# SUMMARY OF RISK MANAGEMENT PLAN FOR JYSELECA (FILGOTINIB)

This is a summary of the risk management plan (RMP) for Jyseleca. The RMP details Important risks of Jyseleca, how these risks can be minimized, and how more information will be obtained about Jyseleca's risks and uncertainties (missing information).

Jyseleca's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Jyseleca should be used.

This summary of the RMP for Jyseleca should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Jyseleca's RMP.

## I. The Medicine and What is it Used for

Jyseleca is authorized for monotherapy or in combination with methotrexate for the treatment of adult patients with moderately to severely active rheumatoid arthritis (see SmPC for the full indication). It contains filgotinib as the active substance and it is given orally.

Further information about the evaluation of Jyseleca's benefits can be found in Jyseleca's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/jyseleca.

## II. Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of Jyseleca, together with measures to minimize such risks and the proposed studies for learning more about Jyseleca's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the public (e.g. with or without prescription) can help to minimises its risks.

Together, these measures constitute routine risk minimization measures.

In the case of Jyseleca, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Jyseleca is not yet available, it is listed under 'missing information' below.

## II.A. List of important risks and missing information

Important risks of Jyseleca are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Jyseleca. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

**Table Part VI.1. List of Important Risks and Missing Information**

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| **Important Identified Risks** | Serious and opportunistic infections |
| | Herpes zoster |
| **Important Potential Risks** | Embryolethality and teratogenicity |
| | Impaired spermatogenesis, leading to possible reduction in male fertility |
| | Malignancy |
| | Venous thromboembolism (deep venous thrombosis and pulmonary embolism) |
| | Gastrointestinal (GI) perforation |
| | Non-melanoma skin cancer (NMSC) |
| | MACE |
| | Hyperlipidemia |
| | Varicella zoster |
| **Missing Information** | Use in patients with evidence of untreated chronic infection with hepatitis B or C |
| | Effect on vaccination efficacy |
| | Use in the very elderly (>75 years) |

## II.B. Summary of Important Risks

Jyseleca has been assigned the legal status of a medicine subject to medical prescription in the European Union (EU), whereby therapy should be initiated by a doctor experienced in the management of rheumatoid arthritis (RA) (as described in section 4.2 of the SmPC).

**Table Part VI.2. Summary of Important Risk(s) and Missing Information**

| **Important identified risk** | **Serious and Opportunistic Infections** |
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| **Evidence for linking the risk to the medicine** | Serious and opportunistic infections have been reported with the use of other Janus kinase (JAK) inhibitors and other immunomodulatory drugs used to treat rheumatoid arthritis, such as tumor necrosis factor (TNF) inhibitors. However, from the pivotal clinical trial data for filgotinib in the Integrated Safety Summary (ISS), the rate of serious infections is lower than the published rate for biological DMARDS. |
| **Risk factors and risk groups** | Patients with rheumatoid arthritis (RA) are at increased risk of developing infections, particularly septic arthritis and pulmonary infections, compared to those without RA. The reasons are multifactorial, including a poorly functioning immune system and concomitant use of immunosuppressant medications such as glucocorticoids.<br>Tuberculosis (TB) and other opportunistic infections (OIs) occur more frequently in patients with RA, and this risk is elevated by the use of glucocorticoids and certain biologic DMARDs.<br>Patients with RA who are elderly, >65 years, on concomitant immunosuppressive therapy, or who have comorbid conditions such as diabetes, may be at increased risk of infection. |
| **Risk Minimization Measure(s)** | *Routine risk communication:*<br>SmPC section 4.2, 4.3, 4.4, 4.8<br>PL section 2<br>*Routine risk minimization activities recommending specific clinical measures to address the risk:*<br>PL Section 2 provides guidance for the patient on signs and symptoms of infection and when to contact a healthcare professional.<br>Section 4.3 of the SmPC contraindicates filgotinib in active TB and active serious infections.<br>Recommendation in SmPC Section 4.2 to avoid initiation or interrupt treatment in patients with a serious infection, an absolute lymphocyte count <0.5 x $10^9$ cells/L or an absolute neutrophil count <1.0 x $10^9$ cells/L. Recommendation in SmPC Section 4.4 on the management of infections in patients receiving filgotinib, and advice on patients at increased risk of infection.<br>Recommendation in SmPC Section 4.4 to screen for TB and to initiate antimycobacterial therapy in patients with latent TB before administering filgotinib, and not to administer filgotinib to patients with active TB. The warning also recommends that patients are monitored for signs and symptoms of TB, including patients who tested negative for latent TB prior to initiating treatment. Section 4.4 also provides advice on the management of viral reactivation, including Herpes zoster and viral hepatitis.<br>Recommendation in SmPC section 4.8 that a starting dose of 100 mg is administered to patients aged 75 years and older as there was a higher incidence of serious infections in this age group, although data are limited.<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA.<br>*Additional risk minimization measures:*<br>Healthcare professional guide, Patient Alert Card |

