**Cibinqo® (abrocitinib)**

# Category

Best Pharmaceutical Agent

# Drug or Device Name

Cibinqo®

# Compound Technical Name

abrocitinib

# Trade Name

Cibinqo®

# Date of Approval

January 14, 2022

# Therapeutic Categories

Dermatology, Inflammation

# Indications

CIBINQO is a Janus kinase (JAK) inhibitor indicated for the treatment of adults with refractory, moderate-to-severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable.

Limitation of Use: CIBINQO is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants.

# Background

Atopic dermatitis (AD), also known as eczema, is one of the most common inflammatory skin diseases, affecting approximately 20% of children and 3% of adults. It is a chronic inflammatory condition characterized by acute flareups of eczematous pruritic lesions over dry skin. The disease often precedes other allergic conditions such as allergic rhinitis and asthma. This sequence of disorders is commonly referred to as the “atopic march”. Symptoms of atopic dermatitis often include patches of red or brownish dry, cracked or scaly skin. In infants it may appear as tiny bumps on the cheeks, whereas older children and adults have lesions on the knees, elbows or the back of the scalp.

Atopic dermatitis poses a significant burden on healthcare resources and quality of life for patients, owing to sleep loss as a result of itching, employment loss, time to care and financial costs of care. The burden from direct and indirect costs of the disease is estimated to be $38 billion (AJMC, June 20, 2017 – Avena-Woods, C. v23i8). Most patients with AD experience itch on a daily basis, and in some cases the degree of itch is associated with mental distress and increased risk of suicidal ideation. Sleep disturbance associated with itch is found in 67% of AD patients, leading to daytime fatigue. In children, these sleep disturbances are associated with higher rates of attention deficit disorder, headaches and short stature.

The pathophysiology of AD is complex, multifactorial and poorly understood. Genetic predisposition, skin barrier disruption, immune system dysregulation and environmental factors are believed to contribute to the disease. Two major theories have been advanced to explain the cause of the disease. The “inside out” hypothesis proposes that allergic triggering leads to a weakened skin barrier that furthers allergen introduction and inflammation. The “outside in” hypothesis invokes an impaired skin barrier that precedes AD and is necessary for immune dysregulation to occur. These theories are not necessarily mutually exclusive.

The epidermis plays a key role in the physical and functional barrier of the skin. It is comprised of several proteins, including filaggrin, transglutaminases, keratin and intracellular proteins. Differences in the protein composition of the epidermis can lead to barrier impairment and penetration of allergens and microbes, leading to further immune and inflammatory response. Loss of function mutations in the FLG gene, which encodes filaggrin, are strongly associated with AD; 10% of the western population and 50% of AD patients carry mutations in FLG.

The immune response observed during the course of AD is biphasic. A Th2-based immune response is predominant in the initial or acute phase of the disease, whereas a Th1-based response is characteristic of chronic AD lesions. Key cytokines in AD pathogenesis are IL-4 and IL-13 although several other cytokines (IL-31, IL-22, TARC) also play a significant role. In addition, regulatory T-cells and the innate immune system are altered in the skin. As a result, microbial defenses are compromised, and *S. aureus* is often found in both diseased and healthy skin of AD patients, which exacerbates lesions.

Treatment of atopic dermatitis frequently begins by recognizing and avoiding triggers of AD exacerbation, which can include viral infections, food allergens, cosmetics, fragrance and extremes of hot or cold weather. Symptom relief may be provided by topical or oral corticosteroids. While effective, chronic use of topical corticosteroids can lead to thinning of the skin. Oral corticosteroids cannot be used chronically due to severe systemic side effects. Local infections of the skin are treated with antibiotic ointments or oral antibiotics. Dupilumab was approved by the FDA for treatment of moderate to severe atopic dermatitis in patients over 6 years of age whose disease is not adequately controlled with topical agents or when those therapies are not advisable. Dupilumab is a dual IL-4 and IL-13 inhibitor. While these are major cytokines associated with the Th2 driven response in AD, inhibiting Th1 and Th2 cytokines offers the potential for greater efficacy.

