

## HEALTH TECHNOLOGY BRIEFING NOVEMBER 2019

### Upadacitinib for atopic dermatitis

<b>NIHRIO ID</b>	13417	<b>NICE ID</b>	9995
<b>Developer/Company</b>	AbbVie Ltd.	<b>UKPS ID</b>	646497

<b>Licensing and market availability plans</b>	Currently in phase II/III clinical trials.
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### SUMMARY

Upadacitinib is in development for the treatment of moderate to severe atopic dermatitis (AD). AD is a chronic inflammatory skin disease that affects both children and adults and is characterised by redness, itchiness, and scaling of the skin. Some people only have small patches of dry skin, but others may experience widespread red, inflamed skin all over the body. Patients with moderate to severe AD may experience sleep disturbances, anxiety, depression, and poor quality of life. Currently, the management of AD involves the removal or treatment of trigger factors that contribute to the development of the disease and topical and/or systemic treatment depending on the severity of the disease.

Upadacitinib acts by selectively blocking a protein called Janus-Associated Kinase 1 (JAK1 and JAK1/3). JAKs contribute to the processes within the cell to produce an immune or inflammatory response. There is an emerging body of evidence establishing that JAK dependent enzymes are major contributors to the progression of immune-mediated diseases such as AD and that blocking such enzymes can be beneficial. Upadacitinib is taken orally and if licensed, it will offer an additional treatment option for patients with moderate to severe AD.

*This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.*

## PROPOSED INDICATION

Treatment for adolescents and adults aged 12 years or over with moderate to severe atopic dermatitis (AD).<sup>1,a</sup>

## TECHNOLOGY

### DESCRIPTION

Upadacitinib (ABT-494; ABT494) is an orally administered Janus kinase (JAK)1 inhibitor.<sup>2</sup> The Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway is recognised as one of the major mechanisms by which cytokine receptors transduce intercellular signals.<sup>3</sup> The binding of ligands to receptors on the cell membrane leads to JAK-STAT activation and its translocation to the nucleus for the initiation of gene transcription.<sup>3</sup> By blocking JAKs, pro-inflammatory cytokines are reduced. The JAK1 pathway (alongside JAK2, JAK3, and tyrosine kinase 2) is implicated in the pathogenesis of atopic dermatitis (AD).<sup>4</sup> Upadacitinib and other JAK inhibitors therefore fight inflammation by binding to JAK proteins to block the pro-inflammatory effects of cytokines on the target cells.<sup>5</sup>

Upadacitinib is in phase II/III clinical development for the treatment of moderate to severe AD (NCT02925117<sup>6</sup>; Heads Up, NCT03738397<sup>1</sup>; Measure Up 1, NCT03569293<sup>7</sup>; Measure Up 2 NCT03607422<sup>8</sup>; AD Up, NCT03568318<sup>9</sup>). In the phase III clinical trials the dose comprised of either 15mg or 30mg upadacitinib administered once daily as an oral treatment.

### INNOVATION AND/OR ADVANTAGES

An overwhelming body of evidence has established that JAK-dependent cytokines are major contributors to immunopathology. It is known that blocking such cytokines with biologics can be beneficial in immune-mediated diseases such as AD.<sup>10</sup> Currently there is only biologic licenced to treat AD (IL4 & IL-13).<sup>11</sup>

### DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Upadacitinib does not currently have Marketing Authorisation in the EU/UK for any indication. However the Committee for Medicinal Products for Human Use (CHMP) recommended granting a marketing authorisation for upadacitinib for the treatment of rheumatoid arthritis in October 2019.<sup>12</sup>

Upadacitinib is in phase II and phase III clinical development for a range of conditions including ulcerative colitis, ankylosing spondylitis, Crohn's disease, systematic lupus erythematosus, giant cell arteritis, rheumatoid arthritis and psoriatic arthritis.<sup>13</sup>

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<sup>a</sup> Information provided by AbbVie Ltd.

