

HEALTH TECHNOLOGY BRIEFING FEBRUARY 2020

Abrocitinib for moderate to severe atopic dermatitis

NIHRIO ID	12772	NICE ID	10108
Developer/Company	Pfizer Limited (UK)	UKPS ID	652035

Licensing and market availability plans	Currently in phase III clinical trials.
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SUMMARY

Abrocitinib is in development for the treatment of moderate to severe atopic dermatitis (AD) in adolescents and adults aged 12 years or over. 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 could suffer from 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.

Abrocitinib is a medicinal product taken by mouth (tablets) and acts by selectively blocking a protein called Janus Kinase 1 (JAK-1). JAKs contribute to cell processes that result in an immune or inflammatory response. JAK dependent enzymes are major contributors to the progression of immune-mediated diseases such as AD. Therefore, blocking these enzymes may be beneficial. Abrocitinib, if licensed, may offer the first oral, once-daily treatment option for patients with moderate to severe AD.

PROPOSED INDICATION

Treatment for adolescents and adults aged 12 years or over with moderate to severe atopic dermatitis (AD).^a

TECHNOLOGY

DESCRIPTION

Abrocitinib (PF-04965842) is an oral Janus Kinase 1 (JAK1) selective inhibitor that inhibits several key cytokine signalling pathways known to have an important role in the pathophysiologic characteristics of AD, including interleukin-4 (IL-4), IL-13, IL-31, and interferon γ .¹

Abrocitinib is currently in phase III clinical development for the treatment of moderate to severe atopic dermatitis, in patients aged 12 years and over. In the phase III clinical trials (JADE Mono-1; NCT03349060, JADE Mono-2; NCT03575871) patients are randomised to either 100mg or 200mg abrocitinib or placebo, given orally as two tablets and taken once daily for 12 weeks.^{2,3} In the phase III trial (JADE Compare; NCT03720470), patients are randomised to either 100mg or 200mg abrocitinib taken orally as two tablets on a background of topical therapies taken once daily for 16 weeks or 600mg dupilumab administered as two 300mg injections as a loading dose on day one, followed by a 300mg injection every 2 weeks until week 16.⁴ In the phase III trial (JADE TEEN; NCT03796676) patients are randomised to either 100mg or 200mg abrocitinib taken orally as two tablets on a background of topical therapies or placebo for 12 weeks.⁵

INNOVATION AND/OR ADVANTAGES

AD is a common chronic inflammatory skin disease characterised by intense pruritus and eczematous lesions. The burden associated with the disease is substantial, encompassing physical, psychological, social, and economic costs. Although emollients and topical anti-inflammatory agents are the cornerstone of AD treatment, they are often insufficient for individuals with moderate to severe disease. Phototherapy and systemic corticosteroids are treatment options, but the former is limited by accessibility, and the latter is not recommended because of safety concerns. Systemic immunosuppressants may be prescribed but are off-label in many countries and are associated with considerable adverse effects that limit treatment duration. Dupilumab was recently approved in several countries for treatment of moderate to severe AD. Although this is an important addition to the treatment landscape, some patients do not respond adequately, and others are unwilling or unable to receive subcutaneous injections. Consequently, there remains a need for alternative therapies for AD.¹

Results from the JADE Mono-1 trial showed that abrocitinib met all the co-primary and key secondary endpoints, which were related to skin clearance and itch relief compared to placebo. Safety data showed that both evaluated doses of abrocitinib (200mg and 100mg) were well tolerated and were consistent with a companion study (JADE MONO-2) from the JAK1 Atopic Dermatitis Efficacy and Safety (JADE) global development program. If licensed, abrocitinib may provide the first oral, once-daily treatment option for patients with moderate to severe AD.⁶

^a Information provided by Pfizer Limited on UK PharmaScan

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Abrocitinib does not currently have a Marketing Authorisation in the EU/UK for any indication.

