XELJANZ®▼ (tofacitinib citrate)
PRESCRIBER TREATMENT MAINTENANCE CHECKLIST

Patient: _____ Date: _____

Introduction

This treatment maintenance checklist intends to remind you of the risks associated with use of tofacitinib and the recommended tests DURING tofacitinib treatment. The checklist should be used in conjunction with the XELJANZ Summary of Product Characteristics (SmPC).

RHEUMATOID ARTHRITIS (RA)

XELJANZ (tofacitinib citrate) is an inhibitor of Janus kinases (JAKs) that was granted a marketing authorisation in the EU (22 March 2017) for use in combination with methotrexate (MTX) in adult patients with moderate to severe active RA who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). Tofacitinib can be given as monotherapy in case of intolerance to MTX or when treatment with MTX is inappropriate. The recommended dose is 5 mg film-coated tablets given twice daily or 11 mg prolonged-release tablets, given once daily, which should not be exceeded.

Treatment with tofacitinib 5 mg film-coated tablets twice daily and tofacitinib 11 mg prolonged-release tablet once daily may be switched between each other on the day following the last dose of either tablet.

PSORIATIC ARTHRITIS (PsA)

Tofacitinib has also received marketing authorisation in the EU for use in combination with MTX in adult patients with active PsA who have had an inadequate response or who have been intolerant to a prior DMARD therapy. The recommended dose is 5 mg film-coated tablets given twice daily or 11 mg prolonged release tablets, given once daily, which should not be exceeded.

Treatment with tofacitinib 5 mg film-coated tablets twice daily and tofacitinib 11 mg prolonged-release tablet once daily may be switched between each other on the day following the last dose of either tablet.

ULCERATIVE COLITIS (UC)

Tofacitinib has also received marketing authorisation in the EU for the treatment of adult patients with moderately to severely active UC who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

Induction treatment for UC (weeks 0 through week 8, with extension to week 16 as necessary)

The recommended dose for UC is 10 mg given orally twice daily for induction for 8 weeks. For patients who do not achieve adequate therapeutic benefit by week 8, the induction dose of 10 mg twice daily can be extended for an additional 8 weeks (16 weeks total), followed by 5 mg twice daily for maintenance. Tofacitinib induction therapy should be discontinued in any patient who shows no evidence of therapeutic benefit by week 16.

Maintenance treatment for UC (post-induction period)

The recommended dose for maintenance treatment is tofacitinib 5 mg given orally twice daily.

Tofacitinib 10 mg twice daily for maintenance treatment is not recommended in patients with UC who have known venous thromboembolism (VTE) risk factors, unless there is no suitable alternative treatment available.

For patients with UC who are not at increased risk for VTE, tofacitinib 10 mg given orally twice daily may be considered if the patient experiences a decrease in response on tofacitinib 5 mg twice daily and failed to respond to alternative treatment options for ulcerative colitis such as tumour necrosis factor inhibitor (TNF inhibitor) treatment. Tofacitinib 10 mg twice daily for maintenance treatment should be used for the shortest duration possible. The lowest effective dose needed to maintain response should be used.

In patients who have responded to treatment with tofacitinib, corticosteroids may be reduced and/or discontinued in accordance with standard of care.

Retreatment in UC: if therapy is interrupted, restarting treatment with tofacitinib can be considered. If there has been a loss of response, reinduction with tofacitinib 10 mg twice daily may be considered. The treatment interruption period in clinical studies extended up to 1 year. Efficacy may be regained by 8 weeks of 10 mg twice daily therapy.

JUVENILE IDIOPATHIC ARTHRITIS (JIA)

Tofacitinib has also received marketing authorization in the EU for the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis (jPsA) in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs.