## PATIENT GROUP

### DISEASE BACKGROUND

Atopic Dermatitis (AD) also known as eczema or atopic eczema, is a chronic inflammatory skin disease characterised by erythema, pruritus, and scaling of skin that affects both children and adults.<sup>14</sup> AD has a complex and heterogeneous aetiology, characterised histologically by skin infiltration of inflammatory cells, predominantly lymphocytes, eosinophils, and mast cells.<sup>15</sup>

Although the pathogenesis and aetiology of AD remain to be completely understood, this multifactorial disease likely results from complex crosstalk between genetic and environmental factors.<sup>16,17</sup> It can run in families and often develops alongside other conditions, such as asthma and hay fever. The symptoms of AD often have certain triggers, such as soaps, detergents, stress and the weather. Sometimes allergies can be started by food.<sup>18</sup> Exaggerated Th2-type response, disruption of the epidermal barrier functions, high level of serum IgE, and decreased production of antimicrobial peptides (AMPs) are the key findings in AD.<sup>16,17</sup>

Some people only have small patches of dry skin, but others may experience widespread red, inflamed skin all over the body. Although AD can affect any part of the body, it most often affects the hands, insides of the elbows, backs of the knees and the face and scalp in children.<sup>18</sup>

For patients with moderate to severe AD, skin lesions encompassing large surface areas are often associated with severe itching. These lesions can cause sleep disturbances and, in turn, symptoms of anxiety, depression, and poor quality of life.<sup>19</sup>

### CLINICAL NEED AND BURDEN OF DISEASE

Although AD presents most frequently in childhood, it can present at any age.<sup>20,21</sup> Estimates vary due to the different population examined, but figures suggest that it affects about 10-30% of children and 2-10% of adults.<sup>21-28</sup> AD affects both males and females equally.<sup>29</sup>

It is indicated that AD affects 1 in 12 adults in the UK.<sup>30</sup> A 2016 international, cross-sectional, web-based survey estimated the prevalence of atopic dermatitis in several countries including the UK. Size of the sample population in the UK was 10,001. The prevalence of atopic dermatitis in this UK cohort was 2.5% (95% confidence interval [CI]: 2.2%, 2.8%). The prevalence was the same among males and females (2.5%). Depending on which scale was used for diagnosis, between 49-56% of cases were moderate, and 4-12% of cases were severe.<sup>31</sup>

According to the 2018-19 Hospital Episodes Statistics data, collectively there were 1,092 admissions which resulted in 542 day cases and 1,132 FCE bed days for other atopic dermatitis and atopic dermatitis unspecified (ICD-10 codes: L20.8 and L20.9 respectively) in England.<sup>32</sup>

## PATIENT TREATMENT PATHWAY

### TREATMENT PATHWAY

AD has several causes, which may influence treatment. Management of AD involves the removal or treatment of contributory factors that may trigger the development of the disease

or worsen a flare. The management of AD may also involve the use of different therapies to ease the symptoms.<sup>18,33</sup>

For the treatment of AD, NICE recommends a stepped approach. Treatment can be stepped up or down according to the severity of the condition and includes a range of therapies such as emollients, bandages, phototherapy, topical and oral corticosteroids, and oral immunomodulators and biologics.<sup>34</sup>

## CURRENT TREATMENT OPTIONS

The following treatment options have been recommended for moderate AD:<sup>34,b</sup>

- Emollients
- Moderate potency topical corticosteroids
- Topical calcineurin inhibitors (tacrolimus or pimecrolimus)
- Bandages
- Biologics (Dupilumab)

The following treatment options have been recommended for severe AD:<sup>34,b</sup>

- Emollients
- Potent topical corticosteroids
- Topical calcineurin inhibitors
- Bandages
- Phototherapy
- Oral corticosteroids
- Oral immunomodulators (Methotrexate/ ciclosporin/ mycophenolate mofetil)
- Biologics (Dupilumab)

## PLACE OF TECHNOLOGY

If licensed, upadacitinib will offer an additional treatment option for adolescents and adults who have moderate to severe AD.

## CLINICAL TRIAL INFORMATION

<b>Trial</b>	<b>Heads Up, <a href="#">NCT03738397</a>, <a href="#">EudraCT: 2018-002264-57</a>; upadacitinib versus dupilumab; phase III</b>
<b>Sponsor</b>	AbbVie Ltd
<b>Status</b>	Ongoing
<b>Source of Information</b>	Trial registry <sup>1,35</sup> , manufacturer
<b>Location</b>	EU countries (incl UK), USA and Canada and other countries
<b>Design</b>	Randomised, parallel assignment, quadruple masking, active-controlled
<b>Participants</b>	n=650 (planned); pts aged 18 to 75 yrs; participant has active moderate to severe AD defined by Eczema Area and Severity Index (EASI), Investigator's Global Assessment (IGA), Body Surface Area (BSA) and pruritus; participant is a candidate for systemic therapy or have recently required systemic therapy for AD.