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| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Important identified risk** | **Herpes zoster** |
| **Evidence for linking the risk to the medicine** | Herpes zoster has been reported with the use of other JAK inhibitors and other immunomodulatory drugs used to treat RA, such as TNF inhibitors. However, from the pivotal clinical trial data for filgotinib in the ISS, the rate of herpes zoster is lower than that published for biological and csDMARDs. The ISS is based on a pooled dataset of Phase 2b and 3 studies in RA of subjects receiving at least 1 dose of filgotinib 100 mg or 200 mg qd to support the marketing authorization application for RA.<br>As RA patients are at a higher risk of herpes zoster, compared to age-matched controls, and the use of immunomodulatory therapy are a possible contributing factor, herpes zoster has been classified as an important identified risk warranting further study as specified in the PV plan of this RMP. |
| **Risk factors and risk groups** | Patients with RA are at increased with of developing herpes zoster compared with age-matched healthy adults. The reasons are multifactorial, including a poorly functioning immune system and concomitant use of immunosuppressant medications such as glucocorticoids, increased age and female sex. |
| **Risk Minimization Measure(s)** | *Routine risk communication:*<br>SmPC section 4.4, 4.8<br>PL section 2<br>*Routine risk minimization activities recommending specific clinical measures to address the risk:*<br>PL Section 2 provides guidance for the patient on signs and symptoms of herpes zoster and when to contact a healthcare professional.<br>Section 4.4 provides advice on the management of viral reactivation, including Herpes zoster.<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA.<br>*Additional risk minimization measures:*<br>Healthcare professional guide, Patient Alert Card |
| **Additional Pharmacovigilance activities** | *Additional pharmacovigilance activities:*<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries<br>See Section II.C of this summary for an overview of the post-authorization development plan. |

| **Important Potential Risk** | **Embryolethality and Teratogenicity** |
|---|---|
| **Evidence for linking the risk to the medicine** | Non-clinical findings of embryolethality and teratogenicity were observed at exposures slightly higher than the human dose of 200 mg once daily.<br>Embryo-fetal development studies were conducted in rats and rabbits. Visceral and skeletal malformations and/or variations were observed at all dose levels of filgotinib and its active metabolite. |
| **Risk factors and risk groups** | Pregnant women and women of childbearing potential. |
| **Risk Minimization Measure(s)** | *Routine risk communication:*<br>SmPC section 4.3, 4.6, 5.3<br>Package leaflet (PL) section 2<br>*Routine risk minimization activities recommending specific clinical measures to address the risk:*<br>Filgotinib is contraindicated in pregnancy. Recommendations on contraceptive measures to be taken by women of childbearing potential are included in SmPC section 4.6 and PL Section 2.<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA.<br>*Additional risk minimization measures:*<br>Healthcare professional guide, Patient Alert Card |
| **Important Potential Risk** | **Impaired spermatogenesis, leading to possible reduction in male fertility** |
| **Evidence for linking the risk to the medicine** | Filgotinib-related findings were observed in the male reproductive system of both rats and dogs, including dose-dependent impairment of spermatogenesis demonstrated by cessation of sperm production, loss of spermatids, and seminiferous atrophy.<br>The histopathological findings were fully reversible in dogs and partially reversible in rats, and sperm counts were not fully reversible in either species. |
| **Risk factors and risk groups** | Men with potential reproductive interest |
| **Risk Minimization Measure(s)** | *Routine risk communication:*<br>SmPC section 4.4, 4.6, 5.3<br>PL section 2<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA.<br>*Additional risk minimization measures:*<br>Healthcare professional guide, Patient Alert Card |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GS-US-418-4279 (MANTA) study to evaluate the testicular safety of filgotinib in adult males with inflammatory bowel disease (IBD)<br>GLPG0634-CL-227 (MANTA RAy) study to evaluate the effect of filgotinib on semen parameters in adult males with rheumatic diseases<br>See Section II.C of this summary for an overview of the post-authorization development plan. |

