HEM/ONC News

By Devon Schuyler

Recombinant Factor IX Approved for Use in Adults and Children With Hemophilia B

The US Food and Drug Administration (FDA) approved the recombinant coagulation factor IX agent nonacog beta pegol (N9-GP; Rebinyn, Novo Nordisk) on May 31 for use in adults and children with hemophilia B. The product is indicated for on-demand treatment and control of episodes of bleeding and for perioperative management of bleeding in patients with hemophilia B. It is not intended for routine prophylaxis of bleeding or for induction of immune tolerance.

N9-GP is given via intravenous infusion, which may be done at a hemophilia treatment center, at a health care provider's office, or in the home after training of the patient or a family member.

Approval of N9-GP was based on results in 115 patients from 4 clinical trials. In an efficacy evaluation that included 597 episodes of bleeding in 105 patients who had been previously treated with factor IX products, treatment with N9-GP was successful in 93.2% of cases.

Common side effects of N9-GP include itching and infusion site reactions such as swelling, pain, rash, and redness. Other possible side effects include allergic reactions, blood clots, and the development of factor IX inhibitors.

Novo Nordisk expects to launch N9-GP in the first half of 2018.

Pembrolizumab Receives Approval for Use in Tumors With Specific Biomarkers

Pembrolizumab (Keytruda, Merck) received accelerated FDA approval on May 23 for use in adult and pediatric patients with unresectable or metastatic solid tumors that have microsatellite instability (MSI) or mismatch repair deficiency (dMMR). This is the first time the FDA has approved a cancer treatment based on a specific biomarker rather than on the location of the primary tumor.

The agent is approved for use in patients who have solid tumors that have progressed despite treatment and who have no satisfactory alternative treatment options, and in patients with colorectal cancer that has progressed despite treatment with certain chemotherapy drugs.

The approval was based on results in 149 patients from 5 single-arm clinical trials who received pembrolizumab for solid tumors with MSI or dMMR—comprising a total of 15 cancer types. A complete or partial response occurred in 39.6% of patients, and the response lasted for at least 6 months in 78% of cases.

Common side effects of pembrolizumab include fatigue, pruritus, diarrhea, decreased appetite, rash, pyrexia, cough, dyspnea, musculoskeletal pain, constipation, and nausea. Pembrolizumab also can cause immune-mediated side effects, including pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis.

MSI and dMMR, which indicate an impaired ability of tumor cells to repair DNA, are most commonly found in colorectal, endometrial, and gastrointestinal cancers. They also may be found in other cancers, including those of the breast, prostate, bladder, and thyroid gland. MSI or dMMR occurs in the tumors of approximately 5% of patients with metastatic colorectal cancer.

Pembrolizumab, which works by targeting the programmed death 1 (PD-1)/programmed death ligand 1 (PD-L1) pathway, previously received approval for the treatment of certain patients with metastatic melanoma, metastatic non–small cell lung cancer, recurrent or metastatic head and neck cancer, refractory classic Hodgkin lymphoma, or urothelial carcinoma.

Additional studies will examine the clinical benefits of pembrolizumab in patients with the relevant biomarkers.

Durvalumab Approved for Use in Urothelial Carcinoma

On May 1, the FDA granted accelerated approval of durvalumab (Imfinzi, AstraZeneca) for the treatment of patients with locally advanced or metastatic urothelial carcinoma. Patients are eligible for treatment if they have disease progression during or after platinum-containing chemotherapy. Durvalumab is an inhibitor of PD-L1.

Approval of durvalumab was based on the results of a single-arm trial of 182 patients with locally advanced or metastatic urothelial carcinoma whose disease had progressed after platinum-containing chemotherapy. The confirmed objective rate of response to durvalumab treatment was 17.0% (95% CI, 11.9%-23.3%) overall, and 26.3% (95% CI, 17.8%-36.4%) among the 95 patients with a high PD-L1 score.

The most common adverse reactions were fatigue, musculoskeletal pain, constipation, decreased appetite, nausea, peripheral edema, and urinary tract infection. Infection and immune-related adverse events such as pneumonitis, hepatitis, colitis, thyroid disease, adrenal insufficiency, and diabetes also occurred.