<sup>b</sup> Information provided by AbbVie Ltd.

<b>Schedule<sup>1,c</sup></b>	<p><b>Experimental: Participants administered with upadacitinib</b> Participants are administered with upadacitinib 30mg from baseline to wk 24 and placebo pre-filled syringe at baseline visit (2 injections) followed by an injection every other wk until wk 22.</p> <p><b>Experimental: Participants administered with dupilumab</b> Participants are administered with dupilumab 300mg (2 injections) at baseline followed by one every other wk until wk 22 and placebo tablets daily from baseline to wk 24.</p>
<b>Follow-up<sup>c</sup></b>	The study is comprised of a 35-day screening period, a 24-week double-blind treatment period, and an end-of-treatment follow-up visit.
<b>Primary Outcomes</b>	Percentage of participants achieving a 75% reduction in EASI (EASI 75) from baseline [Time frame: at wk 16]
<b>Secondary Outcomes</b>	<ul style="list-style-type: none"> <li>• Percent change in worst pruritus numerical rating scale (NRS) [Time frame: from baseline (wk 0) to wk 16]</li> <li>• Percentage of participants achieving a 100% reduction in EASI (EASI 100) [Time frame: At wk 16]</li> <li>• Percentage of participants achieving a 90% reduction in EASI (EASI 90) [Time frame: at wk 16]</li> </ul>
<b>Key Results</b>	
<b>Adverse effects (AEs)</b>	
<b>Expected reporting date</b>	Estimated primary and study completion date September 2020.

<b>Trial</b>	<b>Measure Up 1, <a href="#">NCT03569293</a>, <a href="#">EudraCT: 2017-005125-20</a>; children and adults aged 12 – 75 yrs; upadacitinib vs placebo; phase III</b>
<b>Sponsor</b>	AbbVie Ltd
<b>Status</b>	Ongoing
<b>Source of Information</b>	Trials registry <sup>7,36</sup> , manufacturer
<b>Location</b>	EU countries (incl UK), USA, Canada and other countries
<b>Design</b>	Randomised, parallel assignment, quadruple masked, placebo-controlled
<b>Participants</b>	n=810 (estimated); aged 12-75 yrs; active moderate to severe AD defined by Eczema Area and Severity Index (EASI), Investigator's Global Assessment (IGA), Body Surface Area (BSA) and pruritus; participant is a candidate for systemic therapy or have recently required systemic therapy for AD.
<b>Schedule<sup>7,c</sup></b>	<p><b>Experimental: Arm A</b> Upadacitinib 30mg is administered once daily.</p> <p><b>Experimental: Arm B</b> Upadacitinib 15mg is administered once daily.</p> <p><b>Experimental: Arm C</b> Placebo administered once daily followed by upadacitinib 30mg once daily.</p> <p><b>Experimental: Arm D</b> Placebo administered once daily followed by upadacitinib 15mg once daily.</p>

<sup>c</sup> Information provided by AbbVie Ltd.

<b>Follow-up<sup>d</sup></b>	The study is comprised of a 35-day Screening Period, a 16 wk double-blind treatment period, a Blinded Extension period of up to wk 136, and a 30-day follow-up visit
<b>Primary Outcomes</b>	<ul style="list-style-type: none"> <li>• Proportion of participants achieving at least a 75% reduction in Eczema Area and Severity Index (EASI 75) [Time frame: at wk 16]</li> <li>• Proportion of participants achieving validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) of 0 or 1 with at least two grades of reduction [Time frame: at wk 16]</li> </ul>
<b>Secondary Outcomes</b>	<ul style="list-style-type: none"> <li>• Proportion of participants achieving an improvement (reduction) in worst pruritus Numerical Rating Scale (NRS) <math>\geq</math> 4 [Time frame: at wk 16]</li> <li>• Proportion of participants achieving EASI 90 [Time frame: at wk 16]</li> <li>• Proportion of participants achieving EASI 50 [Time frame: at wk 1]</li> <li>• Proportion of participants achieving an improvement (reduction) in worst pruritus NRS <math>\geq</math> 4 for participants randomized to dose A [Time frame: at day 2]</li> <li>• Proportion of participants achieving an improvement (reduction) in worst pruritus NRS <math>\geq</math> 4 for participants randomized to dose B [Time frame: at day 3]</li> <li>• Proportion of participants achieving an improvement (reduction) in Atopic dermatitis impact scale (ADerm-IS) sleep domain score <math>\geq</math> Minimal clinically important difference (MCID) [Time frame: at wk 16]</li> <li>• Proportion of participants achieving an improvement (reduction) in Atopic dermatitis symptom scale (ADerm-SS) skin pain score <math>\geq</math> MCID [Time frame: at wk 16]</li> <li>• Proportion of participants achieving an improvement (reduction) in ADerm-SS total score <math>\geq</math> MCID [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving an improvement (reduction) in ADerm-IS total score <math>\geq</math> MCID [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving EASI 100 [Time frame: at wk 16]</li> </ul>
<b>Key Results</b>	-
<b>Adverse effects (AEs)</b>	-
<b>Expected reporting date</b>	Estimated primary completion date March 2020. Estimated study completion date August 2022.