Janus kinases (JAKs) are intracellular kinases that mediate cytokine and growth factor signaling in inflammation, immune homeostasis and hematopoiesis. There are four members of the JAK family: JAK1, JAK2, JAK3 and TYK2. Cytokine binding to its cognate receptor initiates a dimerization or multimerization event of the receptor subunits. JAKs associated with those receptor subunits are brought into proximity with each other, leading to transphosphorylation and activation. These phosphorylated kinases in turn phosphorylate tyrosine residues on the intracellular domain of the cytokine receptor, creating docking sites for the recruitment of signal transducer and activator of transcription factor (STAT) proteins. These STAT proteins then dimerize and translocate to the nucleus, where they modulate gene expression.

JAK1 has the broadest cytokine signaling profile among the different JAK family members and is the only isoform that pairs with all three other family members. There are no redundant pathways known for cytokines that signal through JAKs, making this family of proteins very attractive for modulating inflammatory disease. Cytokines important in AD pathogenesis, such as IL-4, IL-13, IL-31, IL-22, and TARC signal through JAK-1. Tofacitinib was the first JAK inhibitor to be approved for clinical use. Originally developed as a selective JAK3 inhibitor, it was later found to be a JAK1 and JAK3 inhibitor with moderate activity on JAK2. Residual JAK2 inhibition with tofacitinib could result in potential for anemia and thrombocytopenia at doses higher than indicated, owing to the interference with EPO and TPO signaling upon inhibition of JAK2. Given the prominent role of JAK1 in inflammatory cytokine signaling, the team sought a selective JAK1 inhibitor to modulate inflammatory processes involved in dermatitis and arthritis while potentially reducing the hematopoietic effects of JAK2 inhibition. It was on this basis that the abrocitinib program started.

# Development

# The abrocitinib development program was designed to test the hypothesis that strong JAK1 inhibition selectivity over JAK2, JAK3 and TYK2 would result in potent efficacy that minimized the occurrence of dose-limiting hematologic toxicities entioned above. The first approved JAK inhibitor, tofacitinib, has excellent selectivity for JAK family proteins relative to other kinases in the human kinome. Much of this selectivity is attributed to the pyrrolopyrimidine hinge-binding motif. As such, this moiety was retained, and different diamines were surveyed as replacements for the 3-aminopiperidine linker. As part of this survey, it was noted that the *cis*-1,3-diaminocylobutane linker bearing a terminal sulfonamide conferred excellent potency for JAK1 while demonstrating selectivity for other JAK family members. As an example, compound 2 demonstrated remarkable JAK1 potency (IC50 = 6 nM) and selectivity over JAK2 (69-fold) in an in vitro kinase activity assay run at the physiologically relevant ATP concentration of 1 mM. However, this compound had unacceptably high intrinsic clearance in human liver microsomes. This issue could be addressed by substituting the phenyl sulfonamide for a small alkyl sulfonamide at the expense of JAK1 potency. On the basis of their outstanding JAK1 activity and selectivity, substituted phenyl sulfonamide analogues were extensively surveyed. However, none of these compounds showed acceptable clearance. Notably, the majority of these compounds did not show appreciable activity against JAK3 (IC50 > 8 uM) and only had modest activity against TYK2 (IC50 > 200 nM). In order to better estimate the required concentrations for efficacy in vivo, potency measurements were also made in a human whole blood (HWB) assay. In general, IC50 values were right-shifted 5- to 35-fold in human whole blood owing to the effects of plasma protein binding. Therefore, smaller and less lipophilic sulfonamides were chosen for further medicinal chemistry focus.

