XELJANZ® (tofacitinib citrate)
PRESCRIBER TREATMENT MAINTENANCE CHECKLIST
(FOR USE DURING FOLLOW-UP VISITS FOR PATIENTS ON XELJANZ TREATMENT)

Patient: _____

Date: _____

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).

Tofacitinib should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of the conditions for which it is indicated, namely:

- Rheumatoid arthritis (RA)
- Psoriatic arthritis (PsA)
- Ankylosing spondylitis (AS)
- Ulcerative colitis (UC)
- Juvenile idiopathic arthritis (JIA)

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 venous thromboembolism (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, cardiovascular risk (excluding myocardial infarction [MI]), MI, herpes zoster, tuberculosis (TB) and other opportunistic infections, malignancy (including lymphoma and lung cancer), all-cause mortality, gastrointestinal perforations, interstitial lung disease, and laboratory abnormalities have also been reported in patients treated with tofacitinib in clinical studies.

Tofacitinib should only be used if no suitable treatment alternatives are available in patients:

- 65 years of age and older;
- patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers);
- patients with malignancy risk factors (e.g. current malignancy or history of malignancy)

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

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

IS THE PATIENT OVER 65 YEARS OF AGE? — Yes ☐ No ☐

If Yes:
Have you considered alternative treatment considering the increased risk of serious infections, myocardial infarction, malignancies and all-cause mortality 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

IS THE PATIENT OVER 65 YEARS OF AGE, A CURRENT OR PAST LONG-TIME SMOKER, OR DO THEY A HISTORY OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE, OR HAVE OTHER CARDIOVASCULAR RISK FACTORS? — Yes ☐ No ☐

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), including MI, 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

IS THE PATIENT OVER 65 YEARS OF AGE, A CURRENT OR PAST LONG-TIME 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)? — Yes ☐ No ☐

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

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

Note the following:

- Tofacitnib should be used with caution in patients with known risk factors for VTE, regardless of indication and dosage
- Refer to the prescriber brochure for the VTE risk factors
- 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

FOR PATIENTS WITH RA WITH KNOWN RISK FACTORS FOR VTE, HAVE YOU PERFORMED TESTING OF D-DIMER LEVELS AFTER APPROXIMATELY 12 MONTHS OF TREATMENT AND 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 ☐

- For patients who are not at increased risk for VTE, MACE and malignancy, tofacitinib 10 mg orally twice daily may be considered if the patient has failed to respond to alternative treatment options for UC such as tumour necrosis factor inhibitor (TNF inhibitor) treatment
- Tofacitinib 10 mg twice daily for maintenance treatment is not recommended in patients with UC who have known VTE, MACE and malignancy risk factors, unless there is no suitable alternative treatment available

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

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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: ☐ ☐

- If a new infection develops during treatment, please take the following recommended actions:
  - Interrupt tofacitinib treatment
  - Prompt and complete diagnostic testing that is appropriate for an immunocompromised patient
  - Initiation of appropriate antimicrobial therapy
  - Close monitoring of the patient and their neutrophil count
- 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 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

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

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

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

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.