University Hospitals of Derby and Burton NHS Foundation Trust

Tofacitinib – IBD - Full Clinical Guideline

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Indication

- Steroid dependent/resistant UC
- Intolerance or resistance to thiopurine
- Use - either before or after anti TNF's/alpha 4 beta 7 inhibitors (Vedo)

Work Up

- Discuss all patients in IBD MDT
- HIV, HBV, HCV
- ZVZ serology
- CMV, PCR blood test
- Stool MC&S
- Flexible sigmoidoscopy
- Baseline cholesterol and lipids
- Assess TB risk history of TB exposure – test for latent TB. Treat latent TB before Tofacitinib

Contraindications

- Infection including TB or latent TB
- Liver disease (Child Pugh class C cirrhosis)
- Pregnancy and lactation
- High risk of thromboembolic disease (e.g. Use of combined hormonal contraceptives or hormone replacement therapy, Heart failure, Previous venous thromboembolism, either deep venous thrombosis or pulmonary embolism, inherited coagulation disorder, malignancy or patients undergoing major surgery)
- Haemoglobin less than 90 g/L, Lymphocyte count <0.75, Neutrophil <1.0
- Viral hepatitis - Tofacitinib studies did not include any patients with viral hepatitis so should be excluded

Vaccination

Vaccinations should be updated prior to treating with Tofacitinib. Live vaccines should be avoided on this drug. Any patient commencing immunosuppression should be considered for the varicella zoster vaccine, Zostavax (see green book recommendations). This vaccine can be given to patients on less than 20mg of Prednisolone and less than 3mg per kilogram per day of Azathioprine, but should not be given to patients on anti TNF or who have had anti TNF in the last 12 months.

Dose

The recommended dosage of tofacitinib for induction is 10 mg taken orally twice daily for 8 weeks, then 5 mg taken twice daily for maintenance.

If adequate therapeutic benefit is not achieved by week 8 the induction dose can be taken for an additional 8 weeks (16 weeks in total). Induction therapy should be stopped if there is no evidence of therapeutic benefit by week 16.

For patients whose disease has responded inadequately to tumour necrosis factor antagonist therapy, consider continuing the 10-mg twice-daily dose for maintenance in order to maintain therapeutic benefit.

If response decreases to tofacitinib 5 mg taken twice daily as maintenance therapy, consider increasing the dose to 10 mg taken twice daily.

Renal Impairment	Creatinine Clearance	Dose Adjustment
Mild	50-80 mL/min	No dose adjustment required.
Moderate	30-49 mL/min	No dose adjustment required.
Severe	< 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. 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

Hepatic Impairment	Classification	Dose Adjustment
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 . 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
Severe	Child Pugh C	Tofacitinib should not be used in patients with severe hepatic impairment

Dose Alterations

- Stop if serious infection

Low Absolute Lymphocyte Count (ALC)	
Lab 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 until ALC is greater than 750. 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, dosing should be interrupted. When ALC is greater than 750, treatment should be resumed as clinically appropriate.
ALC less than 500	If lab value confirmed by repeat testing within 7 days, dosing should be discontinued.

Low Absolute Neutrophil Count (ANC)	
Lab 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 until ANC is greater than 1,000. 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, dosing should be interrupted. When ANC is greater than 1,000, treatment should be resumed as clinically appropriate.
ANC less than 500	If lab value confirmed by repeat testing within 7 days, dosing should be discontinued.

Low Haemoglobin Value	
Lab 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.

Drug Interactions

- Fluconazole & ketoconazole - Tofacitinib dose should be reduced to 5 mg twice daily in patients receiving 10 mg twice daily. Tofacitinib dose should be reduced to 5 mg once daily in patients receiving 5 mg twice daily
- Tacrolimus & ciclosporin – avoid using in combination with tofacitinib.

Blood Monitoring

- Recommend initially full blood count, liver function tests at 4 weeks, 8 weeks then every 3 months
- Repeat fasting lipids at 8 weeks

Pregnancy

The use of Tofacitinib during pregnancy is contraindicated 3

Women of Childbearing Potential/Contraception in Females

- Women of childbearing potential should be advised to use effective contraception during treatment (but not the combined OCP) with Tofacitinib and for at least 4 weeks after the last dose.

Breast-feeding

- The use of Tofacitinib during breast-feeding is contraindicated

Contraception

- Coadministration of Tofacitinib did not have an effect on the PK of oral contraceptives, Levonorgestrel and Ethinyl Estradiol in healthy female volunteers, but the use of Tofacitinib in patients on the combined oral contraceptive is contraindicated because of the thrombosis risk.

References

https://www.medicines.org.uk/emc/product/2500/smpc (EMC XELJANZ 5mg SPC)

Shingles (herpes zoster): the green book, chapter 28a

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/503773/2905109_Green_Book_Chapter_28a_v3_0W.PDF

Documentation Controls

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