FOR ADULT PATIENTS WITH MODERATELY TO SEVERELY ACTIVE UC WHO HAVE HAD AN INADEQUATE RESPONSE OR WHO ARE INTOLERANT TO TNF BLOCKERS[1]

START WITH XELJANZ

FOR RAPID REMISSION

OCTAVE Induction 1 and 2 at Week 8[1,2,a]

- OCTAVE 1: **18%** of patients taking XELJANZ 10 mg twice daily achieved **remission[b]** (primary endpoint) vs **8%** on placebo; *P*<0.01
- OCTAVE 2: **17%** of patients taking XELJANZ 10 mg twice daily achieved **remission[b]** (primary endpoint) vs **4%** on placebo; *P*<0.001

INDICATION

- XELJANZ/XELJANZ XR (tofacitinib) is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response or who are intolerant to TNF blockers.
- Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biological therapies for UC or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

Patients treated with XELJANZ* 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 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 use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ 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.**

*Unless otherwise stated, "XELJANZ" in the Important Safety Information refers to XELJANZ, XELJANZ XR, and XELJANZ Oral Solution.

[a]XELJANZ 10 mg twice daily (n=905); placebo (n=234).[2]

[b]Remission was stringently defined as a total Mayo score ≤2, with no individual subscore >1 **and** a rectal bleeding subscore of 0.[1]

TNF=tumor necrosis factor; UC=ulcerative colitis.

XELJANZ® XR
(tofacitinib)
extended release • 11 mg and 22 mg tablets

Please see full Prescribing Information, including **BOXED WARNING** and Medication Guide, on last pages.

OCTAVE CLINICAL PROGRAM DESIGN[2,3]

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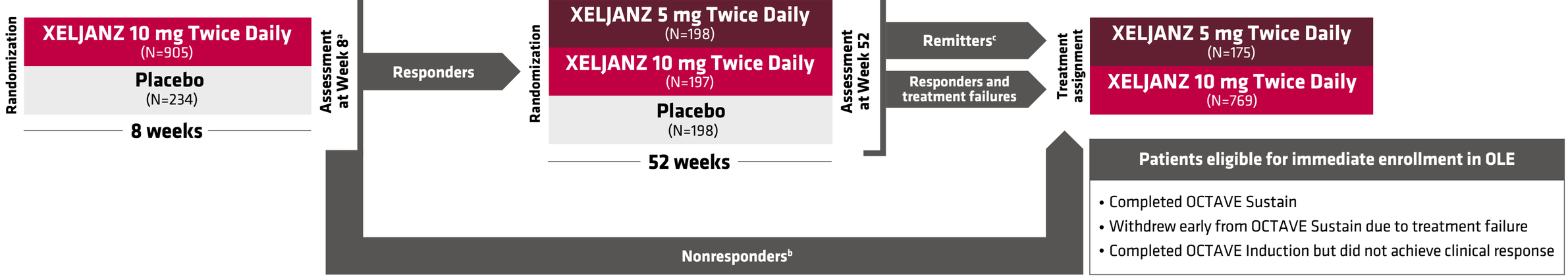

IMPORTANT SAFETY INFORMATION (cont'd)

SERIOUS INFECTIONS (cont'd)

The most common serious infections reported with XELJANZ included pneumonia, cellulitis, herpes zoster, urinary tract infection, diverticulitis, and appendicitis. Avoid use of XELJANZ 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 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. Viral reactivation including herpes virus and hepatitis B reactivation have been reported. 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, 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.

[a]The total number of patients does not include those who received XELJANZ 15 mg twice daily (n=22). **XELJANZ 15 mg twice daily is not an approved dose.**[1]

[b]Patients who completed one of the OCTAVE Induction studies (UC-I or UC-II) but did not achieve clinical response.[3]

[c]Remission was defined as Mayo score ≤2 with no individual subscore >1 **and** rectal bleeding subscore=0.[1]

[d]N values reflect the May 27, 2019, data cut.[2]

BID=twice daily.

