



Pfizer Announces U.S. FDA Approves XELJANZ® (tofacitinib) for the Treatment of Moderately to Severely Active Ulcerative Colitis

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XELJANZ, an Oral Therapy, is the First and Only JAK Inhibitor Approved in the U.S. for This Patient Population

Pfizer Inc. (NYSE: PFE) announced today that the United States (U.S.) Food and Drug Administration (FDA) approved XELJANZ® (tofacitinib) 10 mg twice-daily (BID) for at least eight weeks, followed by XELJANZ 5 mg BID or 10 mg BID, for the treatment of adult patients in the U.S. with moderately to severely active ulcerative colitis (UC).¹

“Ulcerative colitis is a chronic inflammatory bowel disease that can significantly impact the lives of patients and has limited therapeutic options available,” said Michael Goettler, Global President, Inflammation and Immunology, Pfizer. “With the FDA approval of XELJANZ, adults living with moderately to severely active UC now have an oral option that may help achieve and maintain steroid-free remission.”

XELJANZ is indicated for the treatment of adult patients with moderately to severely active UC. Use of XELJANZ in combination with biological therapies for UC or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.¹

This approval was based on data from three pivotal Phase 3 studies from the Oral Clinical Trials for tofacitinib in ulcerative colitis global clinical development program (OCTAVE Induction 1, OCTAVE Induction 2 and OCTAVE Sustain), and OCTAVE Open, an ongoing open label long-term extension study.^{2,3} Data from all three pivotal Phase 3 studies met their respective primary endpoints, showing a statistically significant, greater

proportion of patients in remission at week 8 in the induction studies and in remission at week 52 in the maintenance study in patients with moderately to severely active UC treated with tofacitinib compared to placebo. Remission was defined as a Mayo score of 2 points or lower, with no individual subscore exceeding 1 point, and a rectal bleeding subscore of 0.ⁱ Full results from OCTAVE Induction 1, OCTAVE Induction 2 and OCTAVE Sustain were published in the New England Journal of Medicine in May 2017.

“The FDA approval of XELJANZ is positive news for the ulcerative colitis community, a patient population that can often encounter frequent and debilitating disruptions to their daily lives,” said William J. Sandborn, MD, Chief, Division of Gastroenterology, Professor of Medicine at the University of California San Diego School of Medicine and OCTAVE study investigator. “XELJANZ provides people living with ulcerative colitis and their prescribing physicians with a new oral treatment option.”

Risks observed in the UC clinical program include serious infection, including herpes zoster and opportunistic infections, malignancies (including non-melanoma skin cancer [NMSC] and lymphoproliferative disorders), gastrointestinal perforation and laboratory abnormalities. There was no discernable difference in frequency of gastrointestinal perforation between the placebo and XELJANZ arms in clinical trials of patients with UC, and many of the trial participants were receiving background corticosteroids.

Dose-dependent adverse reactions seen in patients treated with 10 mg BID, in comparison to 5 mg BID, include the following: herpes zoster infections, serious infections, and NMSC.

“What works for one ulcerative colitis patient may not work for another and some struggle with ongoing symptoms. That is why it is so critical that our patients have different treatment options available to them,” said Michael Osso, President & CEO of the Crohn’s & Colitis Foundation. “We are thrilled to have this new treatment option available to ulcerative colitis patients. Every new treatment provides new hope to our community.”

_____ ⁱ Mayo score is a measurement index comprised of four categories (stool frequency, rectal bleeding, findings on endoscopy, physician global assessment) that are each rated from 0 (normal) to 3 (most severe) for a total score that ranges from 0-12.

About Ulcerative Colitis

UC is a chronic and often debilitating inflammatory bowel disease that affects approximately 907,000 people in the U.S.^{4,5} Symptoms of UC can include chronic diarrhea with blood and mucus, abdominal pain and cramping, and weight loss.⁶ UC can

have a significant effect on work, family and social activities.⁷

About XELJANZ (tofacitinib)

XELJANZ is the first and only Janus kinase (JAK) inhibitor approved by the FDA for adult patients with moderately to severely active rheumatoid arthritis (RA), active psoriatic arthritis (PsA) and moderately to severely active UC.

XELJANZ is now approved in more than 80 countries for the treatment of adult patients with moderate to severe RA, with additional applications pending globally for all three respective indications. XELJANZ was also recently approved for moderate to severe UC in Japan and Russia.

As the developer of tofacitinib, Pfizer is committed to advancing the science of JAK inhibition and enhancing understanding of tofacitinib through robust clinical development programs in the treatment of immune-mediated inflammatory conditions.

Please see full Prescribing Information, including BOXED WARNING for XELJANZ/XELJANZ XR available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=959>.

