CIBINQO®
(abrocitinib) tablets

Cibinqo (Abrocitinib)
Prescriber Guide

This Prescriber Brochure contains important safety information that you need to consider when prescribing and maintaining patients on Cibinqo therapy, namely:

- Venous thromboembolism
- Potential risk of Infections (including herpes zoster and serious and opportunistic infections)
- Potential risk of malignancy
- Potential risk of Major Adverse Cardiovascular Events
- Embryofoetal toxicity following exposure in utero

Please read this brochure in full along with the prescribing information for Cibinqo.

Abrocitinib should only be used if no suitable treatment alternatives are available in patients:

- 65 years of age and older;
- patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers);
- patients with malignancy risk factors (e.g., current malignancy or history of malignancy)

About Cibinqo

Cibinqo is a Janus kinase (JAK) 1 inhibitor.

Cibinqo is indicated for treatment of moderate-to-severe atopic dermatitis in adults who are candidates for systemic therapy.

Posology

The recommended starting dose is 100 mg or 200 mg once daily based on individual patient characteristics:

- A starting dose of 100 mg once daily is recommended for patients at higher risk for of venous thromboembolism (VTE), major adverse cardiovascular event (MACE) and malignancy. If the patient does not respond adequately to 100 mg once daily, the dose can be increased to 200 mg once daily.
- A dose of 200 mg once daily may be appropriate for patients who are not at higher risk of VTE, MACE and malignancy with high disease burden or for patients with an inadequate response to 100 mg once daily. Upon disease control, dose should be decreased to 100 mg once daily. If disease control is not maintained after dose reduction, re-treatment with 200 mg once daily can be considered.

The lowest effective dose for maintenance should be considered.

Discontinuation of treatment should be considered in patients who show no evidence of therapeutic benefit after 24 weeks.

Cibinqo can be used with or without medicated topical therapies for atopic dermatitis.

Important points to remember - Patient Safety Information Card

Prior to starting treatment with Cibinqo:

- Provide the Patient Safety Information Card to patients and explain that it contains important safety information that patients should be aware of before, during, and after treatment with Cibinqo.
- Discuss with patient important safety information with Cibinqo treatment mentioned at the start of this document and ensure patient understanding of this important safety information as well as ways to minimize this. Encourage patients asking questions about the Patient Safety Information Card and safe use of Cibinqo.

- Advise patients about the importance of the Patient Safety Information Card and to keep it with them and to have any doctor or pharmacist involved in their care review the Patient Card.
- Advise patients that they should read the Patient Safety Information Card along with the Patient Information Leaflet.

Use in patients 65 years of age and older:

- Considering the increased risk of MACE, malignancies, serious infections, and all-cause mortality in patients 65 years of age and older, as observed in a large, randomised study of tofacitinib (another JAK inhibitor), abrocitinib should only be used in these patients if no suitable treatment alternatives are available.
- The recommended dose is 100 mg once daily.

Venous thromboembolism (VTE):

- Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving Cibinqo.
- In a large randomized active-controlled study of tofacitinib (another JAK inhibitor) in rheumatoid arthritis patients 50 years and older with at least one additional cardiovascular risk factor, a dose dependent higher rate of VTE including DVT and PE was observed with tofacitinib compared to TNF inhibitors.
- A higher rate of VTE was observed with abrocitinib 200 mg compared to abrocitinib 100 mg.
- In patients with cardiovascular or malignancy risk factors abrocitinib should only be used if no suitable treatment alternatives are available.
- In patients with known VTE risk factors other than cardiovascular or malignancy risk factors, abrocitinib should be used with caution.
- VTE risk factors other than cardiovascular or malignancy risk factors include previous VTE, patients undergoing major surgery, immobilisation, use of combined hormonal contraceptives or hormone replacement therapy or inherited coagulation disorder.
- Patients should be re-evaluated periodically during abrocitinib treatment to assess for changes in VTE risk.

If signs and symptoms of VTE occur:

- Promptly evaluate patients and discontinue abrocitinib in patients with suspected VTE, regardless of dose.

Infections/serious infections:

- Cibinqo must not be used in patients with active serious systemic infections, including tuberculosis (TB). The most frequent serious infections in clinical studies were herpes simplex, herpes zoster, and pneumonia.
- As there is a higher incidence of infections in the elderly and in the diabetic populations in general, caution should be used when treating the elderly and patients with diabetes. In patients 65 years of age and older abrocitinib should only be used if no suitable treatment alternatives are available.
- Patients should be closely monitored for the development of signs and symptoms of infection, including viral reactivation, during and after treatment with Cibinqo.
- It is important to tell patients to get immediate medical attention if they have symptoms suggesting infection. This is to ensure rapid evaluation and appropriate treatment.

Before starting Cibinqo:

- The risks and benefits of treatment should be carefully considered prior to initiating in patients:

o with chronic or recurrent infection

o who have been exposed to TB

o with a history of a serious or an opportunistic infection

o who have resided or travelled in areas of endemic TB or endemic mycoses; or

o with underlying conditions that may predispose them to infection.

- Patients should be screened for TB before starting treatment and yearly screening for patients in highly endemic areas for TB should be considered.
- Cibinqo should not be given to patients with active TB. For patients with a new diagnosis of latent TB or prior untreated latent TB, preventive therapy for latent TB should be started prior to initiation of Cibinqo.

- Patients should be screened for viral hepatitis before and during therapy with Cibinqo in accordance with clinical guidelines. If hepatitis B virus DNA is detected while receiving Cibinqo, a liver specialist should be consulted.
- Before, 4 weeks after initiation and during treatment with Cibinqo, patients should be monitored using a complete blood count (including platelets, absolute lymphocyte count, absolute neutrophil count, and haemoglobin).