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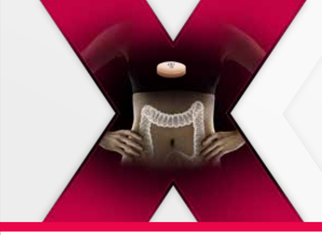

OCTAVE CLINICAL PROGRAM DESIGN (CONT'D)

XELJANZ® XR
[tofacitinib]
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The efficacy and safety of XELJANZ in UC were evaluated in the OCTAVE clinical program, which included 3 phase 3, randomized, double-blind, placebo-controlled clinical trials: OCTAVE Induction 1 (UC-I), OCTAVE Induction 2 (UC-II), and OCTAVE Sustain (UC-III), and an open-label, long-term extension study (UC-IV).[1,2]

All patients in the **O**ral **C**linical **T**rials for tof**A**citinib in ulcerati**VE** colitis (OCTAVE) clinical program were adults with a confirmed diagnosis of moderately to severely active UC for at least 4 months, which was defined as a Mayo score of 6 to 12, with a rectal bleeding subscore ≥1 and an endoscopic subscore ≥2. Patients were required to have experienced treatment failure with or intolerance to at least 1 of the following agents: oral or intravenous corticosteroids, azathioprine, 6-MP, or TNF blocker. Endoscopic results were centrally read in the induction trials and OCTAVE Sustain.

OCTAVE Induction 1 and 2[1]

In 2 identical, 8-week induction studies, 1139 patients with moderately to severely active UC (598 and 541 patients, respectively) were randomized to XELJANZ 10 mg twice daily or placebo (4:1 ratio). The primary endpoint was remission. During the induction trials, patients who were on stable doses of oral aminosalicylates and corticosteroids (prednisone daily dose up to 25 mg equivalent) were permitted to continue on their stable dosing. Concomitant immunosuppressants (immunomodulators or biological therapies) were not permitted.

OCTAVE Sustain[1]

In a 52-week maintenance study, 593 patients who had completed the induction studies and achieved clinical response were rerandomized to XELJANZ 10 mg twice daily, XELJANZ 5 mg twice daily, or placebo (1:1:1 ratio). XELJANZ 5 mg twice daily is the recommended dosage for maintenance therapy. For patients with loss of response during maintenance treatment, a dosage of 10 mg twice daily may be considered and limited to the shortest duration. The primary endpoint was remission. Sustained corticosteroid-free remission was a key secondary endpoint. Patients were permitted to use stable doses of oral aminosalicylates, but initiation of corticosteroid tapering was required upon entrance to this study for patients who were receiving corticosteroids at baseline. Concomitant immunosuppressants (immunomodulators or biological therapies) were not permitted.

Total patient population included patients with and without prior TNF blocker failure[1]

- Prior TNF blocker failure was defined in this program as inadequate response, loss of response, or intolerance to TNF blocker therapy
- Patients without prior TNF blocker failure had failed one or more conventional therapies (corticosteroid, azathioprine, 6-MP) but did not have a history of prior failure of TNF blocker therapy

IMPORTANT SAFETY INFORMATION (cont'd)

MORTALITY

Rheumatoid arthritis (RA)† patients 50 years of age and older with at least one cardiovascular (CV) risk factor treated with XELJANZ 10 mg twice a day had a higher rate of all-cause mortality, including sudden CV death, compared to those treated with XELJANZ 5 mg given twice daily or TNF blockers in a large, ongoing, postmarketing safety study. XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily is not recommended for the treatment of RA or PsA‡. For UC, use XELJANZ at the lowest effective dose and for the shortest duration needed to achieve/maintain therapeutic response.

†RA=rheumatoid arthritis. XELJANZ/XELJANZ XR 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. 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. **XELJANZ 10 mg twice daily is not approved for use in RA.**

‡PsA=psoriatic arthritis. XELJANZ/XELJANZ XR 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. **XELJANZ 10 mg twice daily is not approved for use in PsA.**

6-MP=6-mercaptopurine; TNF=tumor necrosis factor; UC=ulcerative colitis.

Please see full Prescribing Information, including **BOXED WARNING** and Medication Guide, on last pages.

