FDA Approves First Treatment for Post-partum Depression

The U.S. Food and Drug Administration today approved Zulresso (brexanolone) injection for intravenous (IV) use for the treatment of postpartum depression (PPD) in adult women. This is the first drug approved by the FDA specifically for PPD.

"Postpartum depression is a serious condition that, when severe, can be life-threatening. Women may experience thoughts about harming themselves or harming their child. Postpartum depression can also interfere with the maternal-infant bond. This approval marks the first time a drug has been specifically approved to treat postpartum depression, providing an important new treatment option," said Tiffany Farchione, M.D., acting director of the Division of Psychiatry Products in the FDA's Center for Drug Evaluation and Research. "Because of concerns about serious risks, including excessive sedation or sudden loss of consciousness during administration, Zulresso has been approved with a Risk Evaluation and Mitigation Strategy (REMS) and is only available to patients through a restricted distribution program at certified health care facilities where the health care provider can carefully monitor the patient."

PPD is a major depressive episode that occurs following childbirth, although symptoms can start during pregnancy. As with other forms of depression, it is characterized by sadness and/or loss of interest in activities that one used to enjoy and a decreased ability to feel pleasure (anhedonia) and may present with symptoms such as cognitive impairment, feelings of worthlessness or guilt, or suicidal ideation.

Zulresso will be available only through a restricted program called the Zulresso REMS Program that requires the drug be administered by a health care provider in a certified health care facility. The REMS requires that patients be enrolled in the program prior to administration of the drug. Zulresso is administered as a continuous IV infusion over a total of 60 hours (2.5 days). Because of the risk of serious harm due to the sudden loss of consciousness, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring (monitors oxygen levels in the blood). While receiving the infusion, patients must be accompanied during interactions with their child(ren). The need for these steps is addressed in a Boxed Warning in the drug's prescribing information. Patients will be counseled on the risks of Zulresso treatment and instructed that they must be monitored for these effects at a health care facility for the entire 60 hours of infusion. Patients should not drive, operate machinery, or do other dangerous activities until feelings of sleepiness from the treatment have completely gone away.

The efficacy of Zulresso was shown in two clinical studies in participants who received a 60-hour continuous intravenous infusion of Zulresso or placebo and were then followed for four weeks. One study included patients with severe PPD and the other included patients with moderate PPD. The primary measure in the study was the mean change from baseline in depressive symptoms as measured by a depression rating scale. In both placebo controlled studies, Zulresso demonstrated superiority to placebo in improvement of depressive symptoms at the end of the first infusion. The improvement in depression was also observed at the end of the 30-day follow-up period.

The most common adverse reactions reported by patients treated with Zulresso in clinical trials include sleepiness, dry mouth, loss of consciousness and flushing. Health care providers should consider changing the therapeutic regimen, including discontinuing Zulresso in patients whose PPD becomes worse or who experience emergent suicidal thoughts and behaviors.

The FDA granted this application Priority Review and Breakthrough Therapy designation.

Approval of Zulresso was granted to Sage Therapeutics, Inc.

FDA News released March 19, 2019. www.fda.gov.

FDA Approves New Treatment for Osteoporosis in Postmenopausal Women at High Risk of Fracture

The U.S. Food and Drug Administration today approved Evenity (romosozumab-aqqg) to treat osteoporosis in postmenopausal women at high risk of breaking a bone (fracture). These are women with a history of osteoporotic fracture or multiple risk factors for fracture, or those who have failed or are intolerant to other osteoporosis therapies.

More than 10 million people in the U.S. have osteoporosis, which is most common in women who have gone through menopause. People with osteoporosis have weakened bones that are more likely to fracture.

"Today's approval provides women with postmenopausal osteoporosis who are at high risk of fracture with a new treatment that will reduce this risk," said Hylton V. Joffe, M.D, M.M.Sc., director of the Center for Drug Evaluation and Research's Division of Bone, Reproductive and Urologic Products. "But Evenity may increase the risk of heart attack, stroke and cardiovascular death so it's important to carefully select patients for this therapy, which includes avoiding use in patients who have had a heart attack or stroke within the previous year."

Evenity is a monoclonal antibody that blocks the effects of the protein sclerostin and works mainly by increasing new bone formation. One dose of Evenity consists of two injections, one immediately following the other, given once a month by a health care professional. The bone forming effect of Evenity wanes after 12 doses so more than 12 doses should not be used. If osteoporosis therapy is needed after the 12 doses, patients should begin an osteoporosis treatment that reduces bone breakdown.