Tofacitinib can be given in combination with methotrexate (MTX) or as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

The recommended dose in patients 2 years of age and older is based upon the following weight categories:

Body weight (kg)	Dose regimen
10 - < 20	3.2 mg (3.2 mL of oral solution) twice daily
20 - < 40	4 mg (4 mL of oral solution) twice daily
≥ 40	5 mg (5 mL of oral solution or 5 mg film-coated tablet) twice daily

Patients ≥ 40 kg treated with tofacitinib 5 mL oral solution twice daily may be switched to tofacitinib 5 mg film-coated tablets twice daily. Patients < 40 kg cannot be switched from tofacitinib oral solution.

ANKYLOSING SPONDYLITIS (AS)

Tofacitinib has also received marketing authorisation in the EU for the treatment of adult patients with active ankylosing spondylitis who have responded inadequately to conventional therapy. The recommended dose is 5 mg given twice daily.

SPECIAL WARNINGS & PRECAUTIONS

In a randomised post-authorisation safety study in patients with RA who were 50 years of age or older with at least one additional cardiovascular risk factor, an increased incidence of myocardial infarctions (MI) and malignancies (excluding non-melanoma skin cancer), particularly lung cancer and lymphoma, was observed with tofacitinib compared to TNF inhibitors.

Serious VTE events including pulmonary embolism (PE), some of which were fatal, and deep vein thrombosis (DVT) have been observed in patients taking tofacitinib. A dose-dependent increased risk for VTE was observed in the randomised post-authorisation safety study of tofacitinib, compared to TNF inhibitors.

Events of serious infections, herpes zoster, tuberculosis (TB) and other opportunistic infections, malignancy (including lymphoma and lung cancer), non-melanoma skin cancer, gastrointestinal perforations, interstitial lung disease, and laboratory abnormalities have also been reported in patients treated with tofacitinib in clinical studies.

Patients should be closely monitored for any signs and symptoms, and laboratory abnormalities for an early identification of these risks.

In patients over 65 years of age, patients who are current or past smokers, and patients with other cardiovascular or malignancy risk factors, tofacitinib should only be used if no suitable treatment alternatives are available.

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DURING THE TREATMENT WITH TOFACITINIB, PLEASE CHECK THE FOLLOWING AT EACH OFFICE VISIT:

	Yes	No
IS THE PATIENT OVER 65 YEARS OF AGE?	☐	☐
If Yes: Have you considered alternative treatment considering the increased risk of serious infections, myocardial infarction and malignancies with tofacitinib?	☐	☐

Note the following:

- In patients over 65 years of age, tofacitinib should only be used in these patients if no suitable treatment alternatives are available

	Yes	No
IS THE PATIENT OVER 65 YEARS OF AGE, A CURRENT OR PAST SMOKER, OR DO THEY HAVE OTHER CARDIOVASCULAR RISK FACTORS?	☐	☐
If Yes: Are there any suitable treatment alternatives available for the patient?	☐	☐

Note the following:

- Given the increased risk of major adverse cardiovascular events (MACE), tofacitinib should only be used in these patients if no suitable treatment alternatives are available
- Discuss with the patient how to recognise symptoms of MI and to promptly seek medical attention if they experience these

	Yes	No
IS THE PATIENT OVER 65 YEARS OF AGE, A CURRENT OR PAST SMOKER, OR DO THEY HAVE OTHER MALIGNANCY RISK FACTORS (E.G. CURRENT OR HISTORY OF MALIGNANCY OTHER THAN A SUCCESSFULLY TREATED NON-MELANOMA SKIN CANCER)?	☐	☐
If Yes: Are there any suitable treatment alternatives available for the patient?	☐	☐

Note the following:

- Given the increased risk of malignancy, tofacitinib should only be used if no suitable treatment alternatives are available

	Yes	No
HAS THE PATIENT DEVELOPED ANY RISK FACTORS FOR VTE?	☐	☐

Note the following:

