NEW DRUG APPROVAL

Brand Name	Cibinqo™
Generic Name	abrocitinib
Drug Manufacturer	Pfizer Inc.

New Drug Approval

FDA approval date: January 14, 2022

Review designation: Priority

Type of review: Type 1 - New Molecular Entity; New Drug Application (NDA): 213871

Dispensing restriction: Speciality Only

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Atopic dermatitis (AD), which is a specific form of eczema, is the most common chronic inflammatory skin disease. Atopic dermatitis has a complex etiology including genetic and environmental factors which lead to abnormalities in the epidermis and the immune system. This chronic disorder associated with pruritus usually starts in infancy and presents with dry skin, eczematous lesions and lichenification. It is believed that AD is associated with other IgE associated disorders like allergic rhinitis, asthma, and food allergies. AD has significant morbidity, and it appears that the prevalence of the disorder has been increasing over the past few decades. Atopic dermatitis is part of the atopic triad (atopic dermatitis, allergic rhinoconjunctivitis, and asthma) which may start simultaneously or in succession in what is known as the "atopic march." Patients with the atopic triad have a defective barrier of the skin, upper respiratory, and lower respiratory tract which leads to their symptomatology. If one parent is atopic, there is more than a 50% chance that their offspring will develop atopic symptoms. If both parents are affected, up to 80% of offspring will be affected. Genetic alterations include loss of function mutations of filaggrin (Filament Aggregating Protein), an epidermal protein that is broken down into natural moisturization factor. Filaggrin mutations are present in up to 30% of atopic dermatitis patients and may also predispose patients to ichthyosis vulgaris, allergic rhinitis, and keratosis pilaris. Food hypersensitivity may also cause or exacerbate atopic dermatitis in 10% to 30% of patients. Ninety percent of such reactions or flares are caused by eggs, milk, peanuts, soy, and wheat.

According to the National Eczema Association, approximately 7.3% of adults in the United States have AD, and the condition is more common in adult females than males. Additionally, multiracial or White adults tend to have the highest prevalence of AD. Approximately 60%, 29%, and 11% of adult patients have mild, moderate, and severe disease, respectively. In children, AD is estimated to affect about 12% of the population, with approximately 67%, 26%, and 7% having mild, moderate, and severe disease, respectively.

Efficacy

The approval of Cibinqo™ was supported by three placebo-controlled Phase 3 trials in patients with moderate to severe AD. JADE Mono-1 and JADE Mono-2 were monotherapy trials conducted in patients 12 years of age and older (note: Cibinqo™ is only approved in adults). JADE Compare was a combination trial with topical therapies conducted in adults.

The primary endpoints of all 3 trials were met and included the percentage of subjects achieving Investigator Global Assessment score of clear or almost clear skin (IGA 0/1) or at least a 75% improvement in the Eczema Area and Severity Index score (EASI-75) at Week 12 compared with baseline.

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In another Phase 3 trial, JADE Dare, the 200-mg dose of Cibinqo™ demonstrated superior efficacy compared with Regeneron/Sanofi's Dupixent (dupilumab).

Trial-AD-1, Trial-AD-2, and Trial-AD-3 assessed the co-primary endpoints of IGA and EASI-75 responses at Week 12. The designs of the trials are summarized in Table.

Study	JADE Mono-1 (NCT03349060) N = 387	JADE Mono-2 (NCT03575871) N = 391	JADE Compare (NCT03720470) N = 837
Study Population	• A total of 1615 participants with moderate to severe AD as defined by IGA score ≥3, EASI score ≥16, BSA involvement ≥10%, and PP-NRS ≥4 at the baseline visit prior to randomization. JADE Mono-1 and JADE Mono-2 included patients ≥12 years of age[a] and JADE Compare included adults ≥18 years of age. • 53% male • 69% White • 64% had a baseline IGA score of 3 (moderate AD) and 36% had a baseline IGA score of 4 (severe AD) • 8% were 12–17 years of age; 92% were ≥18 years of age		
Interventions	Oral administration of: • Cibinqo 200 mg QD • Cibinqo 100 mg QD • Placebo		Oral administration of: • Cibinqo 200 mg QD • Cibinqo 100 mg QD • Placebo Or SC administration of: • Dupilumab 300 mg Q2W[b] All participants received background topical therapy of TCS, calcineurin inhibitors, or PDE4 inhibitors
Co-Primary Endpoints	• Percentage of participants achieving IGA response of 0 or 1[c] at Week 12 • Percentage of participants achieving EASI-75[d] at Week 12		
Key Secondary Endpoint	• Percentage of participants achieving PP-NRS4[e] at Week 2		

Efficacy Results	**Primary Endpoints**
	Cibinqo 100 mg, 200 mg, and placebo, respectively, at Week 12:
	• JADE Mono-1:
	  ○ IGA 0 or 1: 24%, 44%, and 8%
	  ○ EASI-75: 40%, 62%, and 12%
	• JADE Mono-2
	  ○ IGA 0 or 1: 28%, 38%, and 9%
	  ○ EASI-75: 44%, 61%, and 10%
	• JADE Compare
	  ○ IGA 0 or 1: 36%, 47%, and 14%
	  ○ EASI-75: 58%, 68%, and 27%
	Key Secondary Endpoints
	Cibinqo 100 mg, 200 mg, and placebo, respectively, at Week 2:
	• JADE Mono-1:
	  ○ PP-NRS4: 20%, 46%, and 3%		

