

### **A New Treatment for RA**

XELJANZ<sup>®</sup> (tofacitinib citrate) 5 mg tablets twice daily is an oral Janus kinase (JAK) inhibitor that is approved in the U.S. for the treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate. It may be used as monotherapy (alone) or in combination with methotrexate or other non-biologic disease-modifying antirheumatic drugs (DMARDs). XELJANZ should not be used in combination with biologic DMARDs or with potent immunosuppressives, such as azathioprine and cyclosporine.

XELJANZ is the first new oral DMARD approved for RA in more than 10 years and the first RA treatment in a new class of medicines known as JAK inhibitors.

XELJANZ was discovered by Pfizer scientists in the company's Groton, Connecticut, laboratories and was developed solely by Pfizer. XELJANZ is currently under review by several regulatory agencies around the world, including in Europe and Japan.

### **Treating RA Differently**

RA is characterized by a cycle of inflammation involving different pro-inflammatory cells and processes inside the body. Unlike biologic therapies for RA, which work outside the cell, XELJANZ targets the inflammation associated with RA from inside the cell. Specifically, XELJANZ inhibits the JAK pathways, which are signaling pathways inside cells that are used by pro-inflammatory cytokines (proteins that facilitate communication between cells). The relevance of specific JAK combinations to therapeutic effectiveness is not known.

### **Clinical Research Program for XELJANZ**

Pfizer studied XELJANZ in adults for the treatment of moderately to severely active RA in a large, global clinical development program that included approximately 5,000 patients treated with XELJANZ, yielding approximately 7,000 patient-years of experience with XELJANZ.

The Phase 3 ORAL (Oral Rheumatoid Arthritis Phase 3 TriaLs) program included more than 550 locations in more than 40 countries worldwide. Of the six studies in the ORAL program, five are completed and were included in the New Drug Application for XELJANZ submitted to the U.S. Food and Drug Administration (FDA).

- **ORAL Solo (A3921045):** 6-month study in inadequate responders to a DMARD, non-biologic or biologic, receiving XELJANZ monotherapy, evaluating signs and symptoms and physical function.
- **ORAL Sync (A3921046):** 12-month study in inadequate responders to a DMARD, non-biologic or biologic, receiving XELJANZ and background non-biologic DMARDs, evaluating signs and symptoms and physical function.
- **ORAL Scan (A3921044):** 24-month study in inadequate responders to methotrexate (MTX), receiving XELJANZ and background MTX, including a structural endpoint in addition to evaluating signs and symptoms and physical function.

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- **ORAL Standard (A3921064):** 12-month study in inadequate responders to MTX, receiving XELJANZ and background MTX, with active control of adalimumab and background MTX, evaluating signs and symptoms and physical function.
- **ORAL Step (A3921032):** 6-month study in inadequate responders to TNF-inhibiting therapy, receiving XELJANZ and background MTX, evaluating signs and symptoms and physical function.

There is an ongoing Phase 3 study of XELJANZ, ORAL Start, which was not included in the application to the FDA.

- **ORAL Start (A3921069):** 24-month study in MTX-naïve patients, receiving XELJANZ monotherapy or MTX, including a structural endpoint in addition to evaluating signs and symptoms.

### Long-Term Extension Program:

- **ORAL Sequel (A3921024):** Phase 2/3 open-label, follow-up study evaluating patients who had participated in a prior randomized Phase 2 or Phase 3 study of XELJANZ (monotherapy or in combination with non-biologic DMARDs).
- **Study A3921041:** An open-label, follow-up study (similar to ORAL Sequel), but in Japanese patients only.

### Clinical Trial Results for XELJANZ

In clinical trials, XELJANZ 5 mg twice daily demonstrated clinical efficacy whether it was taken alone or in combination with a non-biologic DMARD(s), such as methotrexate, in patients who had a previous inadequate response to non-biologic or biologic DMARDs, including TNF inhibitors.

XELJANZ was evaluated in patients who represented a broad cross-section of the RA patient population and, in clinical trials, improvements in signs and symptoms and physical function were consistently observed.

### About XELJANZ

XELJANZ is a prescription medicine called a Janus kinase (JAK) inhibitor. XELJANZ is used to treat adults with moderately to severely active rheumatoid arthritis in whom methotrexate did not work well.

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

### Important Safety Information

- **XELJANZ can lower the ability of the immune system to fight infections. Some people have serious infections while taking XELJANZ, 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, and monitor them closely for signs and symptoms of TB and other infections during treatment.**
- **XELJANZ may increase the risk of certain cancers by changing the way the immune system works. Lymphoma and other cancer can happen in patients taking XELJANZ.**
- Some people taking XELJANZ get tears in their stomach or intestines. 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 can cause changes in certain lab test results including low blood cell counts, increases in certain liver tests and increases in cholesterol levels. Normal cholesterol levels are important to good heart health. Healthcare providers may stop XELJANZ treatment because of changes in blood cell counts or liver test results.
- Patients should tell their healthcare providers if they plan to become pregnant or are pregnant.
- It is not known if XELJANZ will harm an unborn baby. To monitor the outcomes of pregnant women exposed to XELJANZ, a pregnancy 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 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. Healthcare providers may do blood tests for hepatitis before and during treatment with XELJANZ.
- Common side effects include upper respiratory tract infections (common cold, sinus infections), headache, diarrhea, nasal congestion, sore throat, and runny nose (nasopharyngitis).

For full prescribing information, including boxed warning and Medication Guide, please visit [www.XELJANZ.com](http://www.XELJANZ.com).

## About XELJANZ

*The information contained in this fact sheet is as of November 2012. Pfizer assumes no obligation to update forward-looking statements contained in this fact sheet as the result of new information or future events or developments.*

*This fact sheet contains forward-looking information that involves substantial risks and uncertainties about a potential indication for a product in development, XELJANZ, as a treatment for moderately to severely active RA that is under review by regulatory authorities in various markets, the EU and Japan, and about other potential indications for XELJANZ. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; decisions by regulatory authorities regarding whether and when to approve drug applications that have been or may be filed for XELJANZ for moderately to severely active RA and any drug applications that may be filed for XELJANZ for other indications, as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; 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, 2011, and in its reports on Form 10-Q and Form 8-K.*