<b>Trial</b>	<b>Measure Up 2, <a href="#">NCT03607422</a>, <a href="#">EudraCT: 2018-001383-28</a>; children and adults aged 12-75 yrs; upadacitinib vs placebo; phase III</b>
<b>Sponsor</b>	AbbVie Ltd
<b>Status</b>	Ongoing
<b>Source of Information</b>	Trial registry <sup>8,37</sup> , manufacturer
<b>Location</b>	EU (incl UK), USA, Canada and other countries
<b>Design</b>	Randomised, parallel group assignment, quadruple masking, placebo-controlled
<b>Participants</b>	n=810 (planned); active moderate to severe AD defined by Eczema Area and Severity Index (EASI), Investigator's Global Assessment (IGA), Body surface area (BSA), and pruritus; candidate for systemic therapy or have recently required systemic therapy for AD

<sup>d</sup> Information provided by AbbVie Ltd.

<b>Schedule<sup>8,e</sup></b>	<p><b>Experimental: Arm A</b> Upadacitinib 30mg is administered once daily.</p> <p><b>Experimental: Arm B</b> Upadacitinib 15mg is administered once.</p> <p><b>Experimental: Arm C</b> Placebo is administered once daily until wk 16 followed by upadacitinib 30mg once daily.</p> <p><b>Experimental: Arm D</b> Placebo is administered once daily until wk 16 followed by upadacitinib 15mg once daily.</p>
<b>Follow-up<sup>e</sup></b>	The study is comprised of a 35-day Screening Period, a 16 week double-blind treatment period, a Blinded Extension period of up to Week 136, and a 30-day Follow-up Visit
<b>Primary Outcomes</b>	<ul style="list-style-type: none"> <li>• Proportion of participants achieving at least a 75% reduction in Eczema Area and Severity Index (EASI 75) [Time frame: at wk 16]</li> <li>• Proportion of participants achieving validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) of 0 or 1 with at least two grades of reduction [Time frame: at wk 16]</li> </ul>
<b>Secondary Outcomes</b>	<ul style="list-style-type: none"> <li>• Proportion of participants achieving an improvement (reduction) in worst pruritus Numerical Rating Scale (NRS) <math>\geq</math> 4 from baseline [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving EASI 90 [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving EASI 50 [Time frame: at wk 1]</li> <li>• Proportion of participants achieving an improvement (reduction) in worst pruritus NRS <math>\geq</math> 4 from baseline at day 2 for participants randomised to 30mg [Time frame: at day 2]</li> <li>• Proportion of participants achieving an improvement (reduction) in worst pruritus NRS <math>\geq</math> 4 from baseline at day 3 for participants randomised to 15mg [Time frame: at day 3]</li> <li>• Proportion of participants achieving an improvement (reduction) in Atopic dermatitis impact scale (ADerm-IS) sleep domain score <math>\geq</math> Minimal clinically important difference (MCID) [Time frame: at wk 16]</li> <li>• Proportion of participants achieving an improvement (reduction) in Atopic dermatitis symptom scale (ADerm-SS) skin pain score <math>\geq</math> MCID [Time frame: at wk 16]</li> <li>• Proportion of participants achieving an improvement (reduction) in ADerm-SS total score <math>\geq</math> MCID [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving an improvement (reduction) in ADerm-IS total score <math>\geq</math> MCID [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving EASI 100 [Time frame: at wk 16]</li> <li>• Proportion of participants achieving vIGA-AD of 0 with a reduction of <math>\geq</math> 2 points [Time frame: at wk 16]</li> <li>• Proportion of participants achieving EASI 75 [Time frame: up to wk 4]</li> </ul>
<b>Key Results</b>	-
<b>Adverse effects (AEs)</b>	-
<b>Expected reporting date</b>	Primary completion date reported as March 2020. Study completion date reported as August 2022.