- VTE risk factors include (but are not limited to):
  - Previous VTE
  - Patients undergoing major surgery
  - Immobilisation
  - Myocardial infarction (within previous 3 months)
  - Heart failure
  - Use of combined hormonal contraceptives or hormonal replacement therapy
  - Inherited coagulation disorder
  - Malignancy
- Additional VTE risk factors that should be considered include:
  - Age
  - Obesity (BMI ≥30)
  - Diabetes
  - Hypertension
  - Smoking status
- Tofacitnib should be used with caution in patients with known risk factors for VTE, regardless of indication and dosage
- Promptly evaluate patients with signs and symptoms of VTE and discontinue tofacitinib in patients with suspected VTE, regardless of dose or indication
- Discuss with the patient how to recognise symptoms of VTE and to promptly seek medical attention if they experience these

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FOR PATIENTS WITH RA WITH KNOWN RISK FACTORS FOR VTE, CONSIDER TESTING D-DIMER LEVELS AFTER APPROXIMATELY 12 MONTHS OF TREATMENT. IS D-DIMER TEST RESULT >2X ULN? Yes ☐ No ☐

If yes:
Do the clinical benefits outweigh the risks of treatment continuation with tofacitinib? ☐ ☐

FOR PATIENTS WITH UC WHO HAVE BEEN TAKING TOFACITINIB FOR 16 WEEKS AND HAVE NOT SHOWN CLINICAL IMPROVEMENT, HAVE YOU CONSIDERED THE FOLLOWING? Yes ☐ No ☐

- Tofacitinib induction therapy should be discontinued in any patient who shows no evidence of therapeutic benefit by week 16

FOR PATIENTS WITH UC WHO HAVE LOST RESPONSE TO TOFACITINIB 5 MG TWICE DAILY MAINTENANCE, HAVE YOU CONSIDERED THE FOLLOWING: Yes ☐ No ☐

- Patients with VTE risk factors - tofacitinib 10 mg twice daily is not recommended for maintenance treatment, unless there is no suitable alternative treatment available
- Patients without VTE risk factors - tofacitinib 10 mg twice daily may be considered if patient has failed to respond to alternative treatment options such as TNF inhibitors

FOR PATIENTS WITH JIA WHO HAVE BEEN TAKING TOFACITINIB FOR 18 WEEKS AND HAVE NOT SHOWN CLINICAL IMPROVEMENT, HAVE YOU CONSIDERED THE FOLLOWING? Yes ☐ No ☐

- Available data suggest that clinical improvement in paediatric patients is observed within 18 weeks of initiation of treatment with tofacitinib. Continued therapy should be carefully reconsidered in a patient exhibiting no clinical improvement within this timeframe

FOR PATIENTS WITH AS WHO HAVE BEEN TAKING TOFACITINIB FOR 16 WEEKS AND HAVE NOT SHOWN CLINICAL IMPROVEMENT, HAVE YOU CONSIDERED THE FOLLOWING? Yes ☐ No ☐

- Available data suggest that clinical improvement in AS is observed within 16 weeks of initiation of treatment. Continued therapy should be carefully reconsidered in a patient exhibiting no clinical improvement within this timeframe

IS THE PATIENT CURRENTLY PREGNANT OR DOES THIS PATIENT INTEND TO BECOME PREGNANT? Yes ☐ No ☐

Note the following:

- Use of tofacitinib during pregnancy is contraindicated
- Women of childbearing potential should be advised to use effective contraception during treatment with tofacitinib and for at least 4 weeks after the last dose

IS THIS PATIENT BREASTFEEDING OR DOES THIS PATIENT INTEND TO BREASTFEED? Yes ☐ No ☐

Note the following:

- Use of tofacitinib during breastfeeding is contraindicated

DOES THIS PATIENT HAVE ANY NEW ONSET SIGNS OR SYMPTOMS OF INFECTIONS? Yes ☐ No ☐

Note the following: ☐ ☐

- Treatment should be interrupted if a patient develops a serious infection, an opportunistic infection, or sepsis
- If a new infection develops during treatment, the following actions are recommended:
  - Prompt and complete diagnostic testing that is appropriate for an immunocompromised patient
  - Initiation of appropriate antimicrobial therapy
  - Close monitoring of the patient
- Patients should be evaluated and tested for latent or active TB infection per applicable guidelines during administration of tofacitinib