INDICATIONS

Rheumatoid Arthritis

XELJANZ/XELJANZ XR (tofacitinib) is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. It may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs). Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Psoriatic Arthritis

XELJANZ/XELJANZ XR (tofacitinib) is indicated for the treatment of adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to methotrexate or other disease-modifying antirheumatic drugs (DMARDs). Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Ulcerative Colitis

XELJANZ (tofacitinib) is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC). Limitations of Use: Use of XELJANZ in combination

with biologic therapies for UC or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

Patients treated with XELJANZ/XELJANZ XR are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.

If a serious infection develops, interrupt XELJANZ/XELJANZ XR until the infection is controlled.

Reported infections include:

Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ/XELJANZ XR use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ/XELJANZ XR use. Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease. Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ/XELJANZ XR in patients with an active, serious infection, including localized infections, or with chronic or recurrent infection.

In the UC population, XELJANZ 10 mg twice daily was associated with greater risk of serious infections compared to 5 mg twice daily. Opportunistic herpes zoster infections (including meningoencephalitis, ophthalmologic, and disseminated cutaneous) were seen in patients who were treated with XELJANZ 10 mg twice daily.

The risks and benefits of treatment with XELJANZ/XELJANZ XR should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection, or those who have lived or traveled in areas of endemic TB or mycoses. Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with XELJANZ/XELJANZ XR, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Caution is also recommended in patients with a history of chronic lung disease, or in those who develop interstitial lung disease, as they may be more prone to infection.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with XELJANZ. Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed at an increased rate in renal transplant patients treated with XELJANZ and concomitant immunosuppressive medications.

Consider the risks and benefits of XELJANZ/XELJANZ XR treatment prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing XELJANZ/XELJANZ XR in patients who develop a malignancy.

Malignancies (including solid cancers and lymphomas) were observed more often in patients treated with XELJANZ 10 mg twice daily dosing in the UC long-term extension study.

Other malignancies were observed in clinical studies and the post-marketing setting including, but not limited to, lung cancer, breast cancer, melanoma, prostate cancer, and pancreatic cancer. NMSC have been reported in patients treated with XELJANZ. In the UC population, treatment with XELJANZ 10 mg twice daily was associated with greater risk of NMSC. Periodic skin examination is recommended for patients who are at increased risk for skin cancer.

GASTROINTESTINAL PERFORATIONS

Gastrointestinal perforations have been reported in XELJANZ clinical trials, although the role of JAK inhibition is not known. In these studies, many patients with rheumatoid arthritis were receiving background therapy with Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). There was no discernable difference in frequency of gastrointestinal perforation between the placebo and the XELJANZ arms in clinical trials of patients with UC, and many of them were receiving background corticosteroids. XELJANZ/XELJANZ XR should be used with caution in patients who may be at increased risk for gastrointestinal perforation

(e.g., patients with a history of diverticulitis or taking NSAIDs).

LABORATORY ABNORMALITIES

Lymphocyte Abnormalities: Treatment with XELJANZ was associated with initial lymphocytosis at one month of exposure followed by a gradual decrease in mean lymphocyte counts. Avoid initiation of XELJANZ/XELJANZ XR treatment in patients with a count less than 500 cells/mm³. In patients who develop a confirmed absolute lymphocyte count less than 500 cells/mm³, treatment with XELJANZ/XELJANZ XR is not recommended. Risk of infection may be higher with increasing degrees of lymphopenia and consideration should be given to lymphocyte counts when assessing individual patient risk of infection. Monitor lymphocyte counts at baseline and every 3 months thereafter.

Neutropenia: Treatment with XELJANZ was associated with an increased incidence of neutropenia (less than 2000 cells/mm³) compared to placebo. Avoid initiation of XELJANZ/XELJANZ XR treatment in patients with an ANC less than 1000 cells/mm³. For patients who develop a persistent ANC of 500-1000 cells/mm³, interrupt XELJANZ/XELJANZ XR dosing until ANC is greater than or equal to 1000 cells/mm³. In patients who develop an ANC less than 500 cells/mm³, treatment with XELJANZ/XELJANZ XR is not recommended. Monitor neutrophil counts at baseline and after 4-8 weeks of treatment and every 3 months thereafter.

Anemia: Avoid initiation of XELJANZ/XELJANZ XR treatment in patients with a hemoglobin level less than 9 g/dL. Treatment with XELJANZ/XELJANZ XR should be interrupted in patients who develop hemoglobin levels less than 8 g/dL or whose hemoglobin level drops greater than 2 g/dL on treatment. Monitor hemoglobin at baseline and after 4-8 weeks of treatment and every 3 months thereafter.

Liver Enzyme Elevations: Treatment with XELJANZ was associated with an increased incidence of liver enzyme elevation compared to placebo. Most of these abnormalities occurred in studies with background DMARD (primarily methotrexate) therapy. If drug-induced liver injury is suspected, the administration of XELJANZ/XELJANZ XR should be interrupted until this diagnosis has been excluded. 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.

