Accelerated Approvals Reconsidered

None

Changes in Dosing/Administration

None

Changes in Labeled Indications

Imfinzi® (*durvalumab*) – AstraZeneca's PD-L1 inhibitor was newly approved for use, in combination with gemcitabine and cisplatin, as treatment for adult patients with locally advanced or metastatic biliary tract cancer (BTC). The expansion beyond lung cancer—where the IO agent had already been approved for both unresectable non-small cell and extensive small cell disease—was supported by data from a large (n=685) trial that enrolled treatment-naïve BTC patients as well as patients who had a recurrence of their BTC more than 6 months after surgery and/or completion of adjuvant therapy. Patients were randomized to receive either Imfinzi® or placebo, each in combination with gemcitabine and cisplatin. Overall survival rates were 42 and 34 percent for the Imfinzi® and placebo groups, respectively; median survival was also slightly longer in the Imfinzi® group (12.8 versus 11.5 months), as was the overall response rate (27 versus 19 percent).

Zejula (*niraparib*) – Citing evidence from "two independent randomized clinical trials" that (non-GSK) PARP inhibitors have "potential detrimental effect on overall survival" when used in heavily pretreated BRCA mutant ovarian cancer", GSK notified healthcare professionals in a Sept 14 letter that it was voluntarily withdrawing use of Zejula as 4th line therapy for this population from the approved indications in its prescribing information. Initial approval had been granted in 2019 based on a 28 percent response rate and an 8-month median duration of response observed in a small (N=98) single arm study. Zejula retains its approvals for use as maintenance therapy for patients with either advanced or recurrent disease who are in complete or partial response to platinum-based chemotherapy.

New Biosimilars and Generics

Full approvals were granted for:

- *Lenalidomide* from Zydus (5, 10, 15, and 25 mg capsules); and
- *Lenalidomide* from CIPLA

Tentative Approvals granted for:

- *Gefitinib* from Apotex*;*
- *Lenalidomide* from Zydus (2.5 and 20 mg capsules); and
- *Mitomycin from Hong Kong*

New Biosimilars:

- *Stimufend® (pegfilgrastim)* from Fresenius Kabi; and
- *Vegzelma® (bevacizumab)* from Celltrion

New Data

Halaven® (*eribulin mesylate*) – In response to a late-2021 request from FDA, Eisai incorporated results from three open-label clinical studies on the safety and effectiveness of use in pediatric populations into the prescribing information for the microtubule inhibitor (in Section 8, Use in Specific Populations, Subsection 8.4, Pediatric Use). While no new safety signals were observed for the 77 patients with relapsed or refractory solid tumors and lymphomas who were enrolled in those studies, the evidence remains insufficient to reach any conclusions regarding the safety or effectiveness of Halaven® use in pediatric populations.

Inlyta® (*axitinib*) – Updated data on overall survival (OS) of patients enrolled in the pivotal trial supporting first-line use of Pfizer's kinase inhibitor in combination with an IO agent (either Keytruda or Bavencio) to treat advanced renal cell carcinoma were added to Table 11 in the prescribing information. The new data show that OS of patients randomized to receive the Inlyta® + IO agent regimen continued to be superior to that of patients treated with *sunitinib* (Hazard Ratio of 0.73 with 95 percent CI of 0.60, 0.88). However, as might be expected with the substantially longer follow-up period, the survival differences were somewhat dampened and the newly reported median survival times of 45.1 and 40.1 months for the Inlyta and *sunitinib* groups, respectively, did not achieve statistical significance.

New Molecular Entities

Lytgobi® (*futibatinib*) – FDA granted accelerated approval for use of Taiho Oncology's novel FGFR inhibitor as treatment for adult patients with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements. The approval was supported by an observed 42 percent

response rate in a single arm trial (n=103). The median time to response in that study was 2.5 months and the median duration of response was 9.7 months (95 percent CI of 7.6 – 17.1 months). Approximately 10-15 percent of the estimated 8,000 cholangiocarcinomas detected annually in the US present with the actionable FGFR2 gene fusion.

Rolvedon (*eflapegrastim-xnst*) – Almost four years after it first applied for a license to market its novel anti-neutropenic agent, Spectrum Pharmaceuticals learned that Rolvedon had been approved for use to "decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non- myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia." The approval, partially delayed by FDA's limited plant inspection capabilities during the COVID pandemic, was for a drug that has a portion of an immunoglobulin G (IgG) molecule affixed to a recombinant human granulocyte colony-stimulating factor (*pegfilgrastim*) analog. (Data from animal models suggest that the Ig G fragment—known as Fc fragment—might increase uptake by the bone marrow and reduce clearance.) Evidence in support of approval came from two randomized "non-inferiority" trials (total n=643) that enrolled early-stage breast cancer patients and randomized them to receive either Rolvedon or *pegfilgrastim* in combination with their chemotherapy. The trials were designed to determine whether Rolvedon was *at least as effective as pegfilgrastim* at limiting the duration of severe neutropenia (DSN) and showed that to be true. In one trial, 16 percent of patients in the Rolvedon arm and 24 percent treated with *pegfilgrastim* developed severe neutropenia and the mean DSN was 0.20 ± 0.5 days and 0.35 days± 0.7 days, respectively, for the two arms. No significant difference in outcomes was observed in the other trial as well where the median DSN for each arm was 0.31 ± 0.70 days (Rolvedon) and 0.39 ± 1.0 days (*pegfilgrastim*). No differences in the safety of the two agents were observed in either study.

Safety-Related Changes

Avastin® (*bevacizumab*) – *Anaphylactic/anaphylactoid-type reactions* were added to the possible infusion-related reactions listed in section 5.9 (Warnings and Precautions) and an explicit statement recommending "Use sterile needle and syringe to prepare Avastin" was added in section 2.10 (Dosage and Administration).

Tagrisso® (*osimertinib*) – A warning regarding the possibility of *aplastic anemia* associated with use was added to the prescribing information for AZ's targeted NSCLC therapy. The warning (added to sections 2.4 Dosage Modifications, 5.7 Warnings and Precautions, 6.2 Postmarketing Experience, and 17 Patient Counseling Information) recommends that clinicians withhold the kinase inhibitor if aplastic anemia is suspected and discontinue it if the condition is confirmed.

Vidaza® (*azacitidine*) – *Pericardial effusion and pericarditis* were added to the bulleted list of adverse events observed during the post-marketing period for Celgene's MDS therapy.

Vyxeos® (*daunorubicin and cytarabine*) – Recommendations for use of Jazz Pharmaceuticals' novel drug combination in patients with renal impairment (in section 8.6 of its prescribing information) were updated to now state that dosage modification is not necessary even for patients with severe

impairment. In addition, *infusion-related reactions* were listed in a new section on adverse events observed during the post-marketing period.

Other Changes

Inlyta® (axitinib) – A number of formatting changes were made in the dose modification guidelines for Pfizer's renal cell carcinoma treatment: a) the recommendations for general dosage increases or decreases were placed in tabular format; b) new tables were created to show recommended dosage modifications for specific adverse reactions encountered with use of Inlyta® either as a single agent or in combination with either *avelumab* or *pembrolizumab*; c) *diarrhea* was added to the adverse events potentially requiring dose modification; and d) new subsections were created to clarify the modifications recommended to avoid drug-drug interactions and for treating patients with hepatic impairment (subsections 2.3 and 2.4,respectively).