Tofacitinib 5 mg, 10 mg film-coated tablets (Xeljanz®) SMC2122

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

Advice: following a full submission

Tofacitinib (Xeljanz®) is accepted for use within NHS Scotland.

Indication under review: For the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

In phase III studies, tofacitinib was superior to placebo in achieving and sustaining remission in adult patients with moderately to severely active ulcerative colitis who had treatment failure with, or were intolerant to, a conventional or biologic medicine.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of tofacitinib. This advice is contingent upon the continuing availability of the PAS in NHS Scotland or a list price that is equivalent or lower.

Indication

For the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

Dosing information

The recommended dose is 10 mg orally twice daily for 8 weeks for induction and 5 mg twice daily for maintenance. For patients who do not achieve adequate therapeutic benefit by week 8, the induction dose 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.

For some patients, such as those who have failed prior tumour necrosis factor (TNF) inhibitor therapy, consideration should be given to continuation of the 10 mg twice daily dose for maintenance in order to maintain therapeutic benefit.

Patients who experience a decrease in response on tofacitinib 5 mg twice daily maintenance therapy may benefit from an increase to tofacitinib 10 mg administered twice daily.

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

Retreatment in ulcerative colitis

If therapy is interrupted, restarting treatment with tofacitinib can be considered. If there has been a loss of response, re-induction 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.

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

References


2. Pfizer Limited. XELJANZ 5 mg film-coated tablets—summary of product characteristics.
   www.medicines.org.uk/emc/product/2500/smpc
Tofacitinib citrate 5 mg film-coated tablets (Xeljanz®) SMC1298/18

Indication: rheumatoid arthritis

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

Advice: following a full submission

Tofacitinib citrate (Xeljanz®) is accepted for restricted use within NHS Scotland.

Indication under review: In combination with methotrexate for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). Tofacitinib can be given as monotherapy in case of intolerance to methotrexate or when treatment with methotrexate is inappropriate.

SMC restriction: In patients with severe disease (a disease activity score [DAS28] greater than 5.1) that has not responded to intensive therapy with a combination of conventional DMARDs. In patients with severe disease inadequately controlled by a tumour necrosis factor (TNF) antagonist, it may be used in patients ineligible to receive rituximab.

In a phase III / IV study in patients with rheumatoid arthritis with an inadequate response to conventional DMARDs, non-inferiority of tofacitinib was demonstrated when compared with a tumour necrosis factor alpha (TNF) inhibitor (both in combination with methotrexate) in relation to proportion of patients achieving an American College of Rheumatology response of at least 50% (ACR50). A phase III study in patients with rheumatoid arthritis with an inadequate response to TNF inhibitors demonstrated that tofacitinib plus methotrexate significantly improved signs and symptoms of RA when compared with placebo plus methotrexate. This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of tofacitinib. This advice is contingent upon the continuing availability of the PAS in NHS Scotland or a list price that is equivalent or lower.

Indication

In combination with methotrexate 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 anti-rheumatic drugs (DMARDs). Tofacitinib can be given as monotherapy in case of intolerance to methotrexate or when treatment with methotrexate is inappropriate.

Dosing information

5 mg administered orally twice daily. 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. It is recommended not to initiate dosing in patients with an absolute lymphocyte count less than 750 cells/mm³.

Treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of RA. Further details are included in the summary of product characteristics (SPO).

References

   www.scottishmedicines.org.uk/medicines-advice/tofacitinib-xeljanz-fullsubmission-129818/

2. Pfizer Limited. XELJANZ 5 mg film-coated tablets–summary of product characteristics.
   www.medicines.org.uk/emc/product/2500/smpc

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The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

**Advice:** following a full submission

Tofacitinib (Xeljanz®) is accepted for restricted use within NHS Scotland.

**Indication under review:** In combination with methotrexate for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy.

**SMC restriction:** for use in patients with psoriatic arthritis whose disease has not responded adequately to at least two conventional DMARDs, given either alone or in combination. Two phase III studies demonstrated superiority of tofacitinib when compared with placebo in reducing signs and symptoms of psoriatic arthritis in patients who had not previously received a TNF inhibitor medication and in those with an inadequate response or intolerance to tumour necrosis factor inhibitors. This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of tofacitinib. This advice is contingent upon the continuing availability of the PAS in NHS Scotland or a list price that is equivalent or lower.

**Dosing information**

The recommended dose is 5 mg orally twice daily. Tofacitinib is given with or without food. Treatment should be interrupted if a patient develops a serious infection until the infection is controlled. Treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of psoriatic arthritis.

**About the SMC**

The purpose of the SMC is to accept for use those newly licensed medicines that clearly represent good value for money to NHS Scotland. SMC analyses information supplied by the medicine manufacturer on the health benefits of the medicine and justification of its price. As the NHS has limited resources, the SMC works to make sure that those medicines which represent good value for money are accepted for routine use as quickly as possible so that they can benefit patients.

**References**


This Guidelines card, which summarises Scottish Medicine Consortium (SMC) advice on Tofacitinib 5 mg film-coated tablet, has been initiated by Pfizer Limited. Pfizer Limited has reviewed this card for technical accuracy and regulatory compliance. The SMC has reviewed this card for technical accuracy and permission request only. The SMC were not involved in the production of this card.

