MEDIA ALERT
MARCH 13, 2017

European League Against Rheumatism (EULAR) Includes Janus Kinase (JAK) Inhibitors in Updated Recommendations for the Management of RA

Pfizer is proud that XELJANZ® (tofacitinib citrate) is included in one of the drug categories recommended in the EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update.[1] This update continues to demonstrate that oral Janus kinase (JAK) inhibitors are an important additional option in helping RA patients manage this chronic disease.

In the publication in *Annals of the Rheumatic Diseases* posted online on March 6, 2017, EULAR recommends the use of targeted synthetic DMARDs (tsDMARDs), such as tofacitinib, as a second-line therapy after conventional synthetic DMARDs (csDMARDs) when poor prognostic factors are present. The recommendations note that tsDMARDs may be combined with csDMARDs or used as monotherapy in patients who cannot tolerate or do not respond to csDMARDs.

Pfizer is pleased to see tsDMARDs recommended as second-line therapy, which is consistent with the current labeling where tofacitinib is approved. The recommendations provide additional guidance to physicians to facilitate treatment decisions for patients with RA.

Tofacitinib is also included in the *2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis* after DMARD failure in patients with established moderate to severe RA.[2]

XELJANZ is the first JAK inhibitor approved globally for the treatment of moderate to severe active RA and it is approved in more than 50 countries around the world.[3]

In January 2017, the CHMP of the European Medicines Agency (EMA) adopted a positive opinion recommending XELJANZ 5 mg twice daily for the treatment of patients with moderate to severe active RA. The CHMP's opinion is now with the European Commission for final decision. In the European Union, XELJANZ is an investigational medicine and has not been approved for use.

XELJANZ®/XELJANZ® XR U.S. Label Information
XELJANZ® (tofacitinib citrate)/XELJANZ® XR (tofacitinib citrate) extended-release is a prescription medicine called a Janus kinase (JAK) inhibitor. XELJANZ/XELJANZ XR is used to treat adults with moderately to severely active rheumatoid arthritis in which methotrexate did not work well. XELJANZ/XELJANZ XR may be used as a single agent or in combination with methotrexate (MTX) or other non-biologic disease-modifying antirheumatic drugs (DMARDs). Use of XELJANZ/XELJANZ XR in combination with biologic DMARDs or potent immunosuppressants, such as azathioprine and cyclosporine, is not recommended.

- It is not known if XELJANZ/XELJANZ XR is safe and effective in people with hepatitis B or C.
- XELJANZ/XELJANZ XR is not for people with severe liver problems.
- It is not known if XELJANZ/XELJANZ XR is safe and effective in children.

Important Safety Information

- **XELJANZ/XELJANZ XR can lower the ability of the immune system to fight infections. Some people can have serious infections while taking XELJANZ/XELJANZ XR, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses that can spread throughout the body. Some people have died from these infections. Healthcare providers**

should test patients for TB before starting XELJANZ/XELJANZ XR, and monitor them closely for signs and symptoms of TB and other infections during treatment. People should not start taking XELJANZ/XELJANZ XR if they have any kind of infection unless their healthcare provider tells them it is okay.

- **People may be at a higher risk of developing shingles.**

- **XELJANZ/XELJANZ XR may increase the risk of certain cancers by changing the way the immune system works. Lymphoma and other cancers, including skin cancers, can happen in patients taking XELJANZ/XELJANZ XR.**

- The risks and benefits of treatment should be considered prior to initiating XELJANZ/XELJANZ XR in patients with chronic or recurrent infection; who have been exposed to tuberculosis; with a history of a serious or an opportunistic infection; who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or with underlying conditions that may predispose them to infection.

- Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), was observed in clinical studies with XELJANZ.

- Use of live vaccines should be avoided concurrently with XELJANZ/XELJANZ XR. Update immunizations in agreement with current immunization guidelines prior to initiating XELJANZ/XELJANZ XR therapy.

- Some people who have taken XELJANZ with certain other medicines to prevent kidney transplant rejection have had a problem with certain white blood cells growing out of control (Epstein Barr virus-associated post-transplant lymphoproliferative disorder).

- Some people taking XELJANZ/XELJANZ XR can get tears in their stomach or intestines. This happens most often in people who also take nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or methotrexate.

- 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 who have a narrowing within their digestive tract. Patients should tell their healthcare provider right away if they have fever and stomach-area pain that does not go away or a change in bowel habits.

- XELJANZ/XELJANZ XR can cause changes in certain lab test results including low blood cell counts, increases in certain liver tests, and increases in cholesterol levels. Healthcare providers should do blood tests before starting patients on XELJANZ/XELJANZ XR and while they are taking XELJANZ/XELJANZ XR, to check for these side effects. Normal cholesterol levels are important to good heart health. Healthcare providers may stop XELJANZ/XELJANZ XR treatment because of changes in blood cell counts or liver test results.

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

- Patients should tell their healthcare providers if they plan to become pregnant or are pregnant.

It is not known if XELJANZ/XELJANZ XR will harm an unborn baby. To monitor the outcomes of pregnant women exposed to XELJANZ/XELJANZ XR, a registry has been established. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-877-311-8972.

- Patients should tell their healthcare providers if they plan to breastfeed or are breastfeeding. Patients and their healthcare provider should decide if they will take XELJANZ/XELJANZ XR or breastfeed. They should not do both.

- In carriers of the hepatitis B or C virus (viruses that affect the liver), the virus may become active while using XELJANZ/XELJANZ XR. Healthcare providers may do blood tests before and during treatment with XELJANZ/XELJANZ XR.

- Common side effects include upper respiratory tract infections (common cold, sinus infections), headache, diarrhea, and nasal congestion, sore throat, and runny nose (nasopharyngitis).

Please click the direct link to the full prescribing information for XELJANZ/XELJANZ XR, including Boxed Warning and Medication Guide: http://labeling.pfizer.com/ShowLabeling.aspx?id=959.

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References

[1] Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;0:1-18. doi:10.1136/annrheumdis-2016-210715

[2] Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis & Rheumatology*. doi: 10.1002/art.39480

[3] Data on file. Pfizer Inc, New York, NY. XELJANZ Worldwide Registration Status 2016