The safety and efficacy of Evenity were demonstrated in two clinical trials involving a total of more than 11,000 women with postmenopausal osteoporosis. In the first trial, one year of treatment with Evenity lowered the risk of a new fracture in the spine (vertebral fracture) by 73% compared to placebo. This benefit was maintained over the second year of the trial when Evenity was followed by one year of denosumab (another osteoporosis therapy) compared to placebo followed by denosumab. In the second trial, one year of treatment with Evenity followed by one year of alendronate (another osteoporosis therapy) reduced the risk of a new vertebral fracture by 50% compared to two years of alendronate alone. Evenity followed by alendronate also reduced the risk of fractures in other bones (nonvertebral fractures) compared to alendronate alone.

Evenity increased the risk of cardiovascular death, heart attack and stroke in the alendronate trial, but not in the placebo trial. Therefore, Evenity contains a boxed warning on its labeling stating that it may increase the risk of heart attack, stroke and cardiovascular death and should not be used in patients who have had a heart attack or stroke within the previous year. Health care professionals should also consider whether the benefits of Evenity outweigh its risks in those with other risk factors for heart disease and should discontinue Evenity in any patient who experiences a heart attack or stroke during treatment.

Common side effects of Evenity included joint pain and headache. Injection site reactions were also observed.

The FDA granted the approval of Evenity to Amgen.

FDA News released April 09, 2019. www.fda.gov.

FDA Approves First Targeted Therapy for Metastatic Bladder Cancer

The U.S. Food and Drug Administration today granted accelerated approval to Balversa (erdafitinib), a treatment for adult patients with locally advanced or metastatic bladder cancer that has a type of susceptible genetic alteration known as FGFR3 or FGFR2, and that has progressed during or following prior platinum-containing chemotherapy. Patients should be selected for therapy with Balversa using an FDA-approved companion diagnostic device.

"We're in an era of more personalized or precision medicine, and the ability to target cancer treatment to a patient's specific genetic mutation or biomarker is becoming the standard, with advances being made in new disease types. Today's approval represents the first personalized treatment targeting susceptible FGFR genetic alterations for patients with metastatic bladder cancer," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "FGFRs regulate important biological processes including cell growth and division during development and tissue repair. This drug works by targeting genetic alterations in FGFRs."

The most common type of bladder cancer is transitional cell carcinoma, also called urothelial carcinoma. Bladder cancers are associated with genetic mutations that are present in the patient's bladder or entire urothelium (the lining of the lower urinary tract). Bladder cancer is the sixth most common cancer in the United States. Fibroblast growth factor (FGFR) alterations are present in approximately one in five patients with recurrent and refractory bladder cancer.

The efficacy of Balversa was studied in a clinical trial that included 87 patients with locally advanced or metastatic bladder cancer, with FGFR3 or FGFR2 genetic alterations, that had progressed following treatment with chemotherapy. The overall response rate in these patients was 32.2%, with 2.3% having a complete response and almost 30% having a partial response. The response lasted for an average of approximately five-and-a-half months. About a quarter of patients in the study were previously treated with anti PD-L1/PD-1 therapy, which is a standard treatment for patients with locally advanced or metastatic bladder cancer. Responses to Balversa were seen in patients who had previously not responded to anti PD-L1/PD-1 therapy.

Common side effects reported by patients taking Balversa were increased phosphate level, mouth sores, feeling tired, change in kidney function, diarrhea, dry mouth, nails separating from the bed or poor formation of the nail, change in liver function, low salt (sodium) levels, decreased appetite, change in sense of taste, low red blood cells (anemia), dry skin, dry eyes and hair loss. Other side effects include redness, swelling, peeling or tenderness on the hands or feet (hand foot syndrome), constipation, stomach pain, nausea and muscle pain.

Balversa may cause serious eye problems, including inflamed eyes, inflamed cornea (front part of the eye) and disorders of the retina, an internal part of the eye. Patients are advised to have eye examinations intermittently and to tell their health care professional right away if they develop blurred vision, loss of vision or other visual changes. Health care professionals are advised to check patients' blood phosphate level between 14 and 21 days after starting treatment and monthly, and to increase the dose Balversa in patients whose serum phosphate is below the target level.

Health care professionals are advised to tell male patients with female partners of reproductive potential to use effective contraception during treatment with Balversa and for one month after the last dose. Pregnancy testing is recommended for females of reproductive potential prior to initiating treatment with Balversa. Women who are pregnant or breastfeeding should not take Balversa because it may cause harm to a developing fetus or newborn baby. Balversa must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks.

Balversa received an Accelerated Approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need using clinical trial data that is thought to predict a clinical benefit to patients. Further clinical trials are required to confirm Balversa's clinical benefit and the sponsor is conducting or plans to conduct these studies. Balversa was also granted Breakthrough Therapy designation.

The FDA granted the approval of Balversa to Janssen Pharmaceutical.

The FDA also approved the therascreen FGFR RGQ RT-PCR Kit, developed by QIAGEN Manchester, Ltd., for use as a companion diagnostic with Balversa for this therapeutic indication.

FDA News released April 12, 2019. www.fda.gov.

Source: FDA