XELJANZ (TOFACITINIB)▼
PRESCRIBER TREATMENT MAINTENANCE CHECKLIST
(FOR USE DURING FOLLOW-UP VISITS FOR PATIENTS ON XELJANZ TREATMENT)

Patient: .....

Date: _ _ / _ _ / _ _ _ _

▼ 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.

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Introduction

Rheumatoid Arthritis (RA)

XELJANZ® (tofacitinib citrate) is an inhibitor of Janus kinases (JAKs) that was granted a marketing authorization 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. Tofacitinib can be given as monotherapy in case of intolerance to MTX or when treatment with MTX is inappropriate. The recommended posology is 5 mg film-coated tablets administered twice daily, or 11 mg prolonged-release tablets, administered 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 authorization 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 posology is 5 mg film-coated tablets administered twice daily or 11 mg prolonged release tablets, administered 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

Ankylosing spondylitis

Tofacitinib is indicated for the treatment of adult patients with active ankylosing spondylitis (AS) who have responded inadequately to conventional therapy. The recommended dose of tofacitinib is 5 mg administered twice daily.

Ulcerative Colitis (UC)

Tofacitinib has also received marketing authorization 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.

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

The recommended dose for UC is 10 mg film-coated tablets 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 film-coated tablets twice daily can be extended for an additional 8 weeks (16 weeks total), followed by 5 mg film-coated tablets twice daily for maintenance. Tofacitinib induction therapy should be discontinued in any patient who shows no evidence of therapeutic benefit by week 16.

<u>Maintenance treatment for UC (post induction period)</u>

The recommended dose for maintenance treatment is tofacitinib 5 mg film-coated tablets given orally twice daily.

Tofacitinib 10 mg film-coated tablets 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 film-coated tablets orally twice daily may be considered if the patient experiences a decrease in response on tofacitinib 5 mg film-coated tablets 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 film-coated tablets 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 film-coated tablets 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 film-coated tablets 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:

Table 1: Tofacitinib dose for patients with polyarticular juvenile idiopathic arthritis and juvenile PsA two years of age and older

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.

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 clinical study with tofacitinib, compared to TNF inhibitors.

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 and malignancies (excluding non-melanoma skin cancer), particularly lung cancer and lymphoma, was observed with 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), gastrointestinal perforations, interstitial lung disease, and laboratory abnormalities have 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.

This treatment maintenance checklist intends to remind you of the risks associated with use of tofacitinib and the recommended tests during tofacitinib treatment.

During the treatment of tofacitinib, please check the following at each office visit:

For patients with JIA who have been taking tofacitinib for 18 weeks and have not shown clinical improvement, have you considered the following? Available data suggest that clinical improvement 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	Yes ☐ No ☐
Is the patient currently pregnant or does this patient intends to become pregnant? **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	Yes ☐ No ☐
Is this patient breastfeeding or does this patient intend to breast-feed? **Note the following:** • Use of tofacitinib during breastfeeding is contraindicated	Yes ☐ No ☐
Is the patient over 65 years of age? **If Yes:** **Have you considered alternative treatment considering the increased risk of serious infections, MI and malignancies?** **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 ☐ 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.	Yes ☐ No ☐
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? If yes, do the clinical benefits outweigh the risks of treatment continuation with tofacitinib?	Yes ☐ No ☐ Yes ☐ No ☐
For patients with UC who have lost response to tofacitinib 5mg twice daily maintenance, have you considered the following: • Patients with VTE risk factors - tofacitinib 10mg 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	Yes ☐ No ☐
Does this patient have any new onset signs of symptoms of infections? **Note the following:** • Patients should be evaluated and tested for latent or active infection per applicable guidelines during administration of tofacitinib • 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 - Appropriate antimicrobial therapy should be initiated - Close monitoring of the patient	Yes ☐ No ☐
Given the increased risk of Major Adverse Cardiovascular Events (including MI), is the patient over 65 years of age, a current or past smoker or have other cardiovascular risk factors? **If Yes:** **Are there any suitable treatment alternatives available for the patient?** **Note the following:** Tofacitinib should only be used in these patients if no suitable treatment alternatives are available	Yes ☐ No ☐ Yes ☐ No ☐
Given the increased risk of malignancy, is the patient over 65 years of age, a current or past smoker or 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:** Tofacitinib should only be used if no suitable treatment alternatives are available	Yes ☐ No ☐ Yes ☐ No ☐
Does this patient have any new onset abdominal signs or symptoms? **Note the following:** • Patients presenting with new onset abdominal signs and symptoms should be evaluated promptly for early identification of gastrointestinal perforation	Yes ☐ No ☐

Does this patient have any new onset or worsening of signs or symptoms of interstitial lung disease? **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.	Yes ☐ No ☐
Has the absolute lymphocyte count (ALC) been monitored? **Note the following:** • If lymphocyte count is between 500 and 750 cells/mm^3 (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 750 cells/mm^3, resume tofacitinib as clinically appropriate • If ALC is below 500 cells/mm^3 (confirmed by repeated testing within 7 days), discontinue tofacitinib • Lymphocytes should be measured at baseline and every 3 months thereafter	Yes ☐ No ☐
Has the absolute neutrophil count (ANC) been monitored? **Note the following:** • If the ANC is greater than 1000 cells/mm^3, maintain dose • If the ANC is 500–1000 cells/mm^3 (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 1000 cells/mm^3, resume treatment as clinically appropriate • If the ANC is <500 cells/mm^3 (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	Yes ☐ No ☐
Has the haemoglobin level been monitored? **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	Yes ☐ No ☐
Have lipid parameters been monitored routinely (i.e. after 8 weeks following initiation of tofacitinib therapy)?	Yes ☐ No ☐
Has liver enzyme testing been routinely performed? **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. _	Yes ☐ No ☐