Oral JAK Inhibitors (Xeljanz®/XR, Olumiant®, Rinvoq®) – Safety update

- On September 1, 2021, the FDA announced that after review of a large randomized safety clinical trial, there is an increased risk of serious heart-related events such as heart attack or stroke, cancer, blood clots, and death with Xeljanz, Xeljanz XR (tofacitinib). The FDA believes the other Janus kinase (JAK) inhibitors, Olumiant (baricitinib) and Rinvoq (upadacitinib), have similar risks because they share the same mechanism of action as Xeljanz.
    - The FDA is requiring revisions to the Boxed warning, several sections of the prescribing information and the patient medication guide to reflect these risks.
- Xeljanz, Xeljanz XR, Olumiant and Rinvoq are indicated for the treatment of arthritis; and Xeljanz/Xeljanz XR are also indicated for other inflammatory conditions.
- Xeljanz, Xeljanz XR, Olumiant, and Rinvoq currently carry a boxed warning for serious infections, mortality, malignancy and thrombosis. FDA is revising this boxed warning to include more information about risks of serious events and recommendations for considering benefits and risks for the individual patient.
- The FDA required Pfizer to conduct a safety clinical trial in patients with RA who were 50 years of age or older and had at least one additional cardiovascular risk factor and were taking methotrexate to evaluate the risk of serious heart-related events, cancer, and infections. The trial studied two doses of Xeljanz (5 mg or 10 mg twice daily) vs. a TNF inhibitor. The median on-study follow-up time was 4 years.
    - The data showed evidence of a dose-dependent increased risk for major adverse cardiovascular events, all-cause mortality, and thrombosis at both doses of Xeljanz vs. treatment with TNF blockers.
    - Additionally, the data showed evidence of a non-dose-dependent increased risk for malignancy excluding nonmelanoma skin cancer at both doses of Xeljanz vs. TNF blockers.
    - A prior warning issued in July 2019 based upon earlier results from this trial, reported an increased risk of blood clots and death only seen at the higher dose.
- Two other JAK inhibitors, Jakafi® (ruxolitinib) and Inrebic® (fedratinib), are not indicated for the treatment of arthritis and other inflammatory conditions and so are not a part of the updates being required to the prescribing information for Xeljanz, Xeljanz XR, Olumiant, and Rinvoq.
- Health care professionals should consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Xeljanz/Xeljanz XR, Olumiant, or Rinvoq. This is particularly the case in patients who are current or past smokers, those with other cardiovascular risk factors, those who develop a malignancy, and those with a known malignancy other than a successfully treated nonmelanoma skin cancer.
    - These medicines should be reserved for patients who have had an inadequate response or intolerance to one or more TNF blockers.