FDA expedites review of Novartis drug Promacta® for first-line severe aplastic anemia (SAA)

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- - Promacta receives FDA Priority Review for first-line treatment of SAA based on data showing 52% complete response rate and 85% overall response rate when added to standard immunosuppressive therapy (IST)
- - Regulatory action underscores the treatment potential of Promacta for a rare and serious blood condition

EAST HANOVER, N.J., May 30, 2018 /PRNewswire/ -- Novartis announced today that the US Food and Drug Administration (FDA) has accepted the company's supplemental New Drug Application (sNDA) and granted Priority Review designation to Promacta® (eltrombopag) in combination with standard immunosuppressive therapy (IST) for first-line treatment of severe aplastic anemia (SAA).

Promacta, which is marketed as Revolade® in most countries outside the US, is an oral thrombopoietin receptor agonist (TPO-RA) that is already approved for SAA in the refractory setting for patients who have had an insufficient response to IST. It is also approved for adults and children with chronic immune thrombocytopenia (ITP) for patients who are refractory to other treatments and for the treatment of thrombocytopenia in patients with chronic hepatitis C virus (HCV) infection.

"Promacta is a great example of our drive to develop innovative treatments in serious disease areas where few treatment options exist," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "Thanks to the many individuals and organizations who have helped us to advance the development of this promising medicine. We will continue our work with the FDA to make Promacta available for this potential new indication as quickly as possible."

The Priority Review for first-line SAA is based on Novartis' analysis of research sponsored by the Intramural Research Program of the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) and conducted under a Cooperative Research and Development Agreement (CRADA). The study showed that more than half (52%) of treatment-naïve SAA patients achieved complete response at six months when treated with Promacta concurrently with standard IST, which was an increase of 35% compared to those treated with the standard IST alone[1]. The overall response rate was 85% at six months[2].

Severe aplastic anemia is a rare, life-threatening, acquired blood disorder in which a patient's bone marrow fails to produce enough red blood cells, white blood cells and platelets[3]. As a result, people living with this serious disease may experience debilitating symptoms and complications, such as fatigue, trouble breathing, recurring infections and abnormal bruising or bleeding that can limit their daily activities[4]. Historically, SAA was nearly uniformly a fatal diagnosis due to infection or hemorrhage resulting from prolonged pancytopenia; untreated SAA can result in 80-90% mortality in 1-2 years[5]. The prevalence rates vary for aplastic anemia in the US, but it is believed that 500-1,000 new cases are diagnosed each year[6]. The standard treatment regimen for individuals unable to receive or not eligible candidates for hematopoietic stem cell transplantation (HSCT) in the US for treatment-naïve SAA is IST. With IST as first-line treatment, up to one-third of patients and approximately 40% of those unresponsive to IST die within 5 years of diagnosis[7].

According to FDA guidelines, treatments that receive Priority Review designation are those that address a serious or life threatening disease or condition and, if approved, would provide a significant improvement in treatment safety or efficacy. If a treatment is granted Priority Review designation, the goal of the FDA is to issue a decision within six months of application submission, rather than ten months for standard review.

Promacta (eltrombopag)

Eltrombopag, marketed as Promacta® in the US and Revolade® in countries outside the US, is approved in more than 100 countries worldwide for the treatment of thrombocytopenia in adult patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an inadequate response or are intolerant to other treatments, approved in over 45 countries worldwide for the treatment of patients with severe aplastic anemia (SAA) who are refractory to other treatments, and also approved in more than 50 countries for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow them to initiate and maintain interferon-based therapy. Promacta/Revolade is approved in the US and in the European Union for the treatment of thrombocytopenia in pediatric patients 1 year and older with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids and immunoglobulins.

Important Safety Information

Promacta can cause serious side effects, including liver problems, abnormal liver function tests, high platelet counts and higher risk for blood clots, and new or worsened cataracts (a clouding of the lens in the eye).

Promacta is not for treatment of people with a precancerous condition called myelodysplastic syndromes (MDS). If you have MDS and receive Promacta, your MDS condition may worsen and become AML. If MDS worsens to become AML, you may die sooner from AML.

For patients who have chronic hepatitis C virus and take Promacta with interferon and ribavirin treatment, Promacta may increase the risk of liver problems. Patients should tell a healthcare provider right away if they have any of these signs and symptoms of liver problems including yellowing of the skin or the whites of the eyes (jaundice), unusual darkening of the urine, unusual tiredness, right upper stomach area pain, confusion, swelling of the stomach area (abdomen).

A healthcare provider will order blood tests to check the liver before starting Promacta and during Promacta treatment. In some cases, treatment with Promacta may need to be stopped due to changes in liver function tests.

