PDL NEW DRUG REVIEW

Proprietary Name: Jakafi®
Common Name: ruxolitinib
PDL Category: Antineoplastics- Protein-Tyrosine Kinase Inhibitor

Summary

Indications and Usage: Treatment of those with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia, vera myelofibrosis, and post-essential thrombocythemia myelofibrosis. This is a pregnancy category C medication. The safety and efficacy of use in children under the age of 18 have not been established.

Dosage Forms: Tablets: 5mg, 10mg, 15mg, 20mg, and 25mg.

Drug Interactions: Ruxolitinib is predominantly metabolized by CYP3A4. Jakafi® dose reductions are recommended when used concomitantly with strong CYP3A4 inhibitors, such as ketoconazole. Patients should be closely monitored. Dose adjustments are not required for Jakafi® when used concomitantly with mild or moderate CYP inhibitors. While dose adjustments are not required when Jakafi® is used concomitantly with a CYP3A4 inducer, patients should be monitored closely and dose titrations should be based on safety/efficacy.

Recommended Dosage: The starting dose is based upon platelet count, at a dose of 20mg BID if platelet count (PC) is >200X10^9/L or 15mg BID if PC is 100X10^9/L to 200X10^9/L. A complete blood count (CBC) and PC should be done before initiating therapy, every 2-4 weeks until dose is stabilized, and then as clinically indicated. Therapy should be interrupted if PC is <50X10^9/L. Specific dose reductions and titrations are further outlined in the package insert. Dose reductions are recommended when used in combination with CYP3A4 inhibitors, as discussed above. Dose reductions are recommended for those with end stage renal disease and for those with moderate or severe renal impairment who have a platelet count between 100X10^9/L and 150X10^9/L. Dose reductions are also recommended in those with any degree of hepatic impairment and who have a platelet count between 100X10^9/L and 150X10^9/L.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions = reported % incidence for drug minus reported % incidence for placebo.* The most common adverse events reported with Jakafi® included bruising (8.6%), dizziness (10.8%), headache (9.5%), urinary tract infections (3.7%), weight gain (5.8%), flatulence (4.5%), and herpes zoster (1.2%).

Jakafi® treatment can cause hematologic adverse events, including thrombocytopenia, anemia, and neutropenia. Therefore, a CBC should be performed before starting therapy. Blood transfusions may be required in those who develop anemia, and dose modifications should be considered.

Contraindications: There are currently no contraindications listed in the prescribing information.

Manufacturer: Incyte Corporation

Analysis: Ruxolitinib, the active ingredient of Jakafi®, is the first and only agent approved for the use of myelofibrosis, as well as being the first in a new class of drugs called the JAK inhibitors. Ruxolitinib is a kinase inhibitor that inhibits Janus Associated Kinases (JAKs) JAK1 and JAK2. These arbitrate the signaling of certain cytokines and growth factors important for hematopoiesis and immune function. Thus, it is effective in myelofibrosis, which is a neoplasm known to be associated with dysregulated JAK1 and JAK2 signaling.

There were 2 randomized, placebo-controlled studies (Study 1 N=309; Study 2 N=219) to assess the safety and efficacy of ruxolitinib (Jakafi®) in patients with myelofibrosis. The primary endpoint for Study 1 was the proportion of subjects achieving ≥35% reduction from baseline in spleen volume at week 24, as measured by MRI or CT. The primary endpoint in Study 2 was the proportion of subjects achieving ≥35% reduction from baseline in spleen volume at week 48, as measured by MRI or CT. A significantly greater number achieved ≥35% reduction from baseline in spleen volume in both studies as compared with placebo (Study 1: 41.9% vs 0.7%; Study 2: 28.5% vs 0%; for both comparisons $p<0.0001$, which translates into a Number Needed to Treat (NNT) of 3 and 4 respectively.) Furthermore, 45.9% of those in the Jakafi® group (in study 1) had a ≥50% reduction in total symptom score by week 24 vs 5.3% of the placebo group, which was significantly more ($p<0.0001$), corresponding to a NNT of 3.

It is recommended that Jakafi® be added to the Recommended Drug List as a recommended drug, as it is the only drug FDA approved for the treatment of myelofibrosis.

PDL Placement:
- ☐ **Preferred**
- ☐ **Non-Preferred**
- ☒ **Recommended**

References

[1] Jakafi [package insert]. Wilmington, DE: Incyte Corporation; 2011.

[2] Incyte Corporation. Jakafi. Website: http://www.incyte.com/jakafi. Accessed June 5th, 2012.