Lipid Elevations: Treatment with XELJANZ was associated with dose-dependent increases in lipid parameters, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Maximum effects were generally observed

within 6 weeks. There were no clinically relevant changes in LDL/HDL cholesterol ratios. Manage patients with hyperlipidemia according to clinical guidelines. Assessment of lipid parameters should be performed approximately 4-8 weeks following initiation of XELJANZ/XELJANZ XR therapy.

VACCINATIONS

Avoid use of live vaccines concurrently with XELJANZ/XELJANZ XR. The interval between live vaccinations and initiation of tofacitinib therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. Update immunizations in agreement with current immunization guidelines prior to initiating XELJANZ/XELJANZ XR therapy.

PATIENTS WITH GASTROINTESTINAL NARROWING

Caution should be used when administering XELJANZ XR to patients with pre-existing severe gastrointestinal narrowing. There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of other drugs utilizing a non-deformable extended release formulation.

HEPATIC and RENAL IMPAIRMENT

Use of XELJANZ/XELJANZ XR in patients with severe hepatic impairment is not recommended.

For patients with moderate hepatic impairment or with moderate or severe renal impairment taking XELJANZ 5 mg twice daily, reduce to XELJANZ 5 mg once daily.

For UC patients with moderate hepatic impairment or with moderate or severe renal impairment taking XELJANZ 10 mg twice daily, reduce to XELJANZ 5 mg twice daily.

ADVERSE REACTIONS

The most common serious adverse reactions were serious infections. The most commonly reported adverse reactions during the first 3 months in controlled clinical trials in patients with rheumatoid arthritis (RA) with XELJANZ 5 mg twice daily and placebo, respectively, (occurring in greater than or equal to 2% of patients treated with XELJANZ with or without DMARDs) were upper respiratory tract infection, nasopharyngitis, diarrhea, headache, and hypertension. The safety profile observed in patients with active psoriatic arthritis treated with XELJANZ was consistent with the safety profile observed in RA patients.

Adverse reactions reported in $\geq 5\%$ of patients treated with either 5 mg or 10 mg twice daily of XELJANZ and $\geq 1\%$ greater than reported in patients receiving placebo in either the induction or maintenance clinical trials for ulcerative colitis were: nasopharyngitis, elevated cholesterol levels, headache, upper respiratory tract infection, increased blood creatine phosphokinase, rash, diarrhea, and herpes zoster.

USE IN PREGNANCY

Available data with XELJANZ/XELJANZ XR use in pregnant women are insufficient to establish a drug associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. There are risks to the mother and the fetus associated with rheumatoid arthritis and UC in pregnancy. In animal studies, tofacitinib at 6.3 times the maximum recommended dose of 10 mg twice daily demonstrated adverse embryo-fetal findings. The relevance of these findings to women of childbearing potential is uncertain. Consider pregnancy planning and prevention for females of reproductive potential.

Working together for a healthier world ®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

DISCLOSURE NOTICE: The information contained in this release is as of May 30, 2018. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about XELJANZ and a new indication in the U.S. for the treatment of adult patients with moderately to severely active UC (the "new indication"), including its potential benefits, that involves substantial risks and

uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of XELJANZ and XELJANZ XR, including for the new indication for XELJANZ; the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any applications for the new indication or any other potential indications for XELJANZ or XELJANZ XR may be filed with regulatory authorities in any additional jurisdictions; whether and when regulatory authorities in any other jurisdictions may approve any applications that may be pending or filed for the new indication or for any other indications for XELJANZ or XELJANZ XR, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of XELJANZ and XELJANZ XR, including the new indication for XELJANZ; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2017 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

1 XELJANZ Prescribing Information. May, 2018. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=959>.

2 Sandborn WJ, Su C, Sands B, et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. *N Engl J Med*. 2017;376(18):1723-1736.

3 Long-Term Study Of CP-690,550 In Subjects With Ulcerative Colitis (OCTAVE). <https://clinicaltrials.gov/ct2/show/NCT01470612?term=octave+open&rank=1>. Accessed

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4 Crohn's and Colitis Foundation. What is Ulcerative Colitis.

<http://www.crohnscolitisfoundation.org/what-are-crohns-and-colitis/what-is-ulcerative-colitis/>. Accessed May 30, 2018.

5 Kappelman MD, et al. Recent trends in the prevalence of Crohn's disease and ulcerative colitis in a commercially insured US population. *Digestive Diseases and Sciences*. 2013;58:519-525.

6 Hanauer SB. Inflammatory bowel disease. *N Engl J Med*. 1996;334(13):841-8.

7 Irvine EJ. Quality of Life of Patients with Ulcerative Colitis: Past, Present, and Future. *Inflammatory Bowel Diseases*. 2008;14(4):554-563.

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