The risk of getting a blood clot is increased if the platelet count is too high during treatment with Promacta. The risk of getting a blood clot may also be increased during treatment with Promacta if platelet counts are normal or low. Some forms of blood clots, such as clots that travel to the lungs or that cause heart attacks or strokes can cause severe problems or death. A healthcare provider will check blood platelet counts, and change the dose of Promacta or stop Promacta, if platelet counts get too high. Patients should tell a healthcare provider right away if they have signs and symptoms of a blood clot in the leg, such as swelling, pain, or tenderness in the leg.

People with chronic liver disease may be at risk for a type of blood clot in the stomach area. Patients should tell a healthcare provider right away if they have stomach area pain that may be a symptom of this type of blood clot.

New or worsened cataracts have happened in people taking Promacta. A healthcare provider will check the patient's eyes before and during treatment with Promacta. Patients should tell a healthcare provider about any changes in eyesight while taking Promacta.

Patients should tell a healthcare provider about all the medicines they take, including prescription and over-

the-counter medicines, vitamins, and herbal supplements. Promacta may affect the way certain medicines work. Certain medicines may keep Promacta from working correctly. Patients should take Promacta at least 2 hours before or 4 hours after taking products such as antacids used to treat stomach ulcers or heartburn and multivitamins or products that contain iron, calcium, aluminum, magnesium, selenium, and zinc, which may be found in mineral supplements. Patients should ask a healthcare provider if they are not sure if the medicine is one that is listed above.

Patients should avoid situations and medications that may increase the risk of bleeding while taking Promacta.

The most common side effects of Promacta when used to treat chronic ITP in adults are: nausea; diarrhea; upper respiratory tract infection (symptoms may include runny nose, stuffy nose, and sneezing); vomiting; muscle aches; urinary tract infection (symptoms may include frequent or urgent need to urinate, low fever in some people, pain or burning with urination); pain or swelling (inflammation) in the throat or mouth (oropharyngeal pain and pharyngitis); abnormal liver function tests; back pain; flu-like symptoms (influenza), including fever, headache, tiredness, cough, sore throat, and body aches; skin tingling, itching, or burning; and rash.

The most common side effects of Promacta in children 1 year and older when used to treat chronic ITP are: upper respiratory tract infections (symptoms may include runny nose, stuffy nose, and sneezing); pain or swelling (inflammation) in the nose and throat (nasopharyngitis); cough; diarrhea; pyrexia; runny, stuffy nose (rhinitis); stomach (abdominal) pain; pain or swelling (inflammation) in the throat or mouth; toothache; abnormal liver function tests; rash; runny nose (rhinorrhea).

The most common side effects when Promacta is used in combination with other medicines to treat chronic HCV are: low red blood cell count (anemia); fever; tiredness; headache; nausea; diarrhea; decreased appetite; flu-like symptoms (influenza), including fever, headache, tiredness, cough, sore throat, and body aches; feeling weak; trouble sleeping; cough; itching; chills; muscle aches; hair loss; and swelling in the ankles, feet, and legs.

The most common side effects of Promacta when used to treat severe aplastic anemia are: nausea, feeling tired, cough, diarrhea, headache, pain in arms, legs, hands or feet, shortness of breath, fever, dizziness, pain in nose or throat, abdominal pain, bruising, muscle spasms, abnormal liver function tests, joint pain, and runny nose. Laboratory tests may show abnormal changes to the cells in bone marrow.

Please see full US Prescribing Information, including Boxed WARNING and Medication Guide, for Promacta.

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development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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References

1. Townsley DM et al. Eltrombopag added to standard immunosuppression for aplastic anemia. N Engl J Med 2017 Apr 20; 376:1540.
2. Novartis Data on File.
3. National Heart, Lung and Blood Institute (2018). Aplastic Anemia. Available at: https://www.nhlbi.nih.gov/node/80148. Accessed January 18, 2018.
4. Townsley DM, Desmond R, Dunbar CE, et al. Pathophysiology and management of thrombocytopenia in bone marrow failure: possible clinical applications of TPO receptor agonists in aplastic anemia and myelodysplastic syndromes. Int J Hematology. 2013;98(1):48-55.
5. Rosenfeld S et al. Antithymocyte globulin and cyclosporine for severe aplastic anemia: Association between hematologic response and long-term outcome. JAMA. 2003;289(9):1130–1135. doi:10.1001/jama.289.9.1130.
6. National Organization for Rare Diseases (2018). Acquired Aplastic Anemia. Available at: https://rarediseases.org/rare-diseases/acquired-aplastic-anemia/. Accessed March 26, 2018.
7. Valdez JM, Scheinberg P, Nunez O, et al. Decreased infection-related mortality and improved survival in severe aplastic anemia in the past two decades. Clin Infect Dis. 2011; 52(6):726-735.

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