PATIENT GROUP

DISEASE BACKGROUND

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.⁷ AD has a complex and heterogeneous aetiology, characterised histologically by skin infiltration of inflammatory cells, predominantly lymphocytes, eosinophils, and mast cells.⁸

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.^{9,10} The symptoms of AD can have certain triggers, such as soaps, detergents, stress and the weather.¹¹ 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.^{9,10}

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.¹¹

The appearance and location of AD changes with age. In infants it mainly affects the face and limb extensor surfaces. In adolescents and adults, it is most commonly localised and found on the flexural surfaces of the body, anterior and lateral neck, eyelids, forehead, scalp, face, wrists, dorsa of the feet, and hands.⁷

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.¹²

CLINICAL NEED AND BURDEN OF DISEASE

Although AD presents most frequently in childhood, it can present at any age.^{13,14} Estimates vary due to the different populations examined, but figures suggest that it affects about 10-30% of children and 2-10% of adults.¹⁴⁻²¹ AD affects both males and females equally.²²

It is indicated that AD affects 1 in 12 adults in the UK.²³ 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.²⁴

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

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Dermatitis has several causes, which may influence treatment. Management of dermatitis involves the removal or treatment of contributory factors that may trigger the development of the disease or worsen a flare. The management of AD also involves the use of different therapies to ease the symptoms.^{11,26}

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 and topical and oral corticosteroids.²⁷

CURRENT TREATMENT OPTIONS

The following treatment options have been recommended for moderate AD:²⁷

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

The following treatment options have been recommended for severe AD:²⁷

- Emollients
- Potent topical corticosteroids
- Topical calcineurin inhibitors
- Bandages
- Phototherapy
- Oral corticosteroids

PLACE OF TECHNOLOGY

If licensed, abrocitinib will offer an additional treatment option for patient's age 12 years and over who have moderate to severe AD.

CLINICAL TRIAL INFORMATION

Trial	JADE Mono-1; NCT03349060 ; 2017-003651-29 ; A Phase 3 Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multi-Center Study To Evaluate The Efficacy And Safety Of Pf-04965842 Monotherapy In Subjects Aged 12 Years And Older, With Moderate To Severe Atopic Dermatitis. Phase III - completed Locations: EU (incl UK), United States, Canada and other countries.
Trial design	Randomised, parallel assignment, quadruple-blinded.

Population	N=387, moderate to severe AD with inadequate response or inability to tolerate topical AD treatments or require systemic treatments for AD control, aged 12 years or older.
Intervention(s)	<ul style="list-style-type: none"> • Abrocitinib 100mg (oral), administered as one tablet • Abrocitinib 200mg (oral), administered as two 100mg tablets
Comparator(s)	Matched placebo
Outcome(s)	<ul style="list-style-type: none"> • Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response of Clear (0) or Almost Clear (1) and Greater Than or Equal to 2 Points Improvement [Time frame: Baseline, Week 12] • Percentage of Participants Achieving Eczema Area and Severity Index (EASI) Response of at least 75% Improvement From Baseline at Week 12 [Time frame: Baseline, Week 12] <p>See trial record for full list of other outcomes</p>
Results (efficacy)	Both doses of abrocitinib significantly improved the IGA and EASI-75 dose response outcomes compared to placebo. ⁶
Results (safety)	The most frequently reported treatment-emergent adverse events in abrocitinib-treated patients (200mg, 100mg) were short-lasting nausea (20.1%, 9.0%), headache (9.7%, 7.7%), and nasopharyngitis (11.7%, 14.7%), while for placebo, it was dermatitis (16.9%). Observed serious adverse events (SAEs) for abrocitinib 200mg were inflammatory bowel disease, peritonitis, dehydration, and asthma (2 cases). SAEs seen for the 100mg dose included retinal detachment, acute pancreatitis, appendicitis, dizziness, and seizures. In the placebo arm, SAEs were condition aggravated, appendicitis, meniscal degeneration, and atopic dermatitis. ⁶