FOR ALEXIS, A TNF BLOCKER NONRESPONDER, CONSIDER

XELJANZ FOR RAPID REMISSION

FOR MODERATELY TO SEVERELY ACTIVE UC

Duration of UC

- 4 years

Relevant History

- Recently hospitalized during her last flare
- Corticosteroid and TNF blocker therapy initiated during hospitalization
- Continues to experience increased stool frequency and rectal bleeding after completing TNF blocker induction therapy

Mayo Score

- Total score: 10
  - Stool frequency: 3 (5 or more stools than normal)
  - Rectal bleeding: 2 (obvious blood with stool most of the time)
  - Endoscopic findings: 2 (moderate disease [marked erythema, lack of vascular pattern, any friability, erosions])
  - Physician's Global Assessment: 3 (severe disease)

Not an actual patient.

IMPORTANT SAFETY INFORMATION (cont'd)

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 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 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. NMSCs 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.

TNF=tumor necrosis factor; UC=ulcerative colitis.

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EXPLORE XELJANZ XR/XELJANZ FOR PATIENTS WITH MODERATELY TO SEVERELY ACTIVE UC, INCLUDING TNF BLOCKER NONRESPONDERS, FOR RAPID REMISSION

XELJANZ® XR
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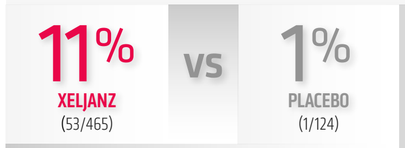
Rapidly Achieve Remission as Early as Week 8 (Primary Endpoint, OCTAVE Induction 1 and 2)[1,2]

- **18%** (88/476) of patients taking XELJANZ 10 mg twice daily achieved remission at Week 8 vs **8%** (10/122) on placebo in OCTAVE 1
- **17%** (71/429) of patients taking XELJANZ 10 mg twice daily achieved remission at Week 8 vs **4%** (4/112) on placebo in OCTAVE 2

XELJANZ induced remission even in difficult-to-treat patients with prior TNF blocker failure[2,a]



For patients with prior TNF blocker failure, more patients achieved remission on XELJANZ 10 mg twice daily vs placebo.

- Prior TNF blocker failure was defined in this program as inadequate response, loss of response, or intolerance to TNF blocker therapy[1]

Exploratory Endpoints, Pooled[a] Data From OCTAVE 1 and 2[1]

- Decreases in rectal bleeding and stool frequency Mayo subscores were observed **as early as Week 2** in patients treated with XELJANZ (exploratory endpoint)

Applicable baseline characteristics of XELJANZ patients from the OCTAVE phase 3 clinical program[2]:

- **51%** (243/476) and **52%** (222/429) of patients had failed a TNF blocker in OCTAVE Induction 1 and 2, respectively
- **74%** (350/476) and **71%** (303/429) of patients had failed corticosteroids in OCTAVE Induction 1 and 2, respectively

ORAL DOSING[1]:

Not an injection or infusion

IMPORTANT SAFETY INFORMATION (cont'd)

THROMBOSIS

Thrombosis, including pulmonary embolism, deep venous thrombosis, and arterial thrombosis, have occurred in patients treated with XELJANZ and other Janus kinase inhibitors used to treat inflammatory conditions. RA patients who were 50 years of age and older with at least one CV risk factor treated with XELJANZ 10 mg twice daily compared to XELJANZ 5 mg twice daily or TNF blockers in a large, ongoing postmarketing safety study had an observed increase in incidence of these events. Many of these events were serious and some resulted in death. Avoid XELJANZ in patients at risk. Discontinue XELJANZ and promptly evaluate patients with symptoms of thrombosis. For patients with UC, use XELJANZ at the lowest effective dose and for the shortest duration needed to achieve/maintain therapeutic response. XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily is not recommended for the treatment of RA or PsA. In a long-term extension study in UC, four cases of pulmonary embolism were reported in patients taking XELJANZ 10 mg twice daily, including one death in a patient with advanced 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 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).

[a]While these subgroup analyses were predefined, the pooled data are post hoc analyses.
TNF=tumor necrosis factor; UC=ulcerative colitis.