| **Important Potential Risk** | **Malignancy** |
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| **Evidence for linking the risk to the medicine** | Patients with RA have an increased risk of some types of malignancy, for example lung, lymphoma, as well as overall malignancy. It is currently unknown if filgotinib affects this risk. The incidence rate for overall malignancies in filgotinib-treated groups for the clinical trial dataset was lower than for published rates in the RA population. However, clinical trial data are insufficient to assess the potential incidence of malignancies. |
| **Risk factors and risk groups** | Patients with familial history of malignancy or lifestyle risk factors, such as tobacco or alcohol use, obesity. The risk of malignancy increases with age. |
| **Risk Minimization Measure(s)** | Routine risk communication:<br>SmPC section 4.4<br>PL section 2<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA. |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048 GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries.<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Important Potential Risk** | **Venous thromboembolism (deep venous thrombosis and pulmonary embolism)** |
| **Evidence for linking the risk to the medicine** | VTEs (deep venous thrombosis and pulmonary embolism) have been observed with filgotinib treatment in patients with RA. However, from the pooled clinical trial data for filgotinib in the indication of RA, no increase in reports of VTEs was seen for filgotinib (100 mg and 200 mg doses) compared to placebo or comparators (MTX, ADA). All patients who developed a VTE had recognized risk factors such as advanced age, immobilization, obesity, smoking, prior history of deep venous thrombosis (DVT) and pulmonary embolism (PE), heart failure or hormone replacement therapy.<br>Population-based cohort studies suggested an increased risk of VTE in RA patients. An incidence rate (IR) of VTE of 0.61 per 100 person-years in RA patients, which was approximately 2.4 times (95% confidence interval [CI] 2.1 – 2.8) higher than the rate in the non-RA population matched for age, sex and index date, was reported in a retrospective US cohort study. A recent epidemiologic analysis based on a US medical claims database indicated an unadjusted VTE IR of 0.58 per patient years of exposure (PYE) (CI 0.59 – 0.60) (Gilead data on file).<br>The exposure-adjusted incidence rate (IR) (0.2 per 100 PYE, 95% CI 0.1 – 0.4 and 0.0 per 100 PYE, 95% CI 0.0 – 0.3 for 200 mg qd and 100 mg qd respectively) of VTEs for filgotinib treatment in the pooled data is within the expected background rate of the target population based on the above literature (0.61 per 100 PYE) and the real-world (claims) data. |
| **Risk factors and risk groups** | The patients who developed VTEs with filgotinib treatment had at least one of the following recognized risk factors including prior history of VTE, advanced age, hormone replacement treatment, obesity, smoking or immobilization. |