# Figure 1: Chemical structures of tofacitinib, abrocitinib and key analogues

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# Additional modifications to the sulfonamide linker included sulfamide, sulfone and reverse sulfonamide linkers. Sulfamide analogues such as 3 demonstrated good JAK1 activity (IC50 = 51 nM), JAK2 selectivity (21x) and human liver microsome apparent intrinsic clearance (10 uL/min/mg). Smaller sulfamide substituents generally showed poorer JAK1 potency and attempts to extend the sulfamide substituent further resulted in lower metabolic stability. Sulfone replacements led to improved JAK1 potency relative to the corresponding sulfamides, but only larger sulfone substituents conferred appreciable JAK2 potency. The *n*-butyl analogue 4 demonstrated potent JAK1 inhibition (IC50 = 9 nM), 24-fold JAK2 selectivity and modest apparent intrinsic clearance in human liver microsomes. When assessed in a human whole blood cytokine release assay, this compound demonstrated potent activity against IFNa (155 nM) and good selectivity vs. EPO (4.1 uM). Reverse sulfonamide analogues such as 5 also demonstrated good JAK1 activity (IC50 = 11 nM) and JAK2 selectivity (18x) but required larger substituents to deliver this profile at the expense of

# Collecting all observations of potency, selectivity and metabolic stability from these analogues generally revealed that alkyl sulfonamides delivered the best overall profiles with larger substituents being preferred for selectivity and compounds with LogD < 2.0 delivering acceptable metabolic stability. Moreover, crystal structures were obtained for one of the simple sulfonamide analogues of 2 (compound 7) bound to JAK1 and to JAK2. The co-structure with JAK1 is shown in Figure 1 and reveals an important hydrogen bond interaction between the sulfonamide NH group and the carbonyl groups of Asn1008 as well as a water mediated hydrogen bond between the pyrrolopyrimidine group and the sidechain of Glu966. This residue is different in JAK2 (Asp939) and therefore requires a more extended network of water molecules to make the interaction with the pyrrolopyrimidine. Moreover, in JAK2 there is a unique water-mediated hydrogen bond between the ligand sulfonamide S=O group and Lys 857. Using this structural information, polar substituents were incorporated on the sulfonamide aliphatic chain. The best of these derivatives is the nitrile 6, which exhibited 15 nM activity against JAK1, 63x selectivity vs. JAK2 and low intrinsic metabolic clearance (<8 ul/min/mg). Its potency in the HWB IFNa assay (IC50 = 220 nM) and was well separated from EPO activity (IC50 > 7 uM). The corresponding unsubstituted compound 7 exhibited comparable JAK1 potency (IC50 = 29 nM), JAK2 selectivity (28x) HWB IFNa activity (IC50 = 190 nM) and selectivity vs. EPO pSTAT3 signaling in HWB (IC50 = 7.2 uM). These two compounds were compared in rat PK and in vivo efficacy studies. In these studies, compound 7 showed superior in vivo clearance and bioavailability, resulting in lower human dose projections than 6. Compound 7 also showed good permeability and solubility in in vitro assays. The in vivo PK-PD relationship was characterized upon oral dosing in naïve Lewis rats. The inhibition of pSTAT3 formation induced by IFNg, IL-21 and IL-6 was directly linked to compound concentration and was not time dependent. The calculated unbound plasma IC50 values were 190 nM, 940 nM and 180 nM respectively. This compound was also active in a rat model of adjuvant induced arthritis with a Cave50 of 1.3 uM. Extensive characterization of kinase selectivity and JAK/STAT signaling activity revealed an excellent profile at the project human dose of 200 mg to deliver average JAK1 inhibition of 80% over the dosing interval as shown in Figure 2. On the basis of these observations, compound 7 (abrocitinib) was selected for clinical development.

# Figure 2: Selectivity profile for the 200 mg abrocitinib dose relative to cytokine signaling through different JAK family members.