<sup>e</sup> Information provided by AbbVie Ltd.



<b>Trial</b>	<b>AD Up, <a href="#">NCT03568318</a>, <a href="#">EudraCT: 2017-005126-37</a>; children and adults aged 12-75 yrs; upadacitinib vs placebo, both in combination with topical corticosteroids (TCS); phase III</b>
<b>Sponsor</b>	AbbVie Ltd
<b>Status</b>	Ongoing
<b>Source of Information</b>	Trials registry <sup>9,38</sup> , manufacturer
<b>Location</b>	EU (incl UK), USA, Canada and other countries
<b>Design</b>	Randomised, parallel assignment, quadruple masked, placebo-controlled
<b>Participants</b>	n=810 (planned); children and adults 12 – 75 yrs old; active moderate to severe AD defined by Eczema Area and Severity Index (EASI), Investigator's Global Assessment (IGA), Body surface area (BSA), and pruritus; candidate for systemic therapy or have recently required systemic therapy for AD.
<b>Schedule<sup>9,f</sup></b>	<b>Experimental: Arm A</b> Upadacitinib 30mg is administered once daily along with TCS. <b>Experimental: Arm B</b> Upadacitinib 15mg is administered once daily along with TCS. <b>Experimental: Arm C</b> Placebo administered once daily and TCS followed by upadacitinib 30mg once daily along with TCS. <b>Experimental: Arm D</b> Placebo administered once daily and TCS followed by upadacitinib 15mg once daily along with TCS.
<b>Follow-up<sup>f</sup></b>	The study is comprised of a 35-day screening period, a 16 wk double-blind treatment period, a blinded extension period of up to wk 136, and a 30-day follow-up visit.
<b>Primary Outcomes</b>	<ul style="list-style-type: none"> <li>• Proportion of participants achieving at least a 75% reduction in Eczema Area and Severity Index (EASI 75) [Time frame: at wk 16]</li> <li>• Proportion of participants achieving validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) of 0 or 1 with at least two grades of reduction [Time frame: at wk 16]</li> </ul>
<b>Secondary Outcomes</b>	<ul style="list-style-type: none"> <li>• Proportion of participants achieving an improvement (reduction) in worst pruritus Numerical Rating Scale (NRS) <math>\geq 4</math> [Time Frame: At wk 16]</li> <li>• Proportion of participants achieving EASI 90 [Time Frame: At wk 16]</li> <li>• Percent change from Baseline of worst pruritus NRS at wk 16;</li> <li>• Percent change in EASI score from Baseline at wk 16.</li> </ul>
<b>Key Results</b>	-
<b>Adverse effects (AEs)</b>	-
<b>Expected reporting date</b>	Primary completion date reported as March 2020 and study completion date reported as August 2022.

<b>Trial</b>	<b><a href="#">NCT02925117</a>, <a href="#">EudraCT: 2016-002451-21</a>; adults aged 18-75 yrs; upadacitinib vs placebo; phase II</b>
<b>Sponsor</b>	AbbVie Ltd
<b>Status</b>	Complete but unpublished

<sup>f</sup> Information provided by AbbVie Ltd.



