Accelerated Approvals Reconsidered

None

Changes in Dosing/Administration

None

Changes in Labeled Indications

Xalkori® (*crizotinib*) – Pfizer received approval to market its kinase inhibitor for the treatment of adult and pediatric patients with ALK-positive unresectable, recurrent, or refractory inflammatory myofibroblastic tumor, a rare soft-tissue malignancy. The approval was based on responses being achieved in 12 of the 14 pediatric patients and in 5 of the 7 adults enrolled in two small single arm trials. Dosing of Xalkori® for the new indication is the same as that for its previously approved uses in treating ALK-positive systemic anaplastic large cell lymphoma and ALK- or ROS1-positive metastatic non-small cell lung cancer.

New Biosimilars and Generics

Full approvals were granted for:

- *Bortezomib* from Accord Healthcare, Dr. Reddy's, Hospira Inc., Intas Pharma USA, Jiangsu Hansoh Pharma, Kindos, Maia Pharm Inc., MSN, and Sandoz;
- *Paclitaxel* from HBT Labs Inc.; and
- *Pemetrexed* from Accord Healthcare Inc.

Tentative Approvals granted for:

- *Bendamustine hydrochloride* from Celerity Pharms;
- *Dasatinib* from Teva;
- *Neratinib maleate* from Sandoz;
- *Paclitaxel* from Teva;

- *Palbociclib* from Eugia Pharmaceutical; and
- *Plerixafor* from AuroMedics

New Data

Bavencio® (*avelumab*) – More mature survival data from the pivotal trial that served as the basis for initial approval for use of the PD-L1 inhibitor in urothelial carcinoma were added to its prescribing information. The updated results from the study—in which 700 patients with unresectable, locally advanced, or metastatic urothelial cancer were randomized to receive either Bavencio® plus best supportive care (BSC) or BSC alone—still support the conclusion that Bavencio® offers an advantage in both median survival time (23.8 versus 15.0 months for treatment and control groups, respectively) and in the probability of survival (Hazard ratio of 0.76 associated with being in treatment group).

Cabometyx® (*cabozantinib*) and **Opdivo®** (*nivolumab*) – Updated data on overall survival from CHECKMATE 9ER--a trial comparing Exelixis' kinase inhibitor in combination with BMS's immuno-oncology agent against *sunitinib* alone as first-line treatment for advanced renal cell carcinoma—were added to the prescribing information of both products. The initial advantage in overall survival (which served as the basis for initial approval) was maintained in the updated data, with patients in the *cabozantinib* + *nivolumab* arm having a median survival of 37.7 months compared to 34.3 months in the *sunitinib* arm. The overall risk reduction associated with the combination therapy was 30 percent. However, in a preliminary analysis, that reduction was shown to be strongest among patients with "poor" or "intermediate/poor" risk scores and did not achieve significance among patients with "favorable" or "intermediate" risk scores (using the International Metastatic Renal Cell Carcinoma Database Consortium or IMDC score).

Cotellic® (*cobimetinib*) – A paragraph on use in pediatric patients was added to the prescribing information for Genentech's kinase inhibitor. The new language states that "(t)he safety and effectiveness of *cobimetinib* were assessed, but not established, in a study in 55 pediatric patients aged 2 to 17 years with solid tumors" and that "(e)xposure in pediatric patients who received *cobimetinib* at the maximum tolerated dosage were lower than those previously observed in adults who received the approved recommended dosage."

New Molecular Entities*

None

Safety-Related Changes

Gazyva® (*obinutuzumab*) – Warnings regarding "*disseminated intravascular coagulation (DIC)*" were added (in newly created subsection 5.9) to the prescribing information for Genentech's CD20-directed cytolytic antibody. The label now warns that both fatal and severe cases of DIC have occurred in chronic lymphocytic leukemia or follicular lymphoma patients treated with Gazyva®,

that the majority of cases occurred with the first infusion, and that most of those cases had spontaneous resolution (usually by Day 8). A new statement in the Warnings and Precautions Highlights encourages clinicians to "(e)valuate cause and monitor for bleeding, thrombosis, and need for supportive care" whenever DIC is encountered or suspected.

Reblozyl® (*luspatercept-aamt*) – A new subsection (5.3) that focuses on the risks of *extramedullary hematopoietic (EMH) masses* was added to the prescribing information for Celgene's growth factor. The new content includes: the rates of occurrence of *EMH masses in beta thalassemia* patients treated with Reblozyl® (3.2 percent); possible risk factors for *EMH masses* (history of masses, splenectomy, splenomegaly, hepatomegaly, or low baseline hemoglobin); and recommendations to discontinue treatment in case of serious complications due to *EMH masses*, as well as to avoid use in patients who have previously required treatment to control the growth of *EMH masses*.

Sarclisa® (*isatuximab-irfc*) – A recommendation to "(i)nitiate antiviral prophylaxis for herpes zoster reactivation based on standard guidelines" was added to the prescribing information for Sanofi's *multiple myeloma* drug.

Turalio® (*pexidartinib*) – Now that a sufficient time since initial approval (August 2019) has elapsed, a section on adverse events observed during the post-marketing period was added to the prescribing information for Daiichi Sankyo's kinase inhibitor. The new section (6.2) includes the single adverse reaction of "Investigations: blood creatine phosphokinase increased."

Other Changes

Rozlytrek® (*entrectinib*) – Links to FDA-approved companion diagnostics have been incorporated into the prescribing information for Genentech's kinase inhibitor in both Section 1 (Indications and Usage) and Section 2 (Dosage and Administration).

**Only five approved to date, putting this year behind recent years (all of which had 13-20 approvals).*