

# Filgotin

Filgotinib Maleate INN



## Composition

**Filgotin 100 Tablet:** Each film coated tablet contains Filgotinib Maleate INN equivalent to Filgotinib 100 mg.

**Filgotin 200 Tablet:** Each film coated tablet contains Filgotinib Maleate INN equivalent to Filgotinib 200 mg.

## Pharmacology

Filgotinib is an adenosine triphosphate (ATP)-competitive and reversible inhibitor of the JAK family. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane. JAK1 is important in mediating inflammatory cytokine signals, JAK2 in mediating myelopoiesis and erythropoiesis and JAK3 plays critical roles in immune homeostasis and lymphopoiesis. Within the signalling pathway, JAKs phosphorylate and activate signal transducers and activators of transcription (STATs) which modulate intracellular activity including gene expression. Filgotinib modulates these signalling pathways by preventing the phosphorylation and activation of STATs. In biochemical assays, filgotinib preferentially inhibited the activity of JAK1 and showed > 5-fold higher potency of filgotinib for JAK1 over JAK2, JAK3 and TYK2.

## Indications

**Rheumatoid arthritis:** Filgotinib is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). Filgotinib may be used as monotherapy or in combination with methotrexate (MTX).

**Ulcerative colitis:** Filgotinib is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic agent.

## Dosage and Administration

**Rheumatoid arthritis:** The recommended dose of Filgotin is 200 mg tablet once a day.

**Ulcerative colitis:** The recommended dose of Filgotin is 200 mg once daily. Patients who have not shown any therapeutic benefit after 22 weeks of treatment should discontinue Filgotinib.

In adults at higher risk of venous thromboembolism, major adverse cardiovascular events and malignancy, the recommended dose for maintenance treatment is 100 mg once daily. In case of flare of the disease, the dose may be escalated to 200 mg once daily. For long term treatment, the lowest effective dose should be used.

## Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Active tuberculosis (TB) or active serious infections
- Pregnancy

## Side Effects

The most frequently reported adverse reactions are nausea, upper respiratory tract infection (URTI), urinary tract infection (UTI), dizziness etc.

## Special warnings and precautions for use

### Immunosuppressive medicinal products

Combination of filgotinib with other potent immunosuppressants such as azathioprine, ciclosporin, tacrolimus, biologic DMARDs (bDMARDs) or other Janus kinase (JAK) inhibitors is not recommended as a risk of additive immunosuppression cannot be excluded.

### Infections

Infections, including serious infections, have been reported in patients receiving filgotinib. The most frequent serious infection reported with filgotinib was pneumonia. Among opportunistic infections, TB, oesophageal candidiasis, and cryptococcosis were reported with filgotinib.

### Viral reactivation

Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical studies. If a patient develops herpes zoster, filgotinib treatment should be temporarily interrupted until the episode resolves. Screening for viral hepatitis and monitoring for reactivation should be performed in accordance with clinical guidelines before starting and during treatment with filgotinib.

### Malignancy

The risk of malignancies is increased in patients with rheumatoid arthritis. Immunomodulatory medicinal products may increase the risk of malignancies.

### Fertility

In animal studies, decreased fertility, impaired spermatogenesis, and histopathological effects on male reproductive organs were observed.

### Vaccinations

Use of live vaccines during, or immediately prior to, filgotinib treatment is not recommended.

### Lipids

Treatment with filgotinib was associated with dose-dependent increase in lipid parameters, including total cholesterol, and high-density lipoprotein (HDL) levels, while low-density lipoprotein (LDL) levels were slightly increased.

### Venous thromboembolism

Consider the risks and benefits prior to treating patients with filgotinib, who may be at increased risk of thrombosis. Promptly evaluate patients with symptoms of thrombosis and treat appropriately.

## Special populations

### Elderly

**Rheumatoid arthritis:** In patients with rheumatoid arthritis aged 65 years of age and older, the recommended dose is 100 mg once daily and may be escalated to 200 mg once daily in case of insufficient disease control. For long term treatment, the lowest effective dose should be used.

**Ulcerative colitis:** In patients with ulcerative colitis aged 65 years of age and older, the recommended dose is 200 mg once daily for the induction treatment and 100 mg once daily for maintenance treatment. In case of flare of the disease, the dose may be escalated to 200 mg once daily. For long term treatment, the lowest effective dose should be used. Filgotinib is not recommended in patients aged 75 years and older as there is no data in this population.

### Renal impairment

No dose adjustment is required in patients with mild renal impairment. A dose of 100 mg of filgotinib once daily is recommended for patients with moderate or severe renal impairment.

### Hepatic impairment

No dose adjustment is required in patients with mild or moderate hepatic impairment.

### Use in Pregnancy

There are no or limited amount of data from the use of filgotinib in pregnant women. Studies in animals have shown reproductive toxicity. Based on findings in animals, filgotinib may cause fetal harm and is therefore contraindicated during pregnancy.

### Women of childbearing potential / Contraception

Women of childbearing potential have to use effective contraception during and for at least 1 week after cessation of filgotinib treatment.

### Lactation

It is unknown whether filgotinib is excreted in human milk. A risk to breastfed newborns/infants cannot be excluded. Therefore, filgotinib should not be used during breast-feeding.

## Drug Interactions

### • Effect of other medicinal products on filgotinib

Filgotinib is primarily metabolised by carboxylesterase 2 (CES2), which can be inhibited in vitro by medicinal products such as fenofibrate, carvedilol, diltiazem or simvastatin. The clinical relevance of this interaction is unknown.

### • Effect of filgotinib on other medicinal products

Filgotinib is not a clinically relevant inhibitor or inducer of most enzymes or transporters commonly involved in interactions such as cytochrome P450 (CYP) enzymes and UDP-glucuronosyltransferases (UGT).

## Overdose

Filgotinib has been administered in clinical studies following single and once daily administration up to 450 mg without dose-limiting toxicity. Adverse reactions were comparable to those seen at lower doses and no specific toxicities were identified. Pharmacokinetic data following a single dose of 100 mg filgotinib in healthy subjects indicate that approximately 50% of the administered dose is eliminated within 24 hours of dosing and 90% of the dose is eliminated within 72 hours. In case of an overdose, it is recommended that a patient be monitored for signs and symptoms of adverse reactions. Treatment of overdose with filgotinib consists of general supportive measures including monitoring of vital signs as well as observation of the clinical status of the patient. It is unknown whether filgotinib can be removed by dialysis.

## Storage

Do not store above 25°C. Protect from light. Keep out of reach of children.

## Packaging

**Filgotin 100 Tablet:** Each box contains 1x8's tablets in blister pack.

**Filgotin 200 Tablet:** Each box contains 1x8's tablets in blister pack.

Manufactured by

**ZISKA PHARMA** Ziska Pharmaceuticals Ltd.  
Kaliakoir, Gazipur, Bangladesh

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