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# The safety, tolerability and pharmacokinetics of abrocitinib were evaluated in a Phase 1 study including 79 healthy participants. There were no serious adverse events; headache (16.4%), nausea (13.9%) and diarrhea (13.9%) were the most frequent treatment-emergent adverse events. Elevated HDL and LDL cholesterol were noted in some subjects. A Phase 2 study in psoriasis showed that abrocitinib at doses of 400 mg QD and especially at 200 mg BID was associated with hematologic toxicities. In a 12-week Phase 2b AD trial, safety and efficacy were evaluated in 267 patients with moderate to severe AD who had a contraindication or inadequate response to topical medications for at least 4 weeks of the prior 12 months using 200 mg QD as maximal dose. At week 12, 43.8% of patients receiving QD 200 mg abrocitinib showed clear or almost clear on the Investigator’s Global Assessment (IGA) with improvement of two or more grades from baseline. Upper respiratory tract infections, headache, nausea, dermatitis atopic and diarrhea were the most frequent TEAEs. Hematologic abnormalities of reduced platelet counts were noted in the 200 mg and 100 mg groups, which trended toward normalization after 4 weeks with continued treatment.

# On the basis of these observations, abrocitinib alone was evaluated in two 12-week Phase 3 studies (JADE MONO-1 and JADE MONO-2) across three treatment groups: 200 mg abrocitinib, 100 mg abrocitinib and placebo (2:2:1). Adults and adolescents were enrolled. According to the JADE MONO-1 study, 333/387 patients completed 12 weeks of treatment. Of these patients, 43.8% in the 200 mg group achieved clear or almost clear on the IGA with at least 2 grades of improvement, compared to 23.7% in the 100 mg group and 7.9% in the placebo group. The percentage of patients achieving EASI-75 (a 75% improvement in severity of disease) at week 12 was 62.7% in the 200 mg group, 39.7% in the 100 mg group and 11.8% in the placebo group. In addition, a PP-NRS (a measure of the severity of itch) improvement of 4 points or more was noted for 55.3% of patients in the 200 mg group, 45.2% in the 100 mg group and 11.5% in the placebo group. A 4-point decrease in itch is considered a clinically significant improvement associated with improvements in quality-of-life. The median time to PP-NRS response was 29 days in the 200 mg group, 58 days in the 100 mg group and 112 days in the placebo group. Adverse event profiles were similar to those seen in earlier studies.

The 16-week Phase 3 JADE-COMPARE study was conducted to evaluate the performance of abrocitinib (200 mg and 100 mg QD) in adults with moderate to severe AD who were receiving background medicated topical therapy. Dupilimab was included as an active control, with a head-to-head comparison on a key secondary endpoint - itch at week 2. Background medicated topical therapy with low or medium potency topical corticosteroids, topical calcineurin inhibitors or topical PDE4 inhibitors was to be applied to areas with active lesions and for 7-days after lesions were under control (clear or almost clear). In total, 837 patients received study drug and were included in the analysis. When administered in combination with background medicated topical therapy, both abrocitinib 100 mg QD and 200 mg QD achieved statistically significant greater responder proportions than placebo for IGA and EASI-75 at Week 12 and Week 16. At Week 2, abrocitinib 200 mg QD relieved itch more effectively (statistically significant greater proportion of PP-NRS4 responders) than placebo and dupilumab. At Week 2, abrocitinib 100 mg QD was statistically significantly more effective in relieving itch than placebo but was not significantly different from dupilumab. Compared with placebo, a significant decrease in POEM (Patient Oriented Eczema Measure) scores were observed with abrocitinib at both doses at weeks 12 and 16 (Week 16 LSM change from baseline: -12.5 for 200 mg abrocitinib, -9.2 for 100 mg abrocitinib, -10.8 for dupilumab, -5.0 for placebo (vs. both abrocitinib groups p<0.0001)). There was also a significant decrease in AD symptom severity as measured by the PSAAD scale (range 0-10, 10=extreme) from week 1 with abrocitinib, and this improvement was maintained through week 16. At week 16, LSM change from baseline PSAAD was -3.6 for abrocitinib 200 mg, -2.8 for abrocitinib 100 mg, -3.4 for dupilumab and -1.7 for placebo (vs. both abrocitinib groups p<0.0001). The proportion of patients meeting the criteria for clinically meaningful improvement (≥4-point improvement from baseline) on the NTIS severity item (range 0–10 [10 = worst itch imaginable]) with both abrocitinib doses was significantly higher compared with placebo from week 2 to 16. At week 16, proportions achieving clinically meaningful improvement were 64.3% for abrocitinib 200 mg, 52.4% for abrocitinib 100 mg, 54.0% for dupilumab, and 34.4% for placebo (vs. abrocitinib groups, P < 0.0001 and P = 0.007, respectively). In exploratory analyses, patients treated with abrocitinib 200 mg or 100 mg had significant improvement in LSM SCORAD sleep loss visual analog scale, and significant differences in LSM scores on both HADS anxiety and depression symptom subscales. In each of these studies at weeks 12 and 16, a higher proportion of patients had clinically meaningful improvements with abrocitinib 200 mg than with dupilumab or abrocitinib 100 mg. The proportion of patients with clinically meaningful improvements in PROs with abrocitinib 100 mg was similar to that with dupilumab for POEM, PtGA, NTIS severity, and HADS-Depression and was numerically lower than dupilumab for PSAAD, SCORAD sleep, and HADS-Anxiety at week 16. The study was not designed to evaluate the superiority of abrocitinib over dupilumab using statistical testing in these PRO endpoints. Patients who have failed to achieve a response with dupilumab were then randomized to abrocitinib 100 or 200 mg QD. The proportion of patients who responded to abrocitinib after having failed dupilumab was similar to the percentage of responders to each dose of abrocitinib among patients who did not have dupilumab experience.

