Journal Academy Formulary (JACF)

Journal Academy

Drug Review: Abrocitinib

Registrations: Abrocitinib had been registered in the following countries United States of America (USA), United Kingdom (U.K.), Canada, and Saudi Arabia (SA).

Trade name (USA.); CIBINQO®

Registration number (S.A.); Not Available.

Insurance Drug Formulary (S.A.); Not covered (28.1.2023).

General Information:

Registered Company: By Pfizer company.

Regulatory Status: R.X.

Mechanism of Action:

It is an oral small-molecule inhibitor of Janus kinase 1 (JAK1).

Indication

Approved (Labeled) indication

Atopic dermatitis (Moderate to Severe), Refractory to other systemic drug products, including biologics, or when the use of such therapies is inadvisable.[3]

Route of Administration: orally.

Dosage Forms: Oral Tablet: 50 M.G., 100 MG, 200 MG.

Dosing/Administration: Oral.

- May be taken with or without food at approximately the same time each day.
- Do not crush, split, or chew tablets; swallow them whole with water.
- Missed dosage: If a dose is missed, provide it as soon as possible unless there are less than 12 hr between the missed dose and the subsequent dose, in which case skip it. After that, start dosing again at the usual time.

Dose: Usual dosage: 100 mg orally once daily; if the response adequate is not achieved after 12 weeks, consider increasing to 200 mg orally once daily; discontinue if the inadequate response after the dosage increase.

Dose in Renal/Hepatic failure:

Renal impairment (moderate, eGFR 30 to 59 mL/min): 50 mg orally once daily; if the response is adequate is not achieved after 12 weeks, the dose can be increased to 100 mg once daily

- Hepatic impairment (mild or moderate, Child-Pugh B or C): No dosage adjustment is required.
- Hepatic impairment (severe, Child-Pugh C): Use not recommended.

Geriatric Dose: No dosage adjustment is needed.

Adjustment required in Specific population

- Renal impairment (mild, estimated GFR [eGFR] 60 to 89 mL/min): No dosage adjustment is needed.
- Renal impairment (moderate, eGFR 30 to 59 mL/min): 50 mg orally once daily; if the response is adequate and is not achieved after 12 weeks, the dose can be increased to 100 mg once daily.
- Renal impairment (severe, eGFR 15 to 29 mL/min) or ESRD: Use not recommended.
- Hepatic impairment (mild or moderate, Child-Pugh B or C): No dosage adjustment is required.
- Hepatic impairment (severe, Child-Pugh C): Use not recommended.
- Dialysis: Use is not recommended in patients on renal replacement therapy.
- Hematologic abnormality (Absolute Lymphocyte Count [ALC] less than 500/mm(3)): Temporarily discontinue and may restart once ALC returns above this value.
- Hematologic abnormality (Absolute Neutrophil Count [ANC] less than 1000/mm(3)): Temporarily discontinue and may restart once ANC returns above this value.
- Hematologic abnormality (Hb less than 8 g/dL): Temporarily suspend and may resume once Hb returns above this value.
- Infections, severe or opportunistic: Discontinue therapy and control the infection; evaluate risks/benefits before reinitiating therapy.
- Myocardial infarction, stroke, or symptoms of Thrombosis: Discontinue use.

Indicated for pediatrics: Safety and effectiveness not established in pediatric patients.

Pharmacokinetic:

Absorption

- T_{max}, oral: Within 1 hr.
- Bioavailability, oral: 60%.
- Effects of food: No effect.

Distribution

- Protein binding, albumin: 64%; 37% (M1); 29% (M2).
- Vd, IV: 100 L.

Metabolism

- Liver: Extensive via CYP enzymes.
- Substrate of CYP2C19, CYP2C9, CYP3A4, and OAT3.
- OCT1 and P-gp inhibitor.
- M1 (major): Active.
- M2 (major): Active.

Excretion

- Renal excretion: Less than 1% as unchanged drug.

Elimination Half-Life

- 3 to 5 hr.
- M1 and M2: 3 to 5 hr.

