JYSELECA®▼ (filgotinib)
Healthcare Professional (HCP) Guide

This guide contains safety information and points for discussion when prescribing filgotinib to patients, namely:

- **Serious and opportunistic infections**
- **Potential risk of birth defects if filgotinib is taken during pregnancy**
- **Potential risk of venous thromboembolic events (VTEs)**
- **Potential risk of major adverse cardiovascular events (MACE)**
- **Potential risk of malignancy**
- **Prescribing in elderly patients and in patients with risk factors for VTE, MACE and malignancy**

Please read in conjunction with the Summary of Product Characteristics (SmPC).

About filgotinib

Filgotinib is a competitive and reversible JAK inhibitor. In biochemical assays, the clinical relevance of which is uncertain, filgotinib preferentially inhibited the activity of JAK1 over JAK2, JAK3 and TYK2. Filgotinib is taken orally and is indicated for:

- The treatment of moderate to severe active rheumatoid arthritis (RA) 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)
- The treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic agent

Important points to discuss – Patient Alert Card

- Provide a **Patient Alert Card (PAC)** to each patient and explain that it contains important information they should be aware of before, during and after treatment with filgotinib.
- Advise patients that the PAC should be read in conjunction with the **Patient Information Leaflet**.
- Advise patients that other healthcare professionals involved in their care should read the PAC.

Infections

Filgotinib increases the risk of serious infections, including opportunistic infections, and viral reactivation, such as herpes zoster:

- Filgotinib must not be prescribed (i.e. is contraindicated) in patients with active tuberculosis (TB) or active, serious infections.
- Screen patients for TB before initiating treatment with filgotinib. Do not administer filgotinib to patients with active TB. In patients with latent TB, standard antimycobacterial therapy should be initiated before administering filgotinib.
- There is an increased risk of herpes zoster in patients receiving filgotinib. In rheumatoid arthritis clinical studies, the risk of herpes zoster appeared to be higher in female patients, Asian patients, patients ≥50 years of age, patients with a medical history of herpes zoster, patients with a medical history of chronic lung disease and patients treated with filgotinib 200 mg once daily. Temporarily interrupt filgotinib if a patient develops herpes zoster and treat with appropriate antiviral medication. Do not resume filgotinib treatment until the infection resolves.
- Do not use live, attenuated vaccines during, or immediately prior to starting filgotinib treatment. It is recommended that immunisations, including prophylactic zoster vaccinations, be updated in line with current immunisation guidelines prior to initiating filgotinib treatment. Examples of live, attenuated vaccines are Zostavax™, used to prevent herpes zoster, or the Bacillus Calmette-Guérin (BCG) vaccine to prevent TB.
- Screen patients for viral hepatitis before starting filgotinib and monitor for reactivation in accordance with clinical guidelines during treatment with filgotinib.

If a new infection develops during treatment:

- Carry out diagnostic testing and use appropriate antimicrobial therapy, and closely monitor the patient.
- If the infection is serious or is TB, then stop filgotinib until the infection is resolved.
- If the patient is not responding to antimicrobial therapy, temporarily interrupt filgotinib treatment until the infection is controlled.
- Instruct patients to seek immediate medical attention if they show signs suggesting infection. The PAC provides the patient with information on when to contact their doctor. This is to ensure appropriate treatment is given as soon as possible to bring the infection under control.

Contraception, pregnancy and breastfeeding

Studies in animals have shown reproductive toxicity, including embryolethality and teratogenicity, at filgotinib exposures comparable to the human dose of 200 mg once daily (Section 5.3 of SmPC). Visceral and skeletal malformations and/or variations were observed. There are no or limited amounts of data from the use of filgotinib in pregnant women. Based on findings in animals, filgotinib may cause foetal harm and is therefore contraindicated during pregnancy.

Important points to discuss – women of childbearing potential:

- Filgotinib must not be used during pregnancy (contraindicated). HCPs should actively discuss with patients any current or future pregnancy plans. Filgotinib should not be administered to women who want to become pregnant in the near future (e.g. the next 3 months).
- Female patients who are able to have children must use effective contraception both during treatment and for at least 1 week after stopping filgotinib treatment.
- Tell your patient to stop taking filgotinib immediately and inform you straight away if they think they could be pregnant, or if pregnancy is confirmed.
- Filgotinib should not be used in women who are breastfeeding or intend to breastfeed. It is not known if filgotinib is excreted into human breast milk.

Important points to remember

The PAC reminds female patients of these important points. In particular, consistent use of effective contraceptive methods should be emphasised to female patients of childbearing potential.

Venous thromboembolic events – deep vein thrombosis (DVT) or pulmonary embolism (PE)

Thromboembolic events of DVT and PE have been reported in patients receiving JAK inhibitors, including filgotinib. In patients with cardiovascular or malignancy risk factors, filgotinib should only be used if no suitable treatment alternatives are available for the patient. Like other JAK inhibitors, filgotinib should be used with caution in patients with risk factors for DVT/PE other than cardiovascular or malignancy risk factors, such as a medical history of DVT/PE, patients undergoing major surgery, prolonged immobilisation, use of combined hormonal contraceptives or hormone replacement therapy and inherited coagulation disorder.[1] The PAC contains information for the patient on the symptoms of DVT/PE so that they know when to seek medical attention.