On the basis of these results, the FDA granted approval for abrocitinib for the treatment of adults with refractory, moderate-to-severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable. CIBINQO® is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants. Consistent with other JAK inhibitors, CIBINQO® carries a boxed warning common to other JAK inhibitors, including warnings about potential serious infections, cardiovascular risks and malignancies. Please see important safety information and full prescribing information at [www.cibinqo.com](http://www.cibinqo.com)

# Innovation

# Janus associated kinases (JAKs) form specific pairs upon cytokine binding to its cognate receptor, resulting in the transmission of different cellular signals from the activated JAK protein. As such, tailored JAK inhibitor therapies offer the potential to provide differentiated activity for a variety of inflammatory conditions. Abrocitinib offers an improved selectivity profile vs. JAK2 relative to tofacitinib, which is important given the role of JAK2 signaling in erythropoiesis and platelet production.

# The design of abrocitinib to impart this selectivity required significant innovation in that the only piece retained from tofacitinib was the pyrrolopyrimidine hinge binder to retain selectivity over the broader kinome. While the JAK1 and JAK2 proteins are only 53% identical, most of the residues in the ATP binding pocket are identical between the two enzymes. Those residues that are different are pointed away from the ligand in co-crystal structures, highlighting the challenges with achieving selective JAK1 inhibition. The cis-cyclobutyl linker that was identified in a survey of diamine linker groups is unique in positioning the sulfonamide NH group in the precise orientation for productive hydrogen bonds with Asn1008 (JAK1, Asn 981 in JAK2). Careful structural studies with both JAK1 and JAK2 complexed to abrocitinib, coupled with a survey of the Cambridge Crystallographic Database around the ground state conformation of alkyl sulfonamides, revealed several factors that contribute to its selectivity for JAK1. These factors include:

# Subtle differences in hydrogen bond interactions between the pyrrolopyrimidine group and Glu966(JAK1) vs. Asp939(JAK2), the latter of which requires an extended network of water molecules.

# A unique hydrogen bonding interaction between one of the sulfonamide oxygen atoms and the backbone of Lys857 in the P-loop of JAK2, which likely influences its flexibility.

# A difference in the orientation of the propyl group of the inhibitor in JAK1 and JAK2, suggesting the P-loop of JAK1 is more open than that of JAK2.