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MAYO RECTAL BLEEDING AND STOOL FREQUENCY SUBSCORES

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Patients used a phone-based interactive voice recording system to record daily bowel movement data and rectal bleeding[2,4]

- In the OCTAVE clinical program, patients were asked to record:
  - "Normal" number of stools per day when not having a flare (only at screening)
  - Number of bathroom visits for bowel movements per day
  - Presence of blood in stools (if any)
  - Description of blood in stools (if any)

Daily bowel movement data that were collected from the patients were used to calculate the Mayo stool frequency and rectal bleeding subscores

MAYO SUBSCORES FOR THE ASSESSMENT OF UC ACTIVITY[5]			
Stool Frequency		Rectal Bleeding	
0	Normal number of stools for this patient when disease is not active	0	No blood seen
1	1 to 2 stools more than normal	1	Streaks of blood with stool less than half the time
2	3 to 4 stools more than normal	2	Obvious blood with stool most of the time
3	5 or more stools more than normal	3	Blood alone passes

Mayo rectal bleeding and stool frequency subscores for exploratory endpoints[2]

- Mayo scores were calculated based on the data recorded over the 3 prior consecutive days

Mayo rectal bleeding and stool frequency subscores for post hoc analyses[4]

- Baseline values were derived using average data from 3 of the 5 days before first dose
- Change from baseline was determined based on diary data for each day during the first 15 days of therapy
- Reported for total patient population and TNF blocker subgroups (patients with prior TNF blocker failure and patients without prior TNF blocker failure)
- Limitations exist for post hoc analysis. See limitations on data pages

IMPORTANT SAFETY INFORMATION (cont'd)

HYPERSENSITIVITY

Angioedema and urticaria that may reflect drug hypersensitivity have been observed in patients receiving XELJANZ and some events were serious. If a serious hypersensitivity reaction occurs, promptly discontinue tofacitinib while evaluating the potential cause or causes of the reaction.

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 treatment in patients with a count less than 500 cells/mm^3. In patients who develop a confirmed absolute lymphocyte count less than 500 cells/mm^3, treatment with XELJANZ 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.

TNF=tumor necrosis factor; UC=ulcerative colitis.

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OBSERVED IMPROVEMENTS IN RECTAL BLEEDING

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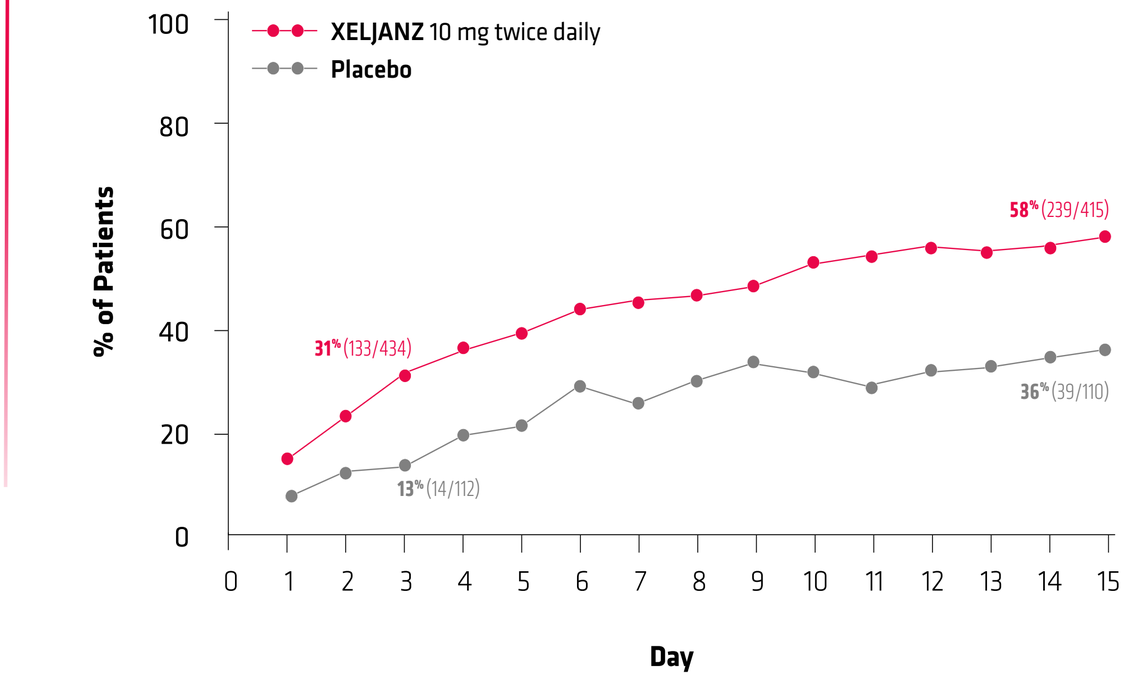
Post Hoc Analysis From OCTAVE Induction Trials