Important points to remember – DVT/PE:

- Patients should be re-evaluated periodically during filgotinib treatment to assess for changes in VTE risk.
- If clinical features of DVT/PE occur, filgotinib treatment should be discontinued regardless of dose and patients should be evaluated promptly, followed by appropriate treatment.

Major adverse cardiovascular events (MACE)

Patients with RA have a significantly higher risk of cardiovascular disease (CVD) compared with the general population that cannot be entirely explained by traditional CVD risk factors, suggesting that RA-specific characteristics (systemic inflammation and disease activity) may be associated with this increase in risk.[2,3] It is unknown whether filgotinib affects the higher CVD risk in RA patients.

Patients with UC have an increased risk of CVD, partly due to conventional risk factors and also due to inflammation based risk factors, such as disease activity.[4,5]

Filgotinib should be used with caution in patients with cardiovascular risk factors. In patients at high risk for MACE filgotinib should only be used if no suitable treatment alternatives are available for the patient. Patients at high risk include patients who are current or past long-time smokers, patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors and patients aged 65 years and older.

Management of conventional cardiovascular risk factors (for example hypertension, smoking, diabetes, obesity) is standard clinical care.[6–10] In Phase 3 randomised

controlled trials, treatment with filgotinib was associated with dose-dependent increases in lipid parameters, including total cholesterol level and high-density lipoprotein (HDL) cholesterol level, while low-density lipoprotein (LDL) cholesterol level was slightly increased. Lipid parameters should be monitored 12 weeks after initiation and thereafter, according to clinical guidelines for hyperlipidaemia.

LDL cholesterol returned to pre-treatment levels in the majority of patients who started statin therapy while taking filgotinib. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined.

Malignancies (including NMSC)

Patients treated with filgotinib might have an increased risk for malignancies, including non-melanoma skin cancer (NMSC). All patients should be monitored for occurrence of NMSC through periodic skin examinations according to local clinical practice.

In patients at high risk for malignancies filgotinib may only be used if no suitable treatment alternatives are available for the patient. Patients at high risk include patients who are current or past long-time smokers, patients with current or history of malignancy and patients aged 65 years and older.

Prescribing in elderly patients and in patients with risk factors for VTE, MACE and malignancy

Patients aged 65 years and above usually have more serious comorbidities, including serious infections, and higher mortality than younger patients. Therefore, for patients with RA aged 65 years and above, and for patients at higher risk of VTE, MACE or malignancy (see risk factors above), a starting dose of 100 mg of filgotinib once daily is recommended.

In case of insufficient disease control the dose may be increased to 200 mg of filgotinib, once daily. For long term treatment the lowest effective dose should be used.

For patients with UC aged 65 years and above, and for patients at higher risk of VTE, MACE or malignancy (see risk factors above), a maintenance dose of 100 mg of filgotinib once daily is recommended. In case of a flare of the disease, the dose may be increased to 200 mg of filgotinib once daily. For long term treatment the lowest effective dose should be used.

There are no data on filgotinib use in patients with UC aged 75 years and above. Therefore, JYSELECA is not recommended for use in this population.

Further information

This guide is not intended as a complete description of the risks associated with the use of filgotinib. Please refer to the Summary of Product Characteristics (SmPC) for a complete description of risks and more details on prescribing filgotinib. The SmPC and additional HCP Guides can be obtained from the **www.hpra.ie** website.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.

Healthcare professionals are asked to report any suspected adverse drug reactions via HPRA Pharmacovigilance.

Website: **www.hpra.ie**

Any suspected adverse reactions to JYSELECA should be reported to Galapagos via email to **DrugSafety.UK.Ireland@glpg.com** or by telephone: 00800 7878 1345.

Please contact Galapagos Medical Information at **medicalinfo@glpg.com** or telephone 00800 7878 1345 if you have any questions or require copies of the Patient Alert Card.

This HCP guide and the SmPC are available online via the Medicines.ie website: **www.medicines.ie**.

References

1. Heit JA. *Nat Rev Cardiol* 2015;12:464–474
2. Crowson CS et al. *Am Heart J* 2013;166:622–628
3. Hollan I et al. *Autoimmun Rev* 2015;14:952–969
4. Feng et al. *J Am Heart Assoc* 2017;6:e005892
5. Singh S, et al. *Clin Gastroenterol Hepatol* 2014;12:382–33
6. Zegkos T, et al. *Ther Adv Musculoskel Dis* 2016;8:86–101
7. Agca R, et al. *Ann Rheum Dis* 2017;76:17–28
8. England BR, et al. *BMJ* 2018;361:k1036
9. Bunu DM, et al. *Gastroenterology Research and Practice*; Vol. 2019, Article ID3012509
10. Fan F, et al. *J Inflamm* 2014;11:29

Date of preparation: March 2023
ROI--FIL-202302-00001