Part VI: Summary of the risk management plan

Summary of risk management plan for Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm (tofacitinib)

This is a summary of the risk management plan (RMP) for **Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm** Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm. The RMP details important risks of T **Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm**, how these risks can be minimised, and how more information will be obtained about **Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm** Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm's risks and uncertainties (missing information).

Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharmshould be used.

Important new concerns or changes to the current ones will be included in updates of Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm’s RMP.

I. The medicine and what it is used for

Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharmis 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 citrate as the active substance and it is given by oral route of administration.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm, together with measures to minimise such risks and the proposed studies for learning more about Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm'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 Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm, 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 Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm is not yet available, it is listed under 'missing information' below

II.A List of important risks and missing information

Important risks of Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm. 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).

List of important risks and missing information	
Important identified risks	• Venous thromboembolic events (Deep vein thrombosis / Pulmonary embolism) • Serious and other important infections • Herpes Zoster reactivation • Lung cancer • Lymphoma • Myocardial infarction • Decrease in haemoglobin levels and anaemia • Non-melanoma skin cancer • Transaminase elevation and potential for drug-induced liver injury • Higher incidence and severity of AEs in the elderly
Important potential risks	• Malignancy • Cardiovascular risk (excl myocardial infarction) • Gastrointestinal perforation

List of important risks and missing information	
	• Interstitial lung disease • Progressive multifocal leukoencephalopathy • All-cause mortality • Fractures • Increased risk of adverse events when tofacitinib is administered in combination with methotrexate 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 course juvemile idiopathic arthritis patients and juvenile psoriatic arthritis patients (e.g., growth or development disturbances)

II.B Summary of important risks

Important identified risks	
Venous thromboembolic events (Deep vein thrombosis / Pulmonary embolism)	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4, 4.8, and 5.1 Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Serious and other important infections	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.2, 4.3, 4.4, 4.8, and 5.1 Prescription only medicine

	Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure)
Herpes Zoster reactivation	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4 and 4.8. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Prescriber Brochure).
Lung cancer	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4, 4.8 and 5.1 Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure)
Lymphoma	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4, 4.8 and 5.1 Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Myocardial infarction	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4, 4.8 and 5.1 Prescription only medicine

	Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure)
Decrease in haemoglobin levels and anaemia	
Risk minimisation measures	Routine risk minimisation measures: Text within sections 4.2, 4.4 and 4.8 of the SmPC Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to prescribers (including Treatment Checklists, Prescriber Brochure).
Non-melanoma skin cancer	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4 and 4.8. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Transaminase elevation and potential for drug-induced liver injury	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4 and 4.8. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure)
Higher incidence and severity of AEs in the elderly	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.2, 4.4, 4.8, and 5.1

	Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Important Potential risks	
Malignancy	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4 and 5.1 Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Cardiovascular risk (excl myocardial infarction)	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4 and 5.1 Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to prescribers (including Treatment Checklists, Prescriber Brochure).
Gastrointestinal perforation	
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Interstitial lung disease	

Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
All-cause mortality	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.4 and 5.1 Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to prescribers (including Treatment Checklists, Prescriber Brochure).
Increased risk of advrse events when tofacitinib is administered in combination with methotrexate in rheumatoid arthritis or psoriatic arthritis patients	
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Prescriber Brochure).
Primary viral infection following live vaccination	
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to prescribers (including Treatment Checklists, Prescriber Brochure).
Missing information	

Effects on pregnancy and the foetus	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.3 and 4.6. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Use in breastfeeding	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.3 and 4.6. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to both patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Effect on vaccination efficacy and the use of live/attenuated vaccines	
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to patients (Patient Alert Card) and prescribers (including Treatment Checklists, Prescriber Brochure).
Use in patients with mild, moderate, or severe hepatic impairment	
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.2, 4.3, and 5.2. Prescription only medicine Additional risk minimisation measures: Development of an educational programme including additional communication to prescribers (including Treatment Checklists, Prescriber Brochure).

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 Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Applicant's Tofacitinib Newbury/Tofacitinib Accord/Tofacitinib Adalvo/Zemik/Tofacitinib Glenmark/Tofacitinib Corapharm.