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NCCN Guidelines Panel: Hairy Cell Leukemia

Dear Sir or Madam:

On behalf of AstraZeneca, this letter is a formal request to the National Comprehensive Cancer Network (NCCN) Panel for "Hairy Cell Leukemia" for the inclusion of LUMOXITI™ (moxetumomab pasudotox-tdfk) for the treatment of adult patients with relapsed or refractory (R/R) hairy cell leukemia (HCL).

Specific Changes:

Request inclusion of LUMOXITI for the treatment of relapsed/refractory HCL (HCL-2).

FDA Clearance:<sup>1</sup>

Moxetumomab pasudotox-tdfk was approved by the FDA on 9/13/2018 under the brand name LUMOXITI for the treatment of adult patients with relapsed or refractory (R/R) hairy cell leukemia who received at least two prior systemic therapies, including treatment with a purine nucleoside analog. Not recommended in patients with severe renal impairment (CrCl ≤ 29 mL/min).<sup>1</sup>

Please refer to the LUMOXITI [prescribing information](#) for complete safety information.

Rationale:

1. There remains an unmet need for R/R HCL therapies that provide a durable response with minimal residual disease (MRD) eradication and less myelo/immunosuppression than what is seen with purine nucleoside analogues PNAs.<sup>2</sup>

2. The FDA based its approval of LUMOXITI based on results from Study 1053. This marks the first new treatment option for R/R HCL patients in over 20 years.<sup>3</sup>

Background and results from publicly available information are as follows:

Background:<sup>1</sup>

- LUMOXITI is a CD22-directed cytotoxin, composed of a recombinant, murine immunoglobulin variable domain genetically fused to a truncated form of *Pseudomonas* exotoxin, PE38, that inhibits protein synthesis.

Study Details and Safety Information:

- Study 1053 is the pivotal, multicenter trial for LUMOXITI. It is a single-arm, open-label study conducted at 32 centers in 14 countries. This is the largest prospective study in third line or beyond R/R HCL and consisted of 80 patients with HCL classical (n=77) or HCL variant (n=3).<sup>2</sup>
- The recommended dose of LUMOXITI is 0.04 mg/kg administered as a 30-minute intravenous infusion on Days 1, 3, and 5 of each 28-day cycle. Continue LUMOXITI treatment for a maximum of 6 cycles, disease progression, or unacceptable toxicity.<sup>1</sup>
- The primary efficacy endpoint in Study 1053 is durable complete response (CR). The endpoint was assessed by the independent review committee (IRC) and defined as maintenance of hematologic remission (hemoglobin ≥ 11 g/dL, neutrophils ≥ 1500/mm<sup>3</sup>, and platelets ≥ 100,000/mm<sup>3</sup> without transfusions or growth factor for at least 4 weeks) more than 180 days after IRC-assessed CR.<sup>1</sup>

- The IRC-assessed durable complete response rate was 30% (95% CI; 20, 41).<sup>1</sup>
- An IRC assessed overall response of 75% (95% CI, 64-84), a complete response (CR) of 41% (95% CI; 30, 53), and a partial response of 34% (95% CI, 24, 45) was seen.<sup>1</sup>
- Of complete responders MRD negativity was seen in 85% of patients (27 of 33).<sup>2</sup>
- LUMOXITI contains a Boxed Warning for capillary leak syndrome (CLS) and hemolytic uremic syndrome (HUS) due to the occurrence of life-threatening events in patients receiving LUMOXITI. For CLS delay dosing or discontinue LUMOXITI as recommended. Discontinue LUMOXITI in patients with HUS.<sup>1</sup>
- The most common non-laboratory adverse reactions ( $\geq 20\%$ ) of any grade were infusion related reactions, edema, nausea, fatigue, headache, pyrexia, constipation, anemia, and diarrhea. The most common Grade 3 or 4 adverse reactions (reported in at least  $\geq 5\%$  of patients) were hypertension, febrile neutropenia, and HUS.<sup>1</sup>
- The most common laboratory abnormalities ( $\geq 20\%$ ) of any grade were creatinine increased, ALT increased, AST increased, hypocalcemia, hypophosphatemia, hemoglobin decreased, neutrophil count decreased, hyponatremia, blood bilirubin increased, hypokalemia, GGT increased, hypomagnesemia, platelet count decreased, hyperuricemia, and alkaline phosphate increased.<sup>1</sup>
- Adverse reactions resulting in permanent discontinuation of LUMOXITI occurred in 15% (12/80) of patients. The most common adverse reaction leading to LUMOXITI discontinuation was HUS (5% or 4/80).<sup>1</sup>
- The most common adverse reactions resulting in dose delays, omissions, or interruptions was pyrexia (3.8%).<sup>1</sup>

A combined safety database of Moxetumomab in HCL studies were used to assess the safety. The results of this analysis formed the basis of the warnings and precautions for LUMOXITI monotherapy and include: capillary leak syndrome, hemolytic uremic syndrome, renal toxicity, infusion related reactions, and electrolyte abnormalities.<sup>1</sup>

These materials may include information that is not found in the currently approved prescribing information for LUMOXITI. The enclosed information is intended to provide pertinent data and should in no way be construed as a recommendation for the use of this product in any manner other than as approved by the Food and Drug Administration and as described in the prescribing information for LUMOXITI. This information is provided to NCCN evaluators for guideline review purposes only.

A copy of the approved [Package Insert](#) and references are submitted in support of this proposed change.

Reference(s):

1. LUMOXITI™ (moxetumomab pasudotox-tdfk) Prescribing Information.
2. Kreitman RJ, Dearden C, Zinzani PL, et al. Moxetumomab pasudotox in relapsed/refractory hairy cell leukemia. *Leukemia*. 2018; 32(8):1768-1777.
3. US Food and Drug Administration. Drugs@FDA: FDA Approved Drug Products. Leustatin (cladribine). Available online. Accessed August 2018.

Sincerely,

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