<b>Source of Information</b>	Conference presentation <sup>39</sup> , trials registry <sup>6,40</sup> , manufacturer
<b>Location</b>	EU (incl UK), USA, Canada and other countries
<b>Design</b>	Randomised, parallel group assignment, quadruple masking, placebo-controlled
<b>Participants</b>	n=166; adults aged 18 to 75 yrs; AD with a diagnosis confirmed by a dermatologist (according to the Hanifin and Rajka criteria) and onset of symptoms at least 1 year prior to baseline; moderate to severe AD defined by an Eczema Area and Severity Index (EASI) $\geq$ 16, Body Surface Area (BSA) $\geq$ 10% and an Investigators Global Assessment (IGA) score $\geq$ 3 at the Baseline visit; documented history (within 1 year prior to the screening visit) of inadequate response to treatment with topical corticosteroids (TCS), or topical calcineurin inhibitors (TCI), or for whom topical treatments are otherwise medically inadvisable (e.g., because of important side effects or safety risks); twice daily use of an additive-free, bland emollient for at least 7 days prior to baseline.
<b>Schedule<sup>6</sup></b>	<p><b>Active comparator: Participants receiving dose 30mg</b> Participants receiving dose 30mg once daily for 16 wks</p> <p><b>Active comparator: Participants receiving dose 15mg</b> Participants receiving dose 15mg once daily for 16 wks</p> <p><b>Placebo comparator: Participants receiving matching placebo</b> Participants receiving matching placebo for 16 wks</p> <p><b>Active comparator: Participants receiving dose 7.5mg</b> Participants receiving dose 7.5mg once daily for 16 wks</p>
<b>Follow-up</b>	Not reported.
<b>Primary Outcomes</b>	<ul style="list-style-type: none"> <li>• Mean Percentage Change in EASI score [Time frame: at wk 16]</li> </ul>
<b>Secondary Outcomes</b>	<ul style="list-style-type: none"> <li>• Percent change in EASI score [Time frame: from day 1 (baseline) and wk 8]</li> <li>• Proportion of participants achieving EASI 75 response [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving EASI 90 response [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving SCORAD 90 response [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving SCORAD 50 response [Time frame: up to wk 16]</li> <li>• Summary of EASI 75 at all visits in Period 2 among those who were re-randomized as EASI 75 non-responders at wk 16 [Time frame: up to wk 88]</li> <li>• Proportion of participants with Dermatology Life Quality Index (DLQI) = "0" or "1" [Time frame: up to wk 16]</li> <li>• Proportion of participants achieving SCORAD 75 response [Time frame: up to wk 16]</li> <li>• Percent change in SCORAD score [Time frame: from day 1 to wk 16]</li> <li>• Time to loss of EASI 50 response relative to Baseline among those who were re-randomized as EASI 75 responders at wk 16 [Time frame: up to wk 88]</li> <li>• Change and percent change from wk 16 (re-randomization) in EASI score at all Period 2 visits [Time frame: up to wk 88]</li> <li>• Proportion of participants achieving EASI 50 response [Time frame: up to wk 16]</li> <li>• Percent change in pruritus/ itch numerical rating scale (NRS) [Time frame: from day 1 (baseline) to wk 16]</li> </ul>