DOES THIS PATIENT HAVE ANY NEW ONSET ABDOMINAL SIGNS OR SYMPTOMS? Yes ☐ No ☐

Note the following:

- Patients presenting with new onset abdominal signs and symptoms should be evaluated promptly for early identification of gastrointestinal perforation

DOES THIS PATIENT HAVE ANY NEW ONSET OR WORSENING OF SIGNS OR SYMPTOMS OF INTERSTITIAL LUNG DISEASE? Yes ☐ No ☐

Note the following:

- Caution is recommended in patients with a history of chronic lung disease as they may be more prone to infections. Events of interstitial lung disease (some of which had a fatal outcome) have been reported in patients treated with tofacitinib

HAS THE ABSOLUTE LYMPHOCYTE COUNT (ALC) BEEN MONITORED? Yes ☐ No ☐

Note the following:

- If lymphocyte count is between 0.5 and 0.75 cells x10^9/L (2 sequential values in this range on routine testing), tofacitinib dosing should be reduced or interrupted. For patients receiving tofacitinib 5 mg twice daily or 11 mg prolonged release tablets once daily, dosing should be interrupted. For patients with UC receiving tofacitinib 10 mg twice daily, dosing should be reduced to tofacitinib 5 mg twice daily
- When ALC is greater than 0.75, resume tofacitinib as clinically appropriate
- If ALC is below 0.5 cells x10^9/L (confirmed by repeated testing within 7 days), discontinue tofacitinib
- Lymphocytes should be measured at baseline and every 3 months thereafter

HAS THE ABSOLUTE NEUTROPHIL COUNT (ANC) BEEN MONITORED? Yes ☐ No ☐

Note the following:

- If the ANC is greater than 1.0 cells x10^9/L, maintain dose
- If the ANC is 0.5–1.0 cells x10^9/L, (2 sequential values in this range on routine testing), reduce or interrupt dosing. For patients receiving tofacitinib 5 mg twice daily or 11 mg prolonged release tablets once daily, dosing should be interrupted. For patients with UC receiving tofacitinib 10 mg twice daily, dosing should be reduced to tofacitinib 5 mg twice daily
- When ANC is greater than 1.0 cells x10^9/L, resume treatment as clinically appropriate
- If the ANC is <0.5 cells x10^9/L (confirmed by repeat testing within 7 days), discontinue treatment
- Neutrophils should be measured at baseline, then after 4 to 8 weeks of treatment, and then every 3 months thereafter

HAS THE HAEMOGLOBIN LEVEL BEEN MONITORED? Yes ☐ No ☐

Note the following:

- If less than or equal to 2 g/dL decrease and greater than or equal to 9.0 g/dL, maintain dose
- If greater than 2 g/dL decrease or less than 8.0 g/dL (confirmed by repeat testing), interrupt the administration of tofacitinib until haemoglobin values have normalised
- Haemoglobin should be monitored at baseline and after 4 to 8 weeks of treatment and every 3 months thereafter

HAVE LIPID PARAMETERS BEEN MONITORED ROUTINELY (I.E. 8 WEEKS FOLLOWING INITIATION OF TOFACITINIB THERAPY)? Yes ☐ No ☐

Note the following:

- Maximum effects on lipid parameters were generally observed within 6 weeks of initiation
- Patients should be managed according to clinical guidelines for hyperlipidaemia; lipid increases associated with tofacitinib may be decreased to pre-treatment levels with statin therapy

HAS LIVER ENZYME TESTING BEEN ROUTINELY PERFORMED? Yes ☐ No ☐

Note the following:

- Routine monitoring of liver tests and prompt investigation of the causes of liver enzyme elevations is recommended to identify potential cases of drug-induced liver injury
- If drug-induced injury is suspected, the administration of tofacitinib should be interrupted until this diagnosis has been excluded

▼ 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 reactions via HPRA Pharmacovigilance. Website: www.hpra.ie. Any suspected adverse reactions may also be reported to Pfizer Medical Information on 1800 633 363.