SeattleGenetics®

IMPORTANT DRUG WARNING

January, 2012

Subject: Important Changes in the ADCETRIS™ (brentuximab vedotin) Prescribing Information

- Progressive Multifocal Leukoencephalopathy (PML) and death
- Increased risk of pulmonary toxicity associated with concomitant use of ADCETRIS and bleomycin

Dear Healthcare Professional:

Seattle Genetics, Inc. would like to inform you of recent changes to the prescribing information for ADCETRIS regarding new important risk information. Additional reports of John Cunningham (JC) virus infection resulting in PML necessitate elevating the existing Warning for PML to a Boxed Warning. In addition, evidence of an increased risk of pulmonary toxicity associated with the use of ADCETRIS in combination with bleomycin has resulted in the inclusion of new risk information to the CONTRAINDICATIONS section of the ADCETRIS prescribing information. This new important risk information in the ADCETRIS prescribing information includes:

Revisions to the Product Labeling Regarding PML and Regarding Pulmonary Toxicity

BOXED WARNING

WARNING: PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

JC virus infection resulting in PML and death can occur in patients receiving ADCETRIS [*see Warnings and Precautions (5.5), Adverse Reactions (6.2)*].

WARNINGS AND PRECAUTIONS

Progressive Multifocal Leukoencephalopathy

JC virus infection resulting in PML has been reported in ADCETRIS-treated patients, including one fatal event. In addition to ADCETRIS therapy, other possible contributory factors include prior therapies and underlying disease that may cause immunosuppression.

Consider the diagnosis of PML in any patient presenting with new-onset signs and symptoms of central nervous system abnormalities. Evaluation of PML includes, but is not limited to, consultation with a neurologist, brain MRI, and lumbar puncture or brain biopsy. Hold ADCETRIS dosing for any suspected case of PML and discontinue ADCETRIS dosing if a diagnosis of PML is confirmed.

CONTRAINDICATIONS

Pulmonary Toxicity

Concomitant use of ADCETRIS and bleomycin is contraindicated due to pulmonary toxicity. In a clinical trial which included the combination of ADCETRIS with ABVD (Adriamycin, bleomycin, vinblastine, dacarbazine), the rate of non-infectious pulmonary toxicity was increased relative to historical observations of ABVD alone. Patients typically reported cough and dyspnea. Interstitial infiltration and/or inflammation were observed on radiographs and computed tomographic imaging of the chest. Most patients responded to corticosteroids.

SUMMARY OF INFORMATION ON RECENT PML CASES

To date, Seattle Genetics has received two reports of confirmed PML and one report of suspected PML in patients who received treatment with ADCETRIS. Presenting signs and symptoms considered to be consistent with PML included speech impairment, problems thinking, memory lapses, unilateral weakness, impairment in coordination and balance, and sensory deficits. The onset of these symptoms occurred following 2, 3 or 8 cycles of ADCETRIS. The patients had multiple risk factors for developing PML, including a history of lymphoproliferative disease (Hodgkin lymphoma or anaplastic large cell lymphoma), prior treatment with multiple chemotherapy regimens, prior targeted radiation therapy and/or prior stem transplantation. PML was diagnosed based on clinical symptoms, MRI findings and detection of JC virus by PCR in the CSF or by histology on biopsy. One of these cases was fatal while the other two patients remain in hospice care.

Physicians should consider a possible diagnosis of PML in any patient currently receiving or who has received ADCETRIS in the past, and presents with new onset of signs or symptoms of CNS abnormalities such as changes in mood, unusual behavior, confusion or other cognitive changes, loss of balance, blurred vision or loss of vision, decreased strength, control, or sensation in one arm or leg or change in the ability to walk or talk. Consultation with a neurologist and performance of a brain MRI and/or lumbar puncture with analysis of cerebrospinal fluid by polymerase chain reaction for JC virus and/or brain biopsy should be considered. Hold ADCETRIS dosing for any suspected case of PML and discontinue ADCETRIS dosing if a diagnosis of PML is confirmed. Instruct patients to report changes in mood or usual behavior, confusion, thinking problems, loss of memory, changes in vision, speech, walking, decreased strength or weakness on one side of the body.

The factors leading to reactivation of latent JC virus are not fully understood. In addition to ADCETRIS, other possible contributory factors include underlying disease and prior therapies that affect the immune system.

SUMMARY OF INFORMATION ON CASES OF PULMONARY TOXICITY REPORTED WITH ADCETRIS

Seattle Genetics is conducting a phase 1 clinical trial of ADCETRIS in combination with Adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) or AVD as front-line therapy for Hodgkin lymphoma (HL). Noninfectious pulmonary toxicity has been observed in some subjects enrolled in the ABVD + ADCETRIS arm of the study. Patients have presented with cough and dyspnea. Interstitial infiltration and/or inflammation have been observed on X-ray and computed tomography of the chest. Most patients have responded favorably to corticosteroid therapy.

The use of ADCETRIS in the front-line HL setting is investigational and is not an approved indication in the prescribing information.

The frequency of pulmonary toxicity in the ABVD + ADCETRIS arm of the phase 1 trial is approximately 40%, compared to a frequency of 10-25% most commonly reported in the literature with bleomycin-based regimens. No pulmonary toxicity has been observed thus far in the AVD + ADCETRIS arm of the study. To date, monotherapy with ADCETRIS has not been associated with a clinically meaningful risk of pulmonary toxicity.

Therefore, ADCETRIS and bleomycin should not be administered concomitantly.

Seattle Genetics will continue to monitor the safety of ADCETRIS through established reporting mechanisms. You can report adverse reactions with ADCETRIS to Seattle Genetics at 855-4SEAGEN (855-473-2436), or to the FDA at www.fda.gov/medwatch or by mail to MedWatch, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852-9787.

IMPORTANT INFORMATION ABOUT ADCETRIS (BRENTUXIMAB VEDOTIN)

INDICATIONS

ADCETRIS is a CD30-directed antibody-drug conjugate indicated for:

- The treatment of patients with Hodgkin lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates.
- The treatment of patients with systemic anaplastic large cell lymphoma after failure of at least one prior multi-agent chemotherapy regimen.

These indications are based on response rate. There are no data available demonstrating improvement in patient reported outcomes or survival with ADCETRIS.

Please see the enclosed ADCETRIS full prescribing information.

If you have any questions or require additional information regarding the use of ADCETRIS, please contact Seattle Genetics Medical Information directly at 855-4SEAGEN (855-473-2436) or medicalinformation@seagen.com.

Sincerely,

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Chief Medical Officer
Seattle Genetics, Inc.