Trial	<p>JADE Mono-2; NCT03575871; 2018-001136-21; A phase 3 randomized, double-blind, placebo-controlled, parallel group, multi-center study to evaluate the efficacy and safety of pf-04965842 monotherapy in subjects aged 12 years and older, with moderate to severe atopic dermatitis.</p> <p>Phase III - Completed</p> <p>Location(s): EU (incl UK), United States, Canada and other countries.</p>
Trial design	Randomised, parallel assignment, quadruple-blinded.
Population	N=391, moderate to severe AD with inadequate response or inability to tolerate topical AD treatments or require systemic treatments for AD control, aged 12 years or older.
Intervention(s)	<ul style="list-style-type: none"> • Abrocitinib 100mg (oral), administered as one tablet • Abrocitinib 200mg (oral), administered as two 100mg tablets
Comparator(s)	Matched placebo.
Outcome(s)	<ul style="list-style-type: none"> • Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response of Clear (0) or Almost Clear (1) and Greater Than or Equal to 2 Points Improvement [Time frame: Baseline, Week 12]

	<ul style="list-style-type: none"> Percentage of Participants Achieving Eczema Area and Severity Index (EASI) Response of at least 75% Improvement From Baseline at Week 12 [Time frame: Baseline, Week 12] <p>See trial record for full list of other outcomes</p>
Results (efficacy)	-
Results (safety)	-

Trial	<p>JADE Compare; NCT03720470; 2018-002573-21; A phase 3 randomized, double-blind, double-dummy, placebo-controlled, parallel group, multi-center study investigating the efficacy and safety of pf-04965842 and dupilumab in comparison with placebo in adult subjects on background topical therapy, with moderate to severe atopic dermatitis.</p> <p>Phase III - ongoing</p> <p>Locations: EU (incl UK), United States, Canada and other countries.</p>
Trial design	Randomised, parallel assignment, quadruple-blinded.
Population	N=759, moderate to severe AD with inadequate response to treatment with medicated topical therapy for AD for at least 4 weeks, or who have required systemic therapies for control of their disease, aged 18 years or older.
Intervention(s)	<ul style="list-style-type: none"> Abrocitinib 100mg (oral), administered as two tablets + placebo (injections), followed by abrocitinib 100mg (oral) alone Abrocitinib 200mg (oral), administered as two tablets + placebo (injections), followed by abrocitinib 200mg (oral) alone
Comparator(s)	<ul style="list-style-type: none"> Dupilumab 600mg (injection) administered as 2x 300mg injections + matched placebo for abrocitinib, followed by matched placebo for abrocitinib alone
Outcome(s)	<ul style="list-style-type: none"> Percentage of Participants Achieving Investigator's Global Assessment (IGA) Response of Clear (0) or Almost Clear (1) and Greater Than or Equal to 2 Points Improvement [Time frame: Baseline, Week 12] Percentage of Participants Achieving Eczema Area and Severity Index (EASI) Response of at least 75% Improvement From Baseline at Week 12 [Time frame: Baseline, Week 12] <p>See trial record for full list of other outcomes</p>
Results (efficacy)	-
Results (safety)	-

Trial	JADE TEEN ; NCT03796676 ; 2018-003804-37 ; A phase 3, randomized, double-blind, placebo-controlled, multi-center study investigating the efficacy and safety of pf-04965842 co-administered with background medicated topical therapy in adolescent participants 12 to <18 years of age with moderate-to-severe atopic dermatitis. Phase III - ongoing Locations: EU (incl UK), United States, Canada and other countries.
Trial design	Randomised, parallel assignment, quadruple-blind.
Population	N=225, moderate to severe AD, aged between 12 and 17 years.
Intervention(s)	<ul style="list-style-type: none"> Abrocitinib 100mg Abrocitinib 200mg
Comparator(s)	Matched placebo.
Outcome(s)	<ul style="list-style-type: none"> Change from baseline response based on IGA score of 0 or 1 and a reduction from baseline of at least 2 points. [Time frame: Day 1 (Baseline), Week 12 (end of treatment/early termination).] Change from baseline response based on the EASI of more than 75% improvement from baseline (EASI-75). [Time frame: Day 1 (Baseline), Week 12 (end of treatment/early termination).] <p>See trial record for full list of other outcomes</p>
Results (efficacy)	-
Results (safety)	-

ESTIMATED COST

The cost of abrocitinib is not yet known.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal guidance in development. Baricitinib for treating moderate to severe atopic dermatitis (ID1622). TBC.
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- NICE technology appraisal guidance in development. Upadacitinib for treating moderate to severe atopic dermatitis in people aged 12 and over (ID3733). TBC.
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- 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

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ADDITIONAL INFORMATION

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