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| **Risk Minimization Measure(s)** | Routine risk communication:<br>SmPC section 4.4<br>PL section 2<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA.<br>*Additional risk minimization measures:*<br>Healthcare professional guide, Patient Alert Card |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries.<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Important Potential Risk** | **Gastrointestinal perforation** |
| **Evidence for linking the risk to the medicine** | GI perforation has been reported with the use of tofacitinib in addition to other immunomodulatory drugs used in the treatment of RA including TNF inhibitors. Although there is a pharmacologically plausible basis for an association between JAK inhibitors and GI perforation, there is insufficient evidence to establish it as an adverse effect of filgotinib treatment at this time. Furthermore, the exposure-adjusted IR (0.1 per 100 PYE, 95% CI 0.0 – 0.4 and 0.0 per 100 PYE, 95% CI 0.0 – 0.2 for 200 mg qd and 100 mg qd respectively) of GI perforation for filgotinib treatment in the pooled data is within the expected background rate of the target population based on real-world (claims) data (0.10, 95% CI 0.10-0.11, per 100 PYE) (Gilead data on file).<br>Patients with RA may be at an increased risk of GI perforation due to prescribed medications (NSAIDs), and/or because of the consequences of the disease process (eg, vasculitis). |
| **Risk factors and risk groups** | Antecedent diverticulitis, use of glucocorticoids, exposure to NSAIDS, increasing age, and other GI conditions represent risk factors for GI perforation. Advanced age and use of immunosuppressive medications are common in the moderately to severely active RA population, therefore placing this population at greater risk. |
| **Risk Minimization Measure(s)** | *Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA. |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries<br>See Section II.C of this summary for an overview of the post-authorization development plan. |

| **Important Potential Risk** | **Non-melanoma skin cancer** |
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| **Evidence for linking the risk to the medicine** | NMSC has been reported with filgotinib treatment in patients with RA. From the pooled clinical trial data for filgotinib in the indication of RA, similar incidence of NMSC was noted across filgotinib (including 100 mg and 200 mg doses) and placebo or comparators. Most NMSC events were reported in white elderly (≥ 65 years old) patients with concomitant medication of methotrexate (MTX). Prior history of NMSC was noted in some patients who developed NMSC during the filgotinib treatment.<br>Epidemiologic studies showed an increased risk of development of NMSC in RA patients, which is in alignment with the result of a meta-analysis showing a relative risk (HR) of 2.02 (95% CI 1.11 to 3.95) for NMSC in RA patients. Development of NMSC in RA patients was associated with use of prednisone (HR 1.28, p = 0.014) alone or with combination MTX and tumor necrosis factor (TNF) inhibitors (HR 1.97, p = 0.001), in addition to established risk factors. A meta-analysis has recently supported the association of increased risk of skin cancers, especially squamous cell cancer (SCC) (RR 1.28, 95% CI 1.19 to 1.3; RR 1.30, 95% CI 1.09 to 1.54 respectively) in RA patients with the use of TNF inhibitors compared to RA patients without anti-TNF drugs.<br>The EAIR (0.2 per 100 PYE, 95% CI 0.1 – 0.4 and 0.1 per 100 PYE, 95% CI 0.0 – 0.4 for filgotinib 200 mg qd and 100 mg qd respectively) for NMSC in the pooled filgotinib data was lower than and a real-world (claims) data (0.57 per 100 PYE, 95% CI 0.56 – 0.58) (Gilead data on file) in the target population of RA patients. However, the filgotinib clinical trial data in the RA population is considered to be insufficient to assess the potential incidence of NMSC. |
| **Risk factors and risk groups** | Advanced age (≥ 65 years old) and Caucasian race were identified as risk factors in the filgotinib RA clinical program. The risk factors that are generally recognized for NMSC also include sun exposure (ie, UV), immunosuppressive therapies, phototherapy, ionizing radiation, male sex, and previous history of NMSC. |
| **Risk Minimization Measure(s)** | Routine risk communication:<br>SmPC section 4.4<br>PL section 2<br>*Routine risk minimization activities recommending specific clinical measures to address the risk:*<br>Recommendation in section 4.4 for periodic skin examination for patients at risk of skin cancer.<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA. |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries.<br>See Section II.C of this summary for an overview of the post-authorization development plan. |