Percent of Patients With a Reduction in the Mayo Rectal Bleeding Subscore ≥1 Point in Patients With Prior TNF Blocker Failure (Pooled Data)[2,4,a]



Separation seen between groups receiving **XELJANZ 10 mg twice daily** and placebo in patients with prior TNF blocker failure[4]

- Prior TNF blocker failure was defined in this program as inadequate response, loss of response, or intolerance to TNF blocker therapy[1]
- At day 3, **32%** (266/830) of the total patient population[b] taking XELJANZ 10 mg twice daily had a reduction from baseline ≥1 point in Mayo rectal bleeding subscore vs 20% (43/214) on placebo[4]
- At day 15, **63%** (494/791) of the total patient population[b] taking XELJANZ 10 mg twice daily had a reduction from baseline of ≥1 point in Mayo rectal bleeding subscore vs 42% (87/209) on placebo[2]

Limitations of post hoc analysis
These analyses were post hoc, and data were based on daily telephone diary entries. Onset of XELJANZ efficacy in the wider population of patients with UC may differ. XELJANZ plasma concentration may not be at steady state until 24 to 48 hours after initial dosing. Therefore, these analyses should be interpreted with caution.

IMPORTANT SAFETY INFORMATION (cont'd)

LABORATORY ABNORMALITIES (cont'd)

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

[a]Proportion of patients with a reduction from baseline in the Mayo rectal bleeding subscore ≥1 point excludes patients with a baseline Mayo rectal bleeding subscore of 0.[4]
[b]Total population includes patients without prior TNF blocker failure. **XELJANZ is not indicated in patients without prior TNF blocker failure.**[1]
TNF=tumor necrosis factor.

Please see full Prescribing Information, including **BOXED WARNING** and Medication Guide, on last pages.

OBSERVED IMPROVEMENTS IN STOOL FREQUENCY

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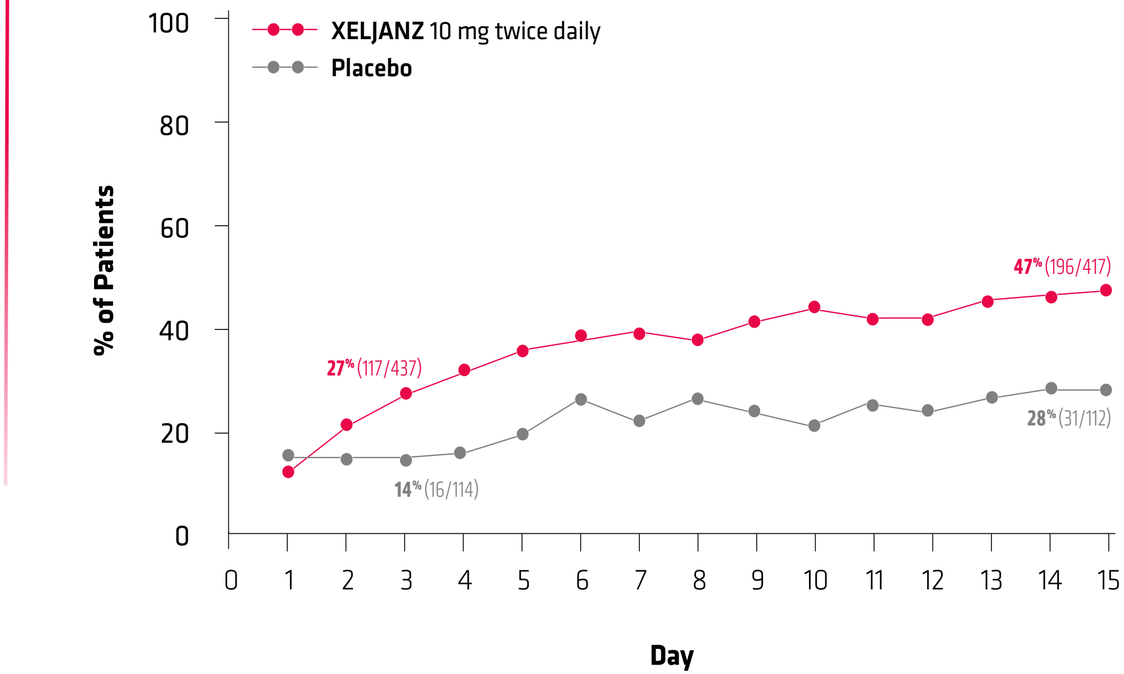
Post Hoc Analysis From OCTAVE Induction Trials