If a new infection develops during treatment with Cibinqo:

- Immediately carry out complete diagnostic testing and initiate appropriate antimicrobial therapy.
- Closely monitor the patient and Cibinqo therapy should be temporarily interrupted if the patient is not responding to standard therapy.

If a patient develops a serious infection, sepsis or opportunistic infection:

- Consider dose interruption of Cibinqo until the infection is controlled.

Vaccines:

- No data are available on the response to vaccination in patients receiving Cibinqo. Before initiating treatment, it is recommended that patients be brought up to date with all immunizations, including prophylactic herpes zoster vaccinations, in agreement with current immunization guidelines.
- Live vaccines (e.g., Zostavax®) should be avoided during Cibinqo treatment, or just before starting Cibinqo treatment.

Malignancy:

- Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including abrocitinib.
- In a large randomized active controlled study of tofacitinib (another JAK inhibitor) in rheumatoid arthritis patients 50 years and older with at least one additional cardiovascular risk factor, a higher rate of malignancies, particularly lung cancer, lymphoma and non-melanoma skin cancer (NMSC) was observed with tofacitinib compared to TNF inhibitors.

- A higher rate of malignancies (excluding non-melanoma skin cancer, NMSC) was observed with abrocitinib 200 mg compared to abrocitinib 100 mg.
- In patients 65 years of age and older, patients who are current or past long-time smokers, or with other malignancy risk factors (e.g., current malignancy or history of malignancy), abrocitinib should only be used if no suitable treatment alternatives are available.
- Non-melanoma skin cancers (NMSCs) have been reported in patients receiving abrocitinib. Periodic skin examination is recommended for all patients, particularly those who are at increased risk for skin cancer.

Major Adverse Cardiovascular Events (MACE):

- Events of MACE have been observed in patients taking abrocitinib.
- In a large randomized active-controlled study of tofacitinib (another JAK inhibitor) in rheumatoid arthritis patients 50 years and older with at least one additional cardiovascular risk factor, a higher rate of major adverse cardiovascular events (MACE), defined as cardiovascular death, non-fatal myocardial infarction (MI) and non-fatal stroke, was observed with tofacitinib compared to TNF inhibitors.
- Therefore, in patients 65 years of age and older, patients who are current or past long-time smokers, and patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors, abrocitinib should only be used if no suitable treatment alternatives are available.
- Lipid parameters should be assessed prior to initiation, after 4 weeks of therapy and thereafter according to patient's risk for cardiovascular disease and clinical guidelines for hyperlipidaemia.
- The effect of lipid parameter elevations on cardiovascular morbidity and mortality has not been determined. Patients with abnormal lipid parameters should be further monitored and managed according to clinical guidelines, due to the known cardiovascular risks associated with hyperlipidaemia.

Embryofoetal toxicity following exposure in utero:

There are no or limited amount of data on the use of Cibinqo in pregnant women. Studies in animals have shown reproductive toxicity.

- Cibinqo is contraindicated during pregnancy and/or breastfeeding.
- Women of reproductive potential should be advised to use effective contraception during and for 1 month following the final dose of Cibinqo. Pregnancy planning and prevention for females of reproductive potential should be encouraged.
- Advise patients to inform their healthcare provider immediately if they think they could be pregnant or if pregnancy is confirmed.

Drug interactions of special interest:

- In patients receiving dual strong inhibitors of CYP2C19 and moderate inhibitors of CYP2C9, or strong inhibitors of CYP2C19 alone (e.g. fluvoxamine, fluconazole, fluoxetine and ticlopidine), the recommended dose should be reduced by half to 100 mg or 50 mg once daily.
- Treatment is not recommended concomitantly with moderate or strong inducers of CYP2C19/CYP2C9 enzymes (e.g. rifampicin, apalutamide, efavirenz, enzalutamide, phenytoin).
- In patients receiving acid reducing agents (e.g. antacids, proton pump inhibitors and H2 receptor antagonists), 200 mg once daily dose of abrocitinib should be considered.
- In vitro, abrocitinib is an inhibitor of P glycoprotein (P-gp). Caution should be exercised for concomitant use of abrocitinib with dabigatran and other P-gp substrates with a narrow therapeutic index, such as digoxin, as their levels may increase.
- Abrocitinib is a moderate inhibitor of CYP2C19 enzyme. Caution should be exercised when using abrocitinib concomitantly with narrow therapeutic index medicines that are primarily metabolised by CYP2C19 enzyme (e.g. S-mephenytoin and clopidogrel).
- Combination with biologic immunomodulators, potent immunosuppressants, such as ciclosporin or other JAK inhibitors, has not been studied. Their concomitant use with abrocitinib is not recommended as a risk of additive immunosuppression cannot be excluded.

Special populations:

- In patients with moderate renal impairment (eGFR 30 to < 60 mL/min), the recommended dose of abrocitinib should be reduced by half to 100 mg or 50 mg once daily.
- In patients with severe renal impairment (eGFR < 30 mL/min), 50 mg once daily is the recommended starting dose. The maximum daily dose is 100 mg.
- Abrocitinib is contraindicated to patients with severe (Child Pugh C) hepatic impairment.
- For patients 65 years of age and older, the recommended dose is 100 mg once daily

ADDITIONAL INFORMATION AND REPORTING OF SUSPECTED ADVERSE REACTIONS

For additional information please refer to the Prescribing Information approved by the Ministry of Health.

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Adverse events can be reported directly to the Ministry of Health using the adverse events reporting portal which is available on the home page of the Ministry of Health website:

www.health.gov.il

or by this link:

https://sideeffects.health.gov.il

Side effects can also be reported to Pfizer by email:

isr.aereporting@pfizer.com

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Pfizer

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