The FDA also approved the Ventana PD-L1 (SP263) Assay as a complementary diagnostic for the assessment of PD-L1 in urothelial carcinoma tissue.

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FDA Approves Midostaurin for Use in Acute Myeloid Leukemia

The FDA approved the use of midostaurin (Rydapt, Novartis) on April 28 in combination with chemotherapy for the treatment of adults with newly diagnosed acute myeloid leukemia (AML) who have the *FLT3* mutation.

The drug is approved for use with a companion diagnostic, the LeukoStrat CDx FLT3 Mutation Assay from Invivoscribe, which is used to detect the *FLT3* mutation in patients with AML. Midostaurin is a multikinase inhibitor that is the first targeted therapy approved for patients with AML.

Midostaurin was approved on the basis of a randomized trial of 717 patients with *FLT3*-mutated disease who had not been treated previously for AML. Survival was longer for patients who received midostaurin plus chemotherapy than for those who received chemotherapy alone, although the researchers were unable to reliably calculate a specific median survival rate. Event-free survival also was longer for patients who received midostaurin plus chemotherapy (median, 8.2 months) than for those who received chemotherapy alone (median, 3.0 months).

Common side effects of midostaurin in patients with AML include febrile neutropenia, nausea, mucositis, vomiting, headache, petechiae, musculoskeletal pain, epistaxis, device-related infection, hyperglycemia, and upper respiratory tract infection. Patients who experience pulmonary toxicity should stop using midostaurin.

The agent received simultaneous approval for adults with aggressive systemic mastocytosis, systemic mastocytosis with associated hematologic neoplasm, or mast cell leukemia. Common side effects of midostaurin in these patients include nausea, vomiting, diarrhea, edema, musculoskeletal pain, abdominal pain, fatigue, upper respiratory tract infection, constipation, fever, headache, and dyspnea.

Midostaurin received breakthrough therapy designation for the AML indication and priority review for the mastocytosis indication.

Regorafenib Approved in Liver Cancer

On April 27, regorafenib (Stivarga, Bayer) received a fast-track FDA indication for use in the second-line treatment of patients with hepatocellular carcinoma (HCC) previously treated with sorafenib (Nexavar, Bayer).

Regorafenib, a multikinase inhibitor, was previously approved for use in selected patients with metastatic colorectal cancer or locally advanced, unresectable, or metastatic gastrointestinal stromal tumors. It is the first new treatment for HCC in a decade.

In the phase 3 RESORCE (Regorafenib for Patients With Hepatocellular Carcinoma Who Progressed on Sorafenib Treatment) trial, which included 573 patients with HCC whose disease had not responded to sorafenib, overall survival was significantly longer with regorafenib than with a placebo (10.6 months vs 7.8 months; hazard ratio, 0.63; 95% CI, 0.50-0.79; $P<.0001$).

The most common side effects in patients treated with regorafenib vs those treated with placebo were pain (55% vs 44%), palmar-plantar erythrodysesthesia (51% vs 7%), asthenia/fatigue (42% vs 33%), diarrhea (41% vs 15%), hypertension (31% vs 6%), infection (31% vs 18%), and decreased appetite and food intake (31% vs 15%).

Other Recent Approvals

- The FDA approved avelumab (Bavencio, EMD Serono/Pfizer) on March 23 for patients aged 12 years and older with metastatic Merkel cell carcinoma, including those who have not received prior chemotherapy, and on May 9 for the second-line treatment of locally advanced or metastatic urothelial carcinoma in patients with disease progression during or after platinum-containing chemotherapy.
- On March 27, the FDA approved niraparib (Zejula, Tesaro) for maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in patients whose tumors have responded to platinum-based chemotherapy.
- The FDA approved ribociclib (Kisqali, Novartis) on March 13 in combination with an aromatase inhibitor in postmenopausal women with advanced or metastatic breast cancer that is hormone receptor–positive and human epidermal growth factor receptor 2–negative.