# The relative rigidity of the P-loop of JAK2 , forcing the propylsulfonamide group into the less favored gauche conformation relative to the JAK1 structure, which shows an energetically favored anti conformation.

# Improved hydrophobic interactions with the P-loop of JAK1 relative to JAK2.

# Achieving this selectivity profile required an extensive survey of diamine linkers and substituents on the distal amine while incorporating property-based features to design for metabolic stability, permeability and solubility to achieve a favorable oral pharmacokinetic profile.

The clinical development program for abrocitinib was also innovative. The combined Single Ascending Dose / Multiple Ascending Dose (SAD/MAD) study provided valuable information early to inform the subsequent clinical development. In this study, adaptive principles were implemented by using the SAD data to make decisions on ongoing basis regarding the doses and number of subjects in the MAD part of the study. By saving time and resources, the SAD/MAD design ensured a very efficient Phase 1 study.

The subsequent Ph2 study in Psoriasis that explored a range of doses and dosing regimens indicated that Abrocitinib dosing up to 200 mg daily preserves JAK-1 selectivity and doesn’t affect JAK2. Based on these results, the top dose in the Phase 2 and 3 studies in AD was set at 200 mg daily.

The Phase 2b study in AD was used not only to establish Proof of Concept (POC) in this indication, but also to validate PSAAD. The PSAAD is a Patient Reported Outcome (PRO) instrument that was developed in accordance with regulatory agency guidance to assess daily AD symptoms during the course of therapy. This instrument includes eleven relevant symptoms (itch, dryness, redness, flaking, discoloration, pain, bleeding, cracking, bumps, swelling, and weeping/oozing) of atopic dermatitis that can be used to measure comprehensibly all the skin manifestations of AD. As a novel PRO, the validated PSAAD is a great new tool for assessment of symptoms in AD clinical trials. The Phase 3 study included adolescents, incorporated an active control agent and used Carrie’s measurement of sleep and nocturnal scratch monitoring. AD is a condition that not only leads to red inflamed skin, but also is characterized by extensive scratching, and sleep disturbances. The use of validated digital wearable technology and associated algorithms provided objective and quantitative measurements of nocturnal scratching and sleep in a home environment over time. The endpoints of nocturnal scratch and sleep were exploratory and optional endpoints in two of the clinical Phase 3 studies. Wrist worn accelerometers and associated novel digital endpoints provided quantitative knowledge regarding pharmacotherapies on the action of nocturnal scratching and sleep quantity in a symptomatic AD population, with low burden and done so passively over time. In addition, these novel digital endpoints will enhance our understanding of AD and provide future opportunities to refine and improve therapies for other conditions.

# The field of JAK inhibitors has expanded dramatically since Pfizer’s introduction of tofacitinib to the market in 2012. CIBINQO® (Abrocitinib) is one of the latest members of this pipeline of JAK inhibitors and offers a new treatment option for patients with atopic dermatitis, a disease that poses a significant burden on patients who have it.

# Publication List:

[(1) Evaluation of a Janus kinase 1 inhibitor, PF-04965842, in healthy subjects: A phase 1, randomized, placebo-controlled, dose-escalation study.](https://pubmed.ncbi.nlm.nih.gov/29672897/) Peeva E, Hodge MR, Kieras E, Vazquez ML, Goteti K, Tarabar SG, Alvey CW, Banfield C. *Br J Clin Pharmacol.* **2018**, *84*,1776-1788.

[(2) Efficacy and safety of the Janus kinase 1 inhibitor PF-04965842 in patients with moderate-to-severe psoriasis: phase II, randomized, double-blind, placebo-controlled study.](https://pubmed.ncbi.nlm.nih.gov/28949012/) Schmieder GJ, Draelos ZD, Pariser DM, Banfield C, Cox L, Hodge M, Kieras E, Parsons-Rich D, Menon S, Salganik M, Page K, Peeva E. *Br J Dermatol.* **2018**,*179*,54.

