

Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for JAKTIFY 5 mg film-coated tablets and JAKTIFY 10 mg film-coated tablets

This is a summary of the risk management plan (RMP) for JAKTIFY 5 mg film-coated tablets and JAKTIFY 10 mg film-coated tablets (hereinafter referred to as Tofacitinib). The RMP details important risks of Tofacitinib, how these risks can be minimised, and how more information will be obtained about Tofacitinib's risks and uncertainties (missing information).

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

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

I. The Medicine and What It is used for

Tofacitinib is authorised for the treatment of adults with moderate to severe active rheumatoid arthritis, active psoriatic arthritis, moderately to severely active ulcerative colitis, active polyarticular juvenile idiopathic arthritis and juvenile psoriatic arthritis, and ankylosing spondylitis (see SmPC for the full indication). It contains Tofacitinib as the active substance and it is given orally.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Tofacitinib, together with measures to minimise such risks and the proposed studies for learning more about Tofacitinib'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 authorised 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 patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Tofacitinib, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed 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 Tofacitinib is not yet available, it is listed under ‘missing information’ below.

II.A List of Important Risks and Missing Information

Important risks of Tofacitinib 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 Tofacitinib. 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 8: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	• Venous thromboembolic events (DVT/PE) • Serious and other important infections • Herpes zoster reactivation • Lung cancer • Lymphoma • Myocardial infarction • Decrease in Hgb levels and anaemia • Non-melanoma skin cancer • Transaminase elevation and potential for drug-induced liver injury • Higher incidence and severity of adverse events in the elderly
Important potential risks	• Malignancy • Cardiovascular risk (excl myocardial infarction) • Gastrointestinal perforation • Interstitial lung disease • Progressive multifocal leukoencephalopathy (PML) • All-cause mortality • Fractures • Increased risk of adverse events when tofacitinib is administered in combination with MTX in rheumatoid arthritis or psoriatic arthritis patients

	• Primary viral infection following live vaccination
Missing information	• Effects on pregnancy and the foetus • Use in breastfeeding • Effect on vaccination efficacy and the use of live/attenuated vaccines • Use in patients with mild, moderate, or severe hepatic impairment • Use in patients with moderate or severe renal impairment • Use in patients with evidence of hepatitis B or hepatitis C infection • Use in patients with malignancy • Long-term safety in polyarticular juvenile idiopathic arthritis patients and juvenile psoriatic arthritis patients (e.g., growth or development disturbances)

II.B Summary of Important Risks

Table 9: Summary of Pharmacovigilance Activities and Additional Risk Minimisation Activities by Safety Concern

Important identified risk: Venous thromboembolic events (deep vein thrombosis/pulmonary embolism)	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC section 4.4, 4.8, and 5.1. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important identified risk: Serious and other important infections	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.2, 4.3, 4.4, 4.8, and 5.1 <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important identified risk: Herpes zoster reactivation	

Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, and 4.8. <u>Additional risk minimisation measures:</u> Prescriber Brochure Patient card
Additional pharmacovigilance activities	None.
Important identified risk: Lung cancer	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, 4.8, and 5.1 <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important identified risk: Lymphoma	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, 4.8, and 5.1 <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important identified risk: Myocardial infarction	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, 4.8, and 5.1 <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important identified risk: Decrease in Hgb levels and anaemia	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.2, 4.4, and 4.8. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists
Additional pharmacovigilance activities	None.

Important identified risk: Non-melanoma skin cancer	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, and 4.8. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important identified risk: Transaminase elevation and potential for drug-induced liver injury	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, and 4.8. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important identified risk: Higher incidence and severity of adverse events in the elderly	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, and 4.8. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important potential risk: Malignancy	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, and 5.1. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important potential risk: Cardiovascular risk (excl myocardial infarction)	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, and 5.1. <u>Additional risk minimisation measures:</u> Prescriber Brochure

	Prescriber checklists
Additional pharmacovigilance activities	None.
Important potential risk: Gastrointestinal perforation	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important potential risk: Interstitial lung disease	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Important potential risk: All-cause mortality	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4, and 5.1. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists
Additional pharmacovigilance activities	None.
Important potential risk: Increased risk of adverse events when tofacitinib is administered in combination with MTX in rheumatoid arthritis or psoriatic arthritis patients	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4. <u>Additional risk minimisation measures:</u> Prescriber Brochure Patient card
Additional pharmacovigilance activities	None.
Important potential risk: Primary viral infection following live vaccination	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4.

	<u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists
Additional pharmacovigilance activities	None.
Missing information: Effects on pregnancy and the foetus	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.3 and 4.6. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Missing information: Use in breastfeeding	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.3 and 4.6. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Missing information: Effect on vaccination efficacy and the use of live/attenuated vaccines	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.4. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists Patient card
Additional pharmacovigilance activities	None.
Missing information: Use in patients with mild, moderate, or severe hepatic impairment	
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Sections 4.2, 4.3, and 5.2. <u>Additional risk minimisation measures:</u> Prescriber Brochure Prescriber checklists
Additional pharmacovigilance activities	None.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which Are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Tofacitinib.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Tofacitinib.