| **Important Potential Risk** | **MACE** |
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| **Evidence for linking the risk to the medicine** | Filgotinib treatment was associated with dose-dependent increases in total cholesterol and high-density lipoprotein (HDL) levels, while low density lipoprotein (LDL) levels were slightly increased. LDL/HDL ratios were generally unchanged. Lipid changes were observed within the first 12 weeks of filgotinib treatment and remained stable thereafter.<br>Long-term exposure to increases in blood lipids in the general population would be expected to be associated with adverse cardiovascular (CV) outcomes including major cardiovascular adverse events (MACE), but published data indicate that they may not be harmful to RA patients as the benefits of suppression of inflammation may outweigh the risk of the lipid changes{Myasoedova 2011}.<br>With RA patients being at a higher risk of CV disease, and the long-term effects of lipid changes on adverse CV outcomes uncertain, MACE has been classified as an important potential risk warranting further study as specified in the PV Plan of this RMP. |
| **Risk factors and risk groups** | Patients with RA have a substantially elevated risk of cardiovascular morbidity and mortality. CV disease risk in older patients (≥ 75 years) with RA has been reported to be more than 3-fold the Framingham-predicted risk for the general population, and female patients with RA have demonstrated a 2-fold higher risk of myocardial infarction compare with female patients without RA. The increased risk of CV disease in the RA population cannot be entirely explained by traditional cardiovascular risk factors, thus indicating that RA-specific characteristics, especially systemic inflammation and disease activity, may be associated with increased cardiovascular risk. Traditional CV risk factors such smoking, dyslipidemia, obesity, hypertension, diabetes mellitus, age and prior CV events may also apply to patients with RA.<br>As the number of patients in whom MACE has been identified in clinical trials remains very low, no specific risk factors for MACE have been identified with filgotinib. |
| **Risk Minimization Measure(s)** | *Routine risk communication:*<br>SmPC section 4.4<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA.<br>*Additional risk minimization measures:*<br>Healthcare professional guide, Patient Alert Card |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Important Potential Risk** | **Hyperlipidaemia** |
| **Evidence for linking the risk to the medicine** | In clinical trials, filgotinib treatment was associated with dose-dependent increases in total cholesterol and high-density lipoprotein (HDL) levels, while low density lipoprotein (LDL) levels were slightly increased. LDL/HDL ratios were generally unchanged. Lipid changes were observed within the first 12 weeks of filgotinib treatment and remained stable thereafter. |

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| **Risk factors and risk groups** | Modifiable risk factors for hyperlipidemia include a diet high in saturated fats, physical inactivity, smoking and obesity. Other risk factors include biliary obstruction, chronic kidney disease, type 2 diabetes mellitus, high blood pressure, and hypothyroidism. Familial hypercholesterolemia (a monogenic disorder) is estimated to occur in 1:500 individuals in the general population. RA itself is an established risk factor for dyslipidemia. |
| **Risk Minimization Measure(s)** | Routine risk communication:<br>SmPC section 4.2, 4.4, 4.8<br>PL section 2<br>*Routine risk minimization activities recommending specific clinical measures to address the risk:*<br>Section 4.2 provides guidance on lipid monitoring and advice on the management of patients with hyperlipidaemia.<br>*Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA. |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries.<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Important Potential Risk** | **Varicella zoster** |
| **Evidence for linking the risk to the medicine** | Primary varicella zoster infection in adults is rare as most people are exposed to the virus in childhood or have been vaccinated. No signal for varicella zoster infection has been detected in the filgotinib RA clinical trial program.<br>As RA patients with no history of prior infection who are being treated with JAK inhibitors or other immunomodulatory drugs are at a higher risk of complications if a primary infection occurs, varicella zoster has been classified as an important potential risk warranting further study as specified in the PV Plan of this RMP. |
| **Risk factors and risk groups** | Patients with RA are at increased risk of developing infections, compared to those without RA. The reasons are multifactorial, including a poorly functioning immune system and concomitant use of immunosuppressant medications such as glucocorticoids. Adult RA patients may be at risk of complications of primary varicella zoster virus infection, which are most commonly pneumonia. |
| **Risk Minimization Measure(s)** | *Other routine risk minimization measures beyond the Product Information:*<br>Medicine's legal status: restricted medical prescription to HCPs experienced in managing patients with RA. |
| **Additional Pharmacovigilance activities** | *Additional pharmacovigilance activities:*<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries.<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Missing information** | **Use in patients with evidence of untreated chronic infection with hepatitis B or C** |