Percent of Patients With a Reduction in the Mayo Stool Frequency Subscore ≥1 Point in Patients With Prior TNF Blocker Failure (Pooled Data)[2,4,a]



Separation seen between groups receiving **XELJANZ 10 mg twice daily** and placebo in patients with prior TNF blocker failure[4]

- Prior TNF blocker failure was defined in this program as inadequate response, loss of response, or intolerance to TNF blocker therapy[1]
- At day 3, **29%** (241/837) of the total patient population[b] taking XELJANZ 10 mg twice daily had a reduction from baseline ≥1 point in Mayo stool frequency subscore vs 18% (39/218) on placebo[4]
- At day 15, **54%** (428/796) of the total patient population[b] taking XELJANZ 10 mg twice daily had a reduction from baseline of ≥1 point in Mayo stool frequency subscore vs 32% (68/212) on placebo[2]

Limitations of post hoc analysis
These analyses were post hoc, and data were based on daily telephone diary entries. Onset of XELJANZ efficacy in the wider population of patients with UC may differ. XELJANZ plasma concentration may not be at steady state until 24 to 48 hours after initial dosing. Therefore, these analyses should be interpreted with caution.

IMPORTANT SAFETY INFORMATION (cont'd)

LABORATORY ABNORMALITIES (cont'd)

Anemia: Avoid initiation of XELJANZ treatment in patients with a hemoglobin level less than 9 g/dL. Treatment with XELJANZ 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 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.

[a]Proportion of patients with a reduction from baseline in the Mayo stool frequency subscore ≥1 point excludes patients with a baseline Mayo rectal bleeding subscore of 0.[4]
[b]Total population includes patients without prior TNF blocker failure. **XELJANZ is not indicated in patients without prior TNF blocker failure.**[1]
TNF=tumor necrosis factor.

Please see full Prescribing Information, including **BOXED WARNING** and Medication Guide, on last pages.

POWERFUL EFFICACY AT WEEK 52

XELJANZ® XR (tofacitinib)
extended release • 11 mg and 22 mg tablets

Significantly More Patients Taking XELJANZ Achieved Remission (Primary Endpoint) at Week 52 vs Placebo[1,2]

- **41%** (80/197) of patients on XELJANZ 10 mg twice daily and **34%** (68/198) of patients on XELJANZ 5 mg twice daily vs **11%** (22/198) on placebo; *P*<0.0001[1,2,a]
- Remission was stringently defined as a total Mayo score ≤2, with no individual subscore >1 **and** a rectal bleeding subscore of 0[1]

Remission at Week 52 even in difficult-to-treat patients with prior TNF blocker failure[1,2]

More patients taking **XELJANZ 10 mg** twice daily and **XELJANZ 5 mg** twice daily who had prior TNF blocker failure achieved remission vs placebo.

- Prior TNF blocker failure was defined in this program as inadequate response, loss of response, or intolerance to TNF blocker therapy[1]
- **XELJANZ 5 mg twice daily is the recommended dosage for maintenance therapy. For patients with loss of response during maintenance treatment, a dosage of 10 mg twice daily may be considered and limited to the shortest duration[1]**

IMPORTANT SAFETY INFORMATION (cont'd)

LABORATORY ABNORMALITIES (cont'd)

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 therapy.

VACCINATIONS

Avoid use of live vaccines concurrently with XELJANZ. 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 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.

[a]Total population includes patients without prior TNF blocker failure. **XELJANZ is not indicated in patients without prior TNF blocker failure**.[1]

Please see full Prescribing Information, including **BOXED WARNING** and Medication Guide, on last pages.