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In Tofacitinib should be used with caution in patients with arterial or venous thromboembolism or pulmonary embolism, inherited coagulation disorder, previous venous thromboembolism or pulmonary embolism, inherited coagulation disorder, malignancy, or patients undergoing major surgery. **Warnings and Precautions:**

- Tofacitinib should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of the condition for which tofacitinib is indicated. Patients treated with tofacitinib should be given a patient alert card. There was a higher incidence of adverse events for the combination of tofacitinib with MTX versus tofacitinib as monotherapy in RA clinical studies. Tofacitinib should be avoided in combination with biologics and potent immunosuppressants such as azathioprine, 6-mercaptopurine, cyclosporine and tacrolimus.

- **Infections:** Serious and sometimes fatal infections have been reported in patients administered tofacitinib. Rheumatoid arthritis patients taking corticosteroids may be predisposed to infection. Patients should be closely monitored for infections, with prompt diagnosis and treatment. Treatment should be interrupted if a serious infection develops. Use carefully in elderly or patients predisposed to, or with a history of infection (e.g., diabetics). **Tuberculosis:** Patients should be evaluated for both active and latent TB prior to being treated with tofacitinib, patients who test positive for latent TB should be treated with standard antimycobacterial therapy before administering tofacitinib. **Viral Reactivation:** In clinical studies viral reactivation and cases of herpes zoster have been observed. The incidence may be increased in patients treated with 10 mg twice daily, screening for viral hepatitis should be performed in accordance with clinical guidelines prior to starting therapy with tofacitinib the impact on chronic viral hepatitis is not known. **Vaccinations:** Prior to initiating tofacitinib, it is recommended that all patients be brought up to date with all immunisations in agreement with current immunisation guidelines. Live vaccines should not be given concurrently with tofacitinib.

- **Malignancy:** Lymphomas and other malignancies have been observed in patients treated with tofacitinib. Patients with highly active disease may be at higher risk than the general population the effect of tofacitinib on the development and course of malignancies is not known. NMSCs have been reported, the risk of NMSC is higher in patients treated with tofacitinib 10 mg twice daily than in patients treated with 5 mg twice daily. Periodic skin examination is recommended in patients at increased risk. **Pulmonary embolism:** Pulmonary embolism (PE) has been observed in patients taking tofacitinib in clinical trials and post marketing reports. Tofacitinib 10 mg twice daily is contraindicated in patients who are at high risk for pulmonary embolism (see also SmPC section 4.3). Additional risk factors that should be considered in determining the patient’s risk for PE are older age, obesity, smoking status and immobilisation. **Interstitial lung disease:** Caution is recommended in patients with a history of chronic lung disease as they may be more prone to infection. Asian patients are known to be at higher risk of ILD caution should be exercised with these patients.

- **Gastrointestinal perforations:** Tofacitinib should be used with caution in patients who may be at increased risk e.g. diverticulitis or concomitant use of corticosteroids or NSAIDs. **Cardiovascular risk:** risk factors should be managed as part of usual standard of care. **Hypersensitivity:** cases of drug hypersensitivity associated with tofacitinib administration have been reported. Allergic reactions included angioedema and urticaria; serious reactions have occurred. If any serious allergic or anaphylactic reaction occurs, tofacitinib should be discontinued immediately.

**Laboratory Parameters:** increased incidence of lymphopenia and neutropenia have been reported and decreases in haemoglobin and should be monitored in accordance with the SmPC. Monitoring of ANC and haemoglobin at baseline, 4-8 weeks and 3 monthly, ALC at baseline and 3 monthly. Tofacitinib has been associated with increases in lipid parameters maximal effects are observed at 6 weeks monitoring should be performed 8 weeks after initiation and managed according to hyperlipidaemia guidelines. Increases in liver enzymes greater than 3x ULN were uncommonly reported, use caution when initiating with potential hepatotoxic medicinal products. **Pregnancy & Lactation:** Use of tofacitinib during pregnancy and breast-feeding is contraindicated.

**Side Effects:** The most common serious adverse reactions were serious infections; pneumonia, cellulitis, herpes zoster, UTs, diverticulitis, appendicitis and opportunistic infections. The most commonly reported adverse reactions in patients receiving tofacitinib 10 mg twice daily in the UC induction studies were headache, upper respiratory tract infections, nasopharyngitis, diaphoresis, nausea and hypertension. The most commonly reported adverse reactions in patients receiving tofacitinib 10 mg twice daily in the UC induction studies were headache, nasopharyngitis, nausea, and arthralgia. Commonly reported adverse reactions (>1/100 to <1/10), were pneumonia, influenza, herpes zoster, urinary tract infection, sinuses, bronchitis, nasopharyngitis, pharyngitis, anaemia, headache, hypertension, cough, abdominal pain, vomiting, diaphoresis, nausea, gastritis, dyspepsia, rash, arthralgia, pyrexia, oedema peripheral, fatigue, blood creatine phosphokinase increased. Refer to SmPC for further information on side effects.

**Legal Category:** POM. **Marketing Authorisation Holder:** Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium. Package quantities, Marketing Authorisation Numbers and Basic NHS Price: XELJANZ 5 mg, 56 film-coated tablets, EU/1/17/1178/003 £690.03; XELJANZ 10 mg, 56 film-coated tablets, EU/1/17/1178/007 £1380.06. Further information is available on request from: Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK. Tel: +44 (0) 1304 616161.