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| **Risk Minimization Measure(s)** | *Routine risk communication:*<br>SmPC section 4.4<br>PL section 2 |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>None |
| **Missing information** | **Effect on vaccination efficacy** |
| **Risk Minimization Measure(s)** | *Routine risk communication:*<br>SmPC section 4.4<br>PL section 2<br>*Routine risk minimization activities recommending specific clinical measures to address the risk:*<br>Section 4.4 provides a recommendation that immunisations are updated in agreement with current guidelines before initiating treatment. |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>None<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Missing information** | **Use in the very elderly (>75 years)** |
| **Risk Minimization Measure(s)** | *Routine risk communication:*<br>SmPC section 4.2, 4.4, 4.8<br>*Routine risk minimization activities recommending specific clinical measures to address the risk:*<br>Section 4.2 provides advice that a starting dose of 100 mg qd is recommended for patients aged 75 years and above as clinical experience is limited.<br>Section 4.4 advises that as there is a higher incidence of serious infections in the very elderly, caution should be used when treating this population.<br>Section 4.8 advises that there was a higher incidence of serious infections in patients 75 years and older, although data are limited.<br>*Additional risk minimization measures:*<br>Healthcare professional guide |
| **Additional Pharmacovigilance activities** | Additional pharmacovigilance activities:<br>GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-US-417-0304 (Finch 4) long-term extension study in RA in subjects who received treatment in the parent studies<br>GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries.<br>See Section II.C of this summary for an overview of the post-authorization development plan. |

## II.C. Post-authorization Development Plan

### II.C.1. Studies which are Conditions of the Marketing Authorization

There are no studies which are conditions of the marketing authorization or specific obligation of Jyseleca.

## II.C.2. Other Studies in Post-Authorization Development Plan

**Table Part VI.3. Other Studies in Post-Authorization Development Plan**

| Short Study Name | Purpose of the Study |
|---|---|
| GS-US-418-4279 (MANTA) study to evaluate the testicular safety of filgotinib in adult males with IBD | To evaluate the effect of filgotinib on testicular function as defined by the proportion of subjects with a ≥50% decrease from baseline in sperm concentration at Week 13 |
| GLPG0634-CL-227 (MANTA RAy) study to evaluate the effect of filgotinib on semen parameters in adult males with rheumatic diseases | To evaluate the effect of filgotinib on testicular function as defined by the proportion of subjects with a ≥50% decrease from baseline in sperm concentration at Week 13 |
| GLPG0634-CL-205 (DARWIN 3) long-term extension study in RA | To evaluate the long-term safety and tolerability of filgotinib for the treatment of RA in subjects who received treatment in the parent studies |
| GS-US-417-0304 (Finch 4) long-term extension study in RA | To evaluate the long-term safety and tolerability of filgotinib for the treatment of RA in subjects who received treatment in the parent studies |
| GS-EU-417-9046, GS-EU-417-9047, GS-EU-417-9048, GS-EU-417-5882, GS-EU-417-5883 Non-interventional post-authorisation safety study of filgotinib in patients with moderate to severe active RA in European registries | To evaluate the incidence rates of infections, malignancy, cardiovascular and other safety events of special interest in rheumatoid arthritis patients initiating treatment with filgotinib. For context, incidence rates will also be calculated in comparator cohorts depending on data availability. |
| GS-EU-417-9050, GS-EU-417-9051, GS-EU-417-9052, GS-EU-417-5884, GS-EU-417-5885 Non-interventional post-authorization safety study evaluating the effectiveness of the additional risk minimization measures for filgotinib use in patients with rheumatoid arthritis using data from European registries. | To evaluate the effectiveness of the additional risk minimization measures for filgotinib use in RA patients who initiate treatment with filgotinib. |