XELJANZ XR/XELJANZ

POWERFUL SUSTAINED EFFICACY

XELJANZ® XR
(tofacitinib)
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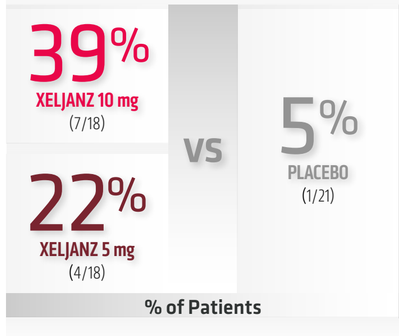
Significantly More Patients Taking XELJANZ Achieved Sustained Corticosteroid-free Remission (Key Secondary Endpoint) vs Placebo[1,2]

- **47%** (26/55) of patients on XELJANZ 10 mg twice daily and **35%** (23/65) of patients on XELJANZ 5 mg twice daily vs **5%** (3/59) on placebo; *P*<0.0001[a]
- Sustained corticosteroid-free remission was defined as remission (a total Mayo score ≤2, with no individual subscore >1 **and** a rectal bleeding subscore of 0) and not taking corticosteroids for at least 4 weeks prior to the visit at both Week 24 and Week 52 among patients in remission at baseline[1]

Sustained corticosteroid-free remission at Week 52 even in difficult-to-treat patients with prior TNF blocker failure[1,2]



More patients taking **XELJANZ 10 mg** twice daily and **XELJANZ 5 mg** twice daily who had prior TNF blocker failure achieved sustained corticosteroid-free remission at Week 52 vs placebo.

- Prior TNF blocker failure was defined in this program as inadequate response, loss of response, or intolerance to TNF blocker therapy[1]
- **XELJANZ 5 mg twice daily is the recommended dosage for maintenance therapy. For patients with loss of response during maintenance treatment, a dosage of 10 mg twice daily may be considered and limited to the shortest duration**[1]

IMPORTANT SAFETY INFORMATION (cont'd)

HEPATIC and RENAL IMPAIRMENT

Use of XELJANZ 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.

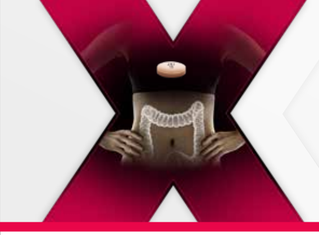
ADVERSE REACTIONS

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 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 PsA treated with XELJANZ was consistent with the safety profile observed in RA patients.

[a]Total population includes patients without prior TNF blocker failure. **XELJANZ is not indicated in patients without prior TNF blocker failure**.[1]

TNF=tumor necrosis factor.

Please see full Prescribing Information, including **BOXED WARNING** and Medication Guide, on last pages.



IMPORTANT SAFETY INFORMATION (CONT'D)

XELJANZ® XR
(tofacitinib)
extended release • 11 mg and 22 mg tablets

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS (cont'd)
Adverse reactions reported in ≥5% of patients treated with either 5 mg or 10 mg twice daily of XELJANZ and ≥1% greater than reported in patients receiving placebo in either the induction or maintenance clinical trials for UC 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 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.

SERIOUS INFECTIONS
Patients treated with XELJANZ* 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 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 use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ 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 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 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. Viral reactivation including herpes virus and hepatitis B reactivation have been reported. 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, 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.

*Unless otherwise stated, "XELJANZ" in the Important Safety Information refers to XELJANZ, XELJANZ XR, and XELJANZ Oral Solution.

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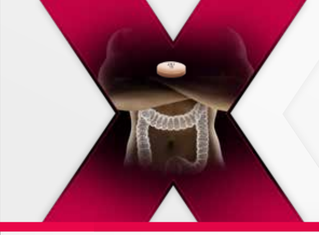

XELJANZ/XELJANZ XR A MARK OF EFFICACY

XELJANZ® XR
(tofacitinib)
extended release • 11 mg and 22 mg tablets

ORAL DOSING[1]

Not an injection, not an infusion

- XELJANZ is available in 5 mg or 10 mg twice-daily doses
- XELJANZ XR is available in 11 mg or 22 mg once-daily doses

Changes between XELJANZ and XELJANZ XR should be made under the supervision of the healthcare provider.