Study	JADE Mono-1 (NCT03349060) N = 387	JADE Mono-2 (NCT03575871) N = 391	JADE Compare (NCT03720470) N = 837
Efficacy Results (cont.)	• JADE Mono-2 ○ PP-NRS4: 23%, 35%, and 4% • JADE Compare ○ PP-NRS4: 32%, 49%, 14%, and 26% (Dupixent)[f]		
Safety Results	• The most common adverse events reported in ≥5% of patients who received Cibinqo included nasopharyngitis (12.4% with Cibinqo 100 mg, 8.7% with Cibinqo 200 mg, and 7.9%, with placebo), nausea (6%, 14.5%, and 2.1%, respectively), and headache (6%, 7.8%, and 3.5%, respectively).		

Sources: Cibinqo Prescribing Information, NCT03349060 (JADE Mono-1), NCT03575871 (JADE Mono-2), NCT03720470 (JADE Compare).

Abbreviations: AD, atopic dermatitis; BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; PDE4, phosphodiesterase 4; PP-NRS, Peak Pruritus Numerical Rating Scale; QD, every day; Q2W, every 2 weeks; SC, subcutaneous; TCS, topical corticosteroid.
[a]Pediatric subjects 12 years of age and older were included in the trial populations for JADE Mono-1 and JADE Mono-2; however, Cibinqo is not approved for use in pediatric patients.
[b]Dupilumab treatment in JADE Compare: an initial dose of 600 mg on Day 1, followed by 300 mg Q2W.
[c]IGA response was based on IGA score of clear (0) or almost clear (1) (on a 5-point scale) and a reduction from baseline of ≥2 points.
[d]EASI-75 was based on ≥75% improvement in EASI from baseline.
[e]PP-NRS4 was defined as an improvement of at least 4 points from baseline on the numeric rating scale for severity of pruritis, which ranged from 0 (no itching) to 10 (worst possible itching).
[f]Difference from Dupixent was superior for Cibinqo 200 mg, but not for Cibinqo 100 mg.

Safety

ADVERSE EVENTS

Most common adverse reactions (≥1%) in subjects receiving 100 mg and 200 mg include: nasopharyngitis, nausea, headache, herpes simplex, increased blood creatinine phosphokinase, dizziness, urinary tract infection, fatigue, acne, vomiting, oropharyngeal pain, influenza, gastroenteritis.

Most common adverse reactions (≥1%) in subjects receiving either 100 mg or 200 mg also include: impetigo, hypertension, contact dermatitis, upper abdominal pain, abdominal discomfort, herpes zoster, and thrombocytopenia.

WARNINGS & PRECAUTIONS

- **Boxed Warning:** Serious infections, risk of all-cause mortality, malignancies, major adverse cardiovascular events (MACEs), and thrombosis.
- **Laboratory Abnormalities**: Laboratory monitoring is recommended due to potential changes in platelets, lymphocytes, and lipids.
- **Immunizations**: Avoid use of live vaccines prior to, during, and immediately after Cibinqo™ treatment.

CONTRAINDICATIONS

Antiplatelet therapies except for low-dose aspirin (≤81 mg daily), during the first 3 months of treatment.

Clinical Pharmacology

MECHANISMS OF ACTION

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Cibinqo™ is a Janus kinase (JAK) inhibitor. Abrocitinib reversibly inhibits JAK1 by blocking the adenosine triphosphate (ATP) binding site. In a cell-free isolated enzyme assay, abrocitinib was selective for JAK1 over JAK2 (28-fold), JAK3 (>340-fold), and tyrosine kinase (TYK) 2 (43-fold), as well as the broader kinome. The relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known. Both the parent compound and the active metabolites inhibit JAK1 activity in vitro with similar levels of selectivity.

Dose & Administration

ADULTS

100 mg orally once daily. If an adequate response is not achieved with 100 mg orally daily after 12 weeks, consider increasing dosage to 200 mg orally once daily.

PEDIATRICS

None

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

Table: Dosage Recommendations in Patients with Renal Impairment

Renal Impairment Stage	Estimated Glomerular Filtration (eGFR)[1]	Dosage
Mild	60 – 89 mL/minute	CIBINQO 100 mg once daily
Moderate	30 – 59 mL/minute	CIBINQO 50 mg once daily
Severe[2]	15 – 29 mL/minute	Not recommended for use
End-Stage Renal Disease[2] (ESRD)	<15 mL/minute	

[1] Glomerular filtration rate was estimated by the Modification of Diet in Renal Disease (MDRD) formula.
[2] Severe Renal Impairment and End-Stage Renal Disease include patients on renal replacement therapy.

HEPATIC IMPAIRMENT

Not recommended for use in patients with severe hepatic impairment.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Tablets: 50 mg, 100 mg, and 200 mg.