Safety:

Common Adverse Reactions (%):

Nausea, headache, acne, herpes, blood creatinine phosphokinase increased > 5 × upper limit of normal, vomiting, dizziness, and upper abdominal pain.

Severe/rare adverse Reactions (%):

- **Cardiovascular:** Myocardial infarction, Nonfatal, Sudden cardiac death.

- **Dermatologic:** Herpes zoster (0.3% to 1.2%).
- **Hematologic:** Arterial Thrombosis, Deep venous Thrombosis (0.3 per 100 patient-years), Lymphocytopenia (1.2 per 100 patient-years), Thrombocytopenia (1.5%), thrombosis.
- **Hepatic:** Hepatitis B.
- **Immunologic:** Herpes simplex (3.3% to 4.2%).
- **Neurologic:** Cerebrovascular accident, Nonfatal.
- **Ophthalmic:** Retinal detachment (0.3 to 0.6 per 100 patient-years).
- **Respiratory:** Pulmonary embolism (0.4 per 100 patient-years).
- **Other:** Infectious disease (91.8 to 168.8 per 100 patient-years; serious, 1.3 to 3.9 per 100 patient-years.

Drug Interactions

Strong CYP2C19 or CYP2C9 inducers diminish the exposure of abrocitinib and its related two active metabolites, M1 and M2, which could lead to clinical response loss or reduction.

The risk or severity of bleeding and Thrombocytopenia can be increased when Clopidogrel is combined with Abrocitinib.

The metabolism of Abrocitinib can be decreased when combined with Clozapine.[4]

Contraindications / Precautions

Concomitant use with antiplatelet therapies, except for low-dose aspirin (81 mg or less daily) during the first three months of treatment

Monitoring Requirements

- Disease stability and improvement are indicative of efficacy.
- CBC: Before initiation of therapy, four weeks after initiation, and four weeks after a dose increase, including differential
- Expression of hepatitis B virus DNA: In patients with inactive hepatitis B virus.

Signs and symptoms of infection: Through and after treatment

- Lipid parameters: 4 weeks after initiation of therapy and according to clinical guidelines.
- Reactivation of viral hepatitis.
- Viral hepatitis: Before treatment.
- Risks and benefits of treatment: Before initiating or continuing therapy with JAK inhibitors, especially in patients who are past smokers or current smokers, or patients with malignancy or cardiovascular risk factors, and those patients successfully treated non-melanoma skin cancer.
- T.B. Skin examination: Consider annual T.B. screening for patients in high-endemic areas before starting treatment.

Sound-Alikes/ Look-Alikes:

Not available.

High Alert: Not available.

Handling of medication: It is not required for hazardous or Antineoplastic precautions.

Boxed warnings or alerts issue

Patients may be more likely to get serious infections that could result in hospitalization or death. Herpes simplex, herpes zoster, and pneumonia were the most serious infections reported.

Active tuberculosis might present with pulmonary or extrapulmonary disease. Test for latent T.B. before and during therapy; treat latent T.B. before use. Monitor all patients for active T.B. during treatment, even those with initial negative latent T.B. tests.

Mortality

In a significant, randomized, post-marketing safety study comparing another JAK inhibitor to TNF blocker treatment in rheumatoid arthritis patients older than 50 with at least one cardiovascular risk factor, a higher mortality rate, including sudden cardiovascular death, was observed. As a result, Abrocetinib use is not permitted in R.A. patients.

Malignancies

Patients taking JAK inhibitors to treat inflammatory diseases have been found to develop lymphoma and other cancers. Excluding Non-Melanoma Skin Cancer [NMSC], A higher rate of malignancies was seen in Rheumatoid arthritis t. patients treated with another JAK inhibitor compared to TNF blockers. Patients who smoke now or in the past are also at higher risk.

Major Adverse Cardiovascular Events

Compared to TNF blockers, a greater rate of Major Adverse Cardiovascular Events (MACE), defined as cardiovascular mortality, myocardial infarction, and stroke, was seen. Patients who smoke now or in the past are also at higher risk. Patients who have had a stroke or myocardial infarction should stop taking abrocitinib.

