פייזר פרמצבטיקה ישראל בע"מ
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יולי 2022

רופא/ה, רוקח/ת נכבד/ה,

חברת פייזר ישראל בע"מ, מבקשת להודיעכם על על שינוי בהתוויות ומשטרי המינון של התכשיר קסלג'אנז 5 מ"ג, ועל הוספת מידע הנוגע לתכשירים קסלג'אנז 10 מ"ג וקסלג'אנז XR לעלוני התכשיר.

הודעה זו מפרטת את העדכונים בהתוויות ומשטרי המינון בלבד. למידע מלא יש לעיין בעלונים.

העלונים מפורסמים במאגר התרופות שבמשרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום:

חברת פייזר פרמצבטיקה ישראל בע"מ, שנקר 9, ת.ד. 12133, הרצליה פיתוח, 46725.

שם התכשיר:

Xeljanz 5mg

Xeljanz 10 mg

Xeljanz XR

הרכב וחוזק:

Xeljanz 5, 10 mg: Each tablet contains tofacitinib citrate, equivalent to 5/10 mg tofacitinib

Xeljanz XR: Each extended-release tablet contains tofacitinib citrate, equivalent to 11 mg tofacitinib

התווית מאושרות:

Rheumatoid arthritis

Tofacitinib in combination with methotrexate (MTX) is indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients 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.

Psoriatic arthritis

Tofacitinib in combination with MTX is indicated for the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy.

Ulcerative colitis

Tofacitinib is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

משטרי המינון המאושרים:

Posology and method of administration

Treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of conditions for which tofacitinib is indicated.

Posology

Rheumatoid arthritis

The recommended dose is 5 mg tablets administered twice daily, or one extended-release tablet (11 mg) which should not be exceeded.

No dose adjustment is required when used in combination with MTX.

For information on switching between tofacitinib tablets and tofacitinib extended-release tablets see Table 1.

Table 1: Switching between tofacitinib tablets and tofacitinib extended-release tablets

Switching between tofacitinib 5 mg tablets and tofacitinib 11 mg extended-release tablet[a]	Treatment with tofacitinib 5 mg tablets twice daily and tofacitinib 11 mg extended-release tablet once daily may be switched between each other on the day following the last dose of either tablet.

[a] See section 5.2 for comparison of pharmacokinetics of extended-release and tablets formulations.

Psoriatic arthritis

The recommended dose is 5 mg tablets administered twice daily, which should not be exceeded.

No dose adjustment is required when used in combination with MTX.

Ulcerative colitis

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

Avoid XELJANZ in patients at increased risk for thrombosis, including pulmonary embolism, deep venous thrombosis, and arterial thrombosis.

For patients with UC who are not at increased risk tofacitinib 10 mg 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.

Dose interruption and discontinuation in adults patients

Tofacitinib treatment should be interrupted if a patient develops a serious infection until the infection is controlled.

Interruption of dosing may be needed for management of dose-related laboratory abnormalities including lymphopenia, neutropenia, and anaemia. As described in Tables 3, 4 and 5 below, recommendations for temporary dose interruption or permanent discontinuation of treatment are made according to the severity of laboratory abnormalities.

It is recommended not to initiate dosing in patients with an absolute lymphocyte count (ALC) less than 750 cells/mm^3.

Low absolute lymphocyte count:

Low absolute lymphocyte count (ALC)	
Laboratory value (cells/mm^3)	**Recommendation**
ALC greater than or equal to 750	Dose should be maintained.
ALC 500-750	For persistent (2 sequential values in this range on routine testing) decrease in this range, dosing should be reduced or interrupted. For patients receiving tofacitinib 10 mg twice daily, dosing should be reduced to tofacitinib 5 mg twice daily. For patients receiving tofacitinib 5 mg twice daily or 11 mg extended-release, dosing should be interrupted. When ALC is greater than 750, treatment should be resumed as clinically appropriate.
ALC less than 500	If laboratory value confirmed by repeat testing within 7 days, dosing should be discontinued.

It is recommended not to initiate dosing in adult patients with an absolute neutrophil count (ANC) less than 1,000 cells/mm^3.

Low absolute neutrophil count:

Low absolute neutrophil count (ANC)	
Laboratory Value (cells/mm^3)	**Recommendation**
ANC greater than 1,000	Dose should be maintained.
ANC 500-1,000	For persistent (2 sequential values in this range on routine testing) decreases in this range, dosing should be reduced or interrupted. For patients receiving tofacitinib 10 mg twice daily, dosing should be reduced to tofacitinib 5 mg twice daily. For patients receiving tofacitinib 5 mg twice daily or 11 mg extended-release , dosing should be interrupted. When ANC is greater than 1,000, treatment should be resumed as clinically appropriate.
ANC less than 500	If laboratory value confirmed by repeat testing within 7 days, dosing should be discontinued.

It is recommended not to initiate dosing in adult patients with haemoglobin less than 9 g/dL.

Low haemoglobin value Table 5:

Low haemoglobin value (see section 4.4)	
Laboratory value (g/dL)	**Recommendation**
Less than or equal to 2 g/dL decrease and greater than or equal to 9.0 g/dL	Dose should be maintained.
Greater than 2 g/dL decrease or less than 8.0 g/dL (confirmed by repeat testing)	Dosing should be interrupted until haemoglobin values have normalised.

Interactions

Tofacitinib total daily dose should be reduced by half in patients receiving potent inhibitors of cytochrome P450 (CYP) 3A4 (e.g., ketoconazole) and in patients receiving 1 or more concomitant medicinal products that result in both moderate inhibition of CYP3A4 as well as potent inhibition of CYP2C19 (e.g., fluconazole) as follows:

- Tofacitinib dose should be reduced to 5 mg once daily in patients receiving 5 mg twice daily or 11 mg extended release once daily.
- Tofacitinib dose should be reduced to 5 mg twice daily in patients receiving 10 mg twice daily.

Special populations

Elderly

No dose adjustment is required in patients aged 65 years and older. There are limited data in patients aged 75 years and older. See section 4.4 for Use in patients over 65 years of age.

Hepatic impairment

Dose adjustment for hepatic impairment

Hepatic impairment category	**Classification**	**Dose adjustment in hepatic impairment for different strength tablets**
Mild	Child Pugh A	No dose adjustment required.
Moderate	Child Pugh B	Dose should be reduced to 5 mg once daily when the indicated dose in the presence of normal hepatic function is 5 mg twice daily or 11 mg extended release once daily. Dose should be reduced to 5 mg twice daily when the indicated dose in the presence of normal hepatic function is 10 mg twice daily (see section 5.2).
Severe	Child Pugh C	Tofacitinib should not be used in patients with severe hepatic impairment (see section 4.3).

Renal impairment

Dose adjustment for renal impairment

Renal impairment category	**Creatinine clearance**	**Dose adjustment in renal impairment for different strength tablets**
Mild	50-80 mL/min	No dose adjustment required.
Moderate	30-49 mL/min	No dose adjustment required.
Severe (including patients undergoing haemodialysis)	< 30 mL/min	Dose should be reduced to 5 mg once daily when the indicated dose in the presence of normal renal function is 5 mg twice daily or 11 mg extended release once daily. Dose should be reduced to 5 mg twice daily when the indicated dose in the presence of normal renal function is 10 mg twice daily. Patients with severe renal impairment should remain on a reduced dose even after haemodialysis.