(3) [Efficacy and Safety of Oral Janus Kinase 1 Inhibitor **Abrocitinib** for Patients With Atopic Dermatitis: A Phase 2 Randomized Clinical Trial.](https://pubmed.ncbi.nlm.nih.gov/31577341/) Gooderham MJ, Forman SB, Bissonnette R, Beebe JS, Zhang W, Banfield C, Zhu L, Papacharalambous J, Vincent MS, Peeva E.*JAMA Dermatol.* **2019**,*155,*1371-1379.

(4) [Development and Content Validation of Pruritus and Symptoms Assessment for Atopic Dermatitis (PSAAD) in Adolescents and Adults with Moderate-to-Severe AD.](https://pubmed.ncbi.nlm.nih.gov/33382444/) Hall R, Lebwohl MG, Bushmakin AG, Simpson EL, Gooderham MJ, Wollenberg A, Gater A, Wells JR, Cappelleri JC, Hsu MA, Papacharalambous J, Peeva E, Tallman AM, Zhang W, Chen *L.Dermatol Ther (Heidelb).* **2021**,*11*, 221-233

1. Identification of N-{cis-3-[Methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino]cyclobutyl}propane-1-sulfonamide (PF-04965842): A Selective JAK1 Clinical Candidate for the Treatment of Autoimmune Diseases. Vazquez ML, Kaila N, Strohbach JW, Trzupek JD, Brown MF, Flanagan ME, Mitton-Fry MJ, Johnson TA, TenBrink RE, Arnold EP, Basak A, Heasley SE, Kwon S, Langille J, Parikh MD, Griffin SH, Casavant JM, Duclos BA, Fenwick AE, Harris TM, Han S, Caspers N, Dowty ME, Yang X, Banker ME, Hegen M, Symanowicz PT, Li L, Wang L, Lin TH, Jussif J, Clark JD, Telliez JB, Robinson RP, Unwalla R. *J Med Chem.* **2018,** *61,* 1130-1152. doi: 10.1021/acs.jmedchem.7b01598.
2. Impact of oral abrocitinib on signs, symptoms and quality of life among adolescents with moderate-to-severe atopic dermatitis: an analysis of patient-reported outcomes. Cork MJ, McMichael A, Teng J, Valdez H, Rojo R, Chan G, Zhang F, Myers DE, DiBonaventura M. *J Eur Acad Dermatol Venereol.* 2022,*36*,422. doi: 10.1111/jdv.17792.
3. Patient-reported outcomes from the JADE COMPARE randomized phase 3 study of abrocitinib in adults with moderate-to-severe atopic dermatitis. Thyssen JP, Yosipovitch G, Paul C, Kwatra SG, Chu CY, DiBonaventura M, Feeney C, Zhang F, Myers D, Rojo R, Valdez H. **J Eur Acad Dermatol Venereol.** *2022*, **36**, 434. doi: 10.1111/jdv.17813.
4. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Simpson EL, Sinclair R, Forman S, Wollenberg A, Aschoff R, Cork M, Bieber T, Thyssen JP, Yosipovitch G, Flohr C, Magnolo N, Maari C, Feeney C, Biswas P, Tatulych S, Valdez H, Rojo R. *Lancet,* **2020**, *396*,255. doi: 10.1016/S0140-6736(20)30732-7. PMID: 32711801.
5. Abrocitinib induction, randomized withdrawal, and retreatment in patients with moderate-to-severe atopic dermatitis: Results from the JAK1 Atopic Dermatitis Efficacy and Safety (JADE) REGIMEN phase 3 trial. Blauvelt A, Silverberg JI, Lynde CW, Bieber T, Eisman S, Zdybski J, Gubelin W, Simpson EL, Valenzuela F, Criado PR, Lebwohl MG, Feeney C, Khan T, Biswas P, DiBonaventura M, Valdez H, Cameron MC, Rojo R. *J Am Acad Dermatol*. **2022**, *86*, 104. doi: 10.1016/j.jaad.2021.05.075.
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