CLINICAL UPDATE

Brand Name	Xeljanz®
Generic Name	tofacitinib
Drug Manufacturer	Pfizer Inc.

Clinical Update

TYPE OF CLINICAL UPDATE

New formulation (1 mg/ml)

FDA APPROVAL DATE

September 28, 2020

LAUNCH DATE

By the end of first quarter 2021

REVIEW DESIGNATION

Priority

TYPE OF REVIEW

Type 3 - New Dosage Form

DISPENSING RESTRICTIONS

Specialty

Overview

INDICATION(S) FOR USE

Xeljanz® Oral Solution is a Janus kinase (JAK) inhibitor indicated for:

- Polyarticular Course Juvenile Idiopathic Arthritis: for the treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older.

Limitations of Use: Use of Xeljanz® Oral Solution in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

MECHANISMS OF ACTION

Tofacitinib is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Tofacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. JAK enzymes transmit cytokine signaling through pairing of JAKs (e.g., JAK1/JAK3, JAK1/JAK2, JAK1/TyK2, JAK2/JAK2). Tofacitinib inhibited the *in vitro* activities of JAK1/JAK2, JAK1/JAK3, and JAK2/JAK2 combinations with IC_{50} of 406, 56, and 1377 nM, respectively. However, the relevance of specific JAK combinations to therapeutic effectiveness is not known.

DOSAGE FORM(S) AND STRENGTH(S)

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- Xeljanz® Oral Solution: 1 mg/mL tofacitinib

DOSE & ADMINISTRATION

Body weight	Dosage
10 kg ≤ body weight < 20 kg	3.2 mg (3.2 mL oral solution) twice daily
20 kg ≤ body weight < 40 kg	4 mg (4 mL oral solution) twice daily
Body weight ≥40 kg	5 mg (one 5 mg tablet or 5 mL oral solution) twice daily

EFFICACY

The efficacy of Xeljanz® for the new indication was based on a 44-week, two-part study (consisting of an 18-week, open-label, run-in phase, followed by a 26-week double-blind, placebo-controlled, randomized withdrawal phase) in 225 patients 2 years to 17 years of age with JIA. Patients received Xeljanz® for 18 weeks (run-in phase) followed by randomization to either Xeljanz® or placebo for 26 weeks (double-blind phase). The primary endpoint was the occurrence of disease flare at week 44 relative to the double-blind phase baseline at week 18.

Xeljanz® treated patients experienced significantly fewer disease flares at week 44 vs. placebo treated patients (31% vs. 55%; p = 0.0007).