Thrombosis

Pulmonary Embolism (P.E.) and Thrombosis, including P.E., DVT, and arterial Thrombosis, have been reported in patients receiving JAK inhibitors to treat inflammatory conditions.

Toxicity if antidote required: Not available.

Storage if there is a special condition

Store in the original package between 20 and 25°C; excursions permitted between 15 and 30°C.

Patient counseling

1. Use the medication as recommended.
2. Take this medication every day at the same time.
3. With water, swallow the tablet whole. Avoid breaking it up or chewing it.
4. Missed dosage: If patients forget to take a dose, they should take it immediately. Then, resume the usual schedule. Skip the missed dose and take the next dose at the scheduled time if there are fewer than 12 hr between doses. To make up for a missed dose, do not take more medication.
5. The medication should be kept at room temperature in a closed container away from heat, moisture, and bright light.
6. During the first three months of treatment, avoid taking this medication with a blood clot preventive.
7. The effects of other drugs may alter how abrocitinib functions. Tell your doctor if you are taking any of the following medications: dabigatran, digoxin, fluconazole, fluvoxamine, metformin, midazolam, rifampin, rosuvastatin, or birth control pills (including ethinyl estradiol and levonorgestrel).
8. Vaccines may be affected by this medication. Before receiving a flu shot or any other vaccination, see your doctor.

Warnings While Using This Medicine

1. Inform the doctor if have any of the following conditions: diabetes, lung disease, HIV, a history of tuberculosis, renal illness, liver disease (including hepatitis B or C), blood issues, cancer, or a history of cancer, or smoke now or in the past, have an ongoing infection, or have an infection that keeps coming back.

2. Before beginning, this medication must have a skin test for Tuberculosis (T.B.). If you or anybody in your home has ever had a positive T.B. skin test or been exposed to T.B., let your doctor know immediately.

3. The skin could become more sun sensitive as a result of this medication. Put on sunblock. Do not use tanning beds or sunlamps.

4. Do routine checkups, Necessary.

5. Keep any medications out of children's reach. Never give anyone else your medication.

6. The following issues could result from this medication:

✓ increased chance of serious bacterial, fungal, or viral infections, such as shingles or herpes.

✓ elevated risk of some malignancies (including lymphoma, lung cancer, and skin cancer).

✓ increased likelihood of developing significant heart or vascular illness (including heart attack, stroke).

✓ Increased risk of blood clots, particularly in people with rheumatoid arthritis who are older than 50 and have heart or blood vessel problems (including arterial Thrombosis, deep vein thrombosis, and pulmonary embolism).

✓ Blood cholesterol levels are high.

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Cost Analysis

Drugs	Drug classes	Approval Indication	Dose	Cost (American Dollar)	Insurance drug formulary(SCHI)
Abrocitinib	Janus kinase (JAK) inhibitors.	Atopic dermatitis (Moderate to Severe).	100 mg orally once daily.	$5,593 for a supply of 30 tablets.	Not Covered
Upadacitinib	Janus kinase (JAK) inhibitors.	Ankylosing spondylitis Atopic dermatitis (Moderate to Severe) Non-radiographic axial spondyloarthritis Psoriatic arthritis Rheumatoid arthritis Ulcerative colitis.	15 mg orally once daily	$6,124.96	Covered
Dupilumab	Monoclonal antibodies.	Moderate-to-Severe. Atopic Dermatitis Moderate-to-Severe. Asthma. Chronic Rhinosinusitis.	Asthma (Moderate to Severe) 400 mg (two 200-mg injections) sub Q once followed by 200 mg every other week or f 600 mg (two 300-mg injections) sub Q once followed by 300 mg every other week. Atopic dermatitis, Moderate to severe 600 mg (two 300-mg injections) sub Q once followed by 300 mg sub Q every other week.	$3,587.92 USD per carton	Covered

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