RAPID REMISSION[1,2]

Significantly more patients taking XELJANZ 10 mg twice daily vs placebo achieved remission[a] as early as Week 8[b]

- OCTAVE 1: **18%** vs **8%** of patients, respectively; *P*<0.01 (primary endpoint)
- OCTAVE 2: **17%** vs **4%** of patients, respectively; *P*<0.001 (primary endpoint)

SYMPTOMATIC IMPROVEMENTS[1,4]

Reductions in rectal bleeding and stool frequency

- Decreases in rectal bleeding and stool frequency Mayo subscores were observed **as early as Week 2** in patients treated with XELJANZ (exploratory endpoint)
- **In a post hoc analysis**, reductions in rectal bleeding and stool frequency subscores ≥1 point were evaluated during the **first 15 days of treatment**

SUSTAINED EFFICACY[1,2]

Significantly more patients taking XELJANZ achieved remission[a] and sustained corticosteroid-free remission[c] vs placebo in a 52-week study[d]

- **Remission[a,e]: 41%** of patients on XELJANZ 10 mg twice daily and **34%** on XELJANZ 5 mg twice daily vs **11%** on placebo; *P*<0.0001 (primary endpoint)
- **Sustained corticosteroid-free remission[c,f]: 47%** of patients on XELJANZ 10 mg twice daily and **35%** on XELJANZ 5 mg twice daily vs **5%** on placebo; *P*<0.0001 (key secondary endpoint)

AFTER AN INADEQUATE RESPONSE OR INTOLERANCE TO A TNF BLOCKER, **START WITH XELJANZ/XELJANZ XR** FOR MODERATELY TO SEVERELY ACTIVE UC

Limitations of post hoc analysis

These analyses were post hoc, and data were based on daily telephone diary entries. Onset of XELJANZ efficacy in the wider population of patients with UC may differ. XELJANZ plasma concentration may not be at steady state until 24 to 48 hours after initial dosing. Therefore, these analyses should be interpreted with caution.

IMPORTANT SAFETY INFORMATION (cont'd)

MORTALITY

Rheumatoid arthritis (RA)† patients 50 years of age and older with at least one cardiovascular (CV) risk factor treated with XELJANZ 10 mg twice a day had a higher rate of all-cause mortality, including sudden CV death, compared to those treated with XELJANZ 5 mg given twice daily or TNF blockers in a large, ongoing, postmarketing safety study. XELJANZ 10 mg twice daily or XELJANZ XR 22 mg once daily is not recommended for the treatment of RA or PsA‡. For UC, use XELJANZ at the lowest effective dose and for the shortest duration needed to achieve/maintain therapeutic response.

Please see full Prescribing Information, including **BOXED WARNING** and Medication Guide, on last pages.

[a]Remission was stringently defined as a total Mayo score ≤2, with no individual subscore >1 **and** a rectal bleeding subscore of 0.1.[1]
[b]XELJANZ 10 mg twice daily (n=905); placebo (n=234).[2]
[c]Sustained corticosteroid-free remission was defined as remission (a total Mayo score ≤2, with no individual subscore >1 **and** a rectal bleeding subscore of 0) and not taking corticosteroids for at least 4 weeks prior to the visit at both Week 24 and Week 52 among patients in remission at baseline.[1]
[d]Use the lowest effective dose to maintain response.[1]
[e]XELJANZ 10 mg twice daily (n=197); XELJANZ 5 mg twice daily (n=198); placebo (n=198).[1]
[f]XELJANZ 10 mg twice daily (n=55); XELJANZ 5 mg twice daily (n=59).[1]

TNF=tumor necrosis factor; UC=ulcerative colitis.

References: 1. XELJANZ [prescribing information]. New York, NY: Pfizer Inc., October 2020. **2.** Data on file. Pfizer Inc., New York, NY. **3.** Sandborn WJ, Su C, Sands BE, et al; for the OCTAVE Induction 1, OCTAVE Induction 2, and OCTAVE Sustain Investigators. Tofacitinib as induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 2017;376(18):1723-1736, 1-77. doi:10.1056/NEJMoa1606910 **4.** Hanauer S, Panaccione R, Danese S, et al. Tofacitinib induction therapy reduces symptoms within 3 days for patients with ulcerative colitis. *Clin Gastroenterol Hepatol*. 2019;17(1):139-147. **5.** Dhanda AD, Creed TJ, Greenwood R, et al. Can endoscopy be avoided in the assessment of ulcerative colitis in clinical trials? *Inflamm Bowel Dis.* 2012;18(11):2056-2062. doi:10.1002/ibd.22879