	<ul style="list-style-type: none"> <li>• Proportion of participants achieving an Investigator Global Assessment (IGA) of "0" or "1" [Time frame: at wk 16]</li> <li>• Change from Baseline in DLQI [Time frame: from day 1 to wk 16]</li> <li>• Proportion of Participants achieving an EASI 75 response [Time frame: at wk 16]</li> </ul>																																
<b>Key Results<sup>39</sup></b>	<p><b>Mean % Improvement from Baseline in EASI Score (primary endpoint at week 16)</b></p> <table border="1" data-bbox="438 405 1198 629"> <tr> <td>30mg Upa</td> <td>74.4%***</td> </tr> <tr> <td>15mg Upa</td> <td>61.7%***</td> </tr> <tr> <td>7.5mg Upa</td> <td>39.4%*</td> </tr> <tr> <td>Placebo</td> <td>23%</td> </tr> </table> <p>***p&lt;0.001, **p&lt;0.01, *p&lt;0.05, UPA vs placebo.</p> <p>Missing data handled by last observation carried forward (LOCF).</p> <p><b>Achievement of EASI 50 at week 16 (% of patients)</b></p> <table border="1" data-bbox="438 792 1198 1016"> <tr> <td>30mg Upa</td> <td>83.3%***</td> </tr> <tr> <td>15mg Upa</td> <td>71.4%***</td> </tr> <tr> <td>7.5mg Upa</td> <td>50%*</td> </tr> <tr> <td>Placebo</td> <td>22%</td> </tr> </table> <p><b>Achievement of EASI 75 at week 16 (% of patients)</b></p> <table border="1" data-bbox="438 1128 1198 1352"> <tr> <td>30mg Upa</td> <td>69.0%</td> </tr> <tr> <td>15mg Upa</td> <td>52.4%</td> </tr> <tr> <td>7.5mg Upa</td> <td>38.6%</td> </tr> <tr> <td>Placebo</td> <td>9.8%</td> </tr> </table> <p><b>Achievement of EASI 90 at week 16 (% of patients)</b></p> <table border="1" data-bbox="438 1464 1198 1688"> <tr> <td>30mg Upa</td> <td>50.0%</td> </tr> <tr> <td>15mg Upa</td> <td>26.2%</td> </tr> <tr> <td>7.5mg Upa</td> <td>14.3%</td> </tr> <tr> <td>Placebo</td> <td>2.4%</td> </tr> </table> <p>Statistical significance: ***P&lt;0.001, **P&lt;0.01, *P&lt;0.05, UPA vs placebo. NRI</p>	30mg Upa	74.4%***	15mg Upa	61.7%***	7.5mg Upa	39.4%*	Placebo	23%	30mg Upa	83.3%***	15mg Upa	71.4%***	7.5mg Upa	50%*	Placebo	22%	30mg Upa	69.0%	15mg Upa	52.4%	7.5mg Upa	38.6%	Placebo	9.8%	30mg Upa	50.0%	15mg Upa	26.2%	7.5mg Upa	14.3%	Placebo	2.4%
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<b>Adverse effects (AEs)<sup>39</sup></b>	<table border="1" data-bbox="438 1816 1390 2004"> <tr> <td data-bbox="438 1816 764 1888"></td> <td data-bbox="764 1816 994 1888"></td> <td colspan="3" data-bbox="994 1816 1390 1888"><b>Upadacitinib (UPA) QD</b></td> </tr> <tr> <td data-bbox="438 1888 764 2004"><b>Patients, n (%)</b></td> <td data-bbox="764 1888 994 2004"><b>Placebo, n=40</b></td> <td data-bbox="994 1888 1086 2004"><b>7.5 mg, n=42</b></td> <td data-bbox="1086 1888 1206 2004"><b>15 mg, n= 42</b></td> <td data-bbox="1206 1888 1390 2004"><b>30 mg, n=42</b></td> </tr> </table>			<b>Upadacitinib (UPA) QD</b>			<b>Patients, n (%)</b>	<b>Placebo, n=40</b>	<b>7.5 mg, n=42</b>	<b>15 mg, n= 42</b>	<b>30 mg, n=42</b>																						
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	Any AE	26 (65.0)	30 (71.4)	32 (76.2)	32 (76.2)
	Serious AE	1 <sup>a</sup> (2.5)	2 <sup>b,c</sup> (4.8)	1 <sup>d</sup> (2.4)	0
	AE leading to study drug discontinuation	2 (5.0)	4 (9.5)	1 (2.4)	4 (9.5)
	Severe AE	1 <sup>a</sup> (2.5)	0	1 <sup>d</sup> (2.4)	0
	AE possibly related to study drug	12 (30.0)	16 (38.1)	15 (35.7)	23 (54.8)
	<b>AEs in ≥10% of patients in any group</b>				
	Upper respiratory tract infection	4 (10.0)	7 (16.7)	5 (11.9)	5 (11.9)
	Atopic dermatitis worsening	3 (7.5)	7 (16.7)	3 (7.1)	5 (11.9)
	Acne	1 (2.5)	4 (9.5)	2 (4.8)	6 (14.3)
<b>Expected reporting date</b>	Previously reported as January 2019.				

## ESTIMATED COST

The cost of upadacitinib is not yet known.

## RELEVANT GUIDANCE

### NICE GUIDANCE

- NICE technology appraisal guidance. Tacrolimus and pimecrolimus for atopic eczema (TA82). August 2004.
- NICE technology appraisal guidance. Frequency of application of topical corticosteroids for atopic eczema (TA81). August 2004.
- NICE Technology Appraisal Guidance. Dupilumab for treating moderate to severe atopic dermatitis (TA534). August 2018.

### NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Specialised Allergy Services (All ages). B09/S/b.
- NHS England. 2013/14 NHS Standard Contract for Specialised Dermatology Services (All ages). A12/S/a.

### OTHER GUIDANCE

- Ring et al. Guidelines for treatment of atopic eczema (atopic dermatitis) Part I. 2012.<sup>41</sup>
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## ADDITIONAL INFORMATION

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