including with ultraviolet (UVB) radiation or psoralen-ultraviolet A (PUVA)
* Immunosuppressive therapies (azathioprine, ciclosporin, and methotrexate)
* Oral steroids
* Best supportive care (combination of emollients, low to mid potency topical corticosteroids, and rescue therapy including higher potency topical or oral corticosteroids or topical calcineurin inhibitors)
* Alitretinoin (in people with atopic dermatitis affecting the hands)
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| Additional comments on the draft scope | **Sanofi** | None. | - |
| **UKCPA** | I do not fully understand the NICE pathway Treating eczema in people over 12 and so I am not able to comment on the potential position of dupilumab in the pathway. In terms of the ‘stepped care’ approach set out in NICE CG 57, dupilumab would be an alternative to other systemic therapies for severe eczema (step 4). | Comments noted. No changes to the scope required. |

**The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope**

Department of Health