Bendeka™ (bendamustine) – New Orphan Drug Approval

- On December 7, 2015, Teva and Eagle Pharmaceuticals announced the **FDA approval** of Bendeka™ (bendamustine), an alkylating agent, for the treatment of patients with chronic lymphocytic leukemia (CLL) and indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

  - In CLL, the efficacy relative to first-line therapies other than chlorambucil has not been established.

- The approval of Bendeka’s CLL indication was based on an open-label trial involving 301 previously-untreated patients with Binet Stage B or C (Rai States I – IV) CLL requiring treatment. Patients received bendamustine or chlorambucil. The endpoints were overall response rate (ORR) and progression-free survival (PFS).

  - Fifty-nine percent of patients treated with bendamustine experienced an ORR (complete or partial shrinkage of their tumors) compared to 26% of patients treated with chlorambucil (p < 0.0001).
  - Additionally, the median PFS was 18 months in the Bendeka group vs. 6 months in the chlorambucil group (HR = 0.27, [95% CI: 0.17, 0.43]; p < 0.0001).

- Bendeka’s approval for NHL was based on a single-arm trial involving 100 patients with indolent B-cell NHL that had progressed during or within six months of treatment with rituximab or a rituximab-containing regimen. The endpoints were ORR and duration of response (DR).

  - Seventy-four percent of patients treated with bendamustine experienced an ORR (95% CI: 64.3, 82.3).
  - Additionally, the median DR was 9.2 months (95% CI: 7.1, 10.8).

- Warnings and precautions for Bendeka include myelosuppression, infections, anaphylaxis and infusion reactions, tumor lysis syndrome, skin reactions, other malignancies, extravasation injury, and embryo-fetal toxicity.

- The most common adverse events (> 5%) with Bendeka use during infusion and within 24 hours post-infusion were nausea and vomiting.

- The most common non-hematologic adverse events (≥ 15%) with Bendeka use for CLL were pyrexia, nausea, and vomiting.

- The most common non-hematologic adverse events (≥ 15%) with Bendeka use for NHL were nausea, fatigue, vomiting, diarrhea, pyrexia, constipation, anorexia, cough, headache, weight decreased, dyspnea, rash, and stomatitis.

- The most common hematologic abnormalities (≥ 15%) with Bendeka use were lymphopenia, anemia, leukopenia, thrombocytopenia, and neutropenia.

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• The recommended dose of Bendeka for CLL is 100 mg/m² infused intravenously over 10 minutes on days 1 and 2 of a 28-day cycle, for up to 6 cycles.

• The recommended dose of Bendeka for NHL is 120 mg/m² infused intravenously over 10 minutes on days 1 and 2 of a 21-day cycle, for up to 8 cycles.

• Teva plans to launch Bendeka in the first quarter of 2016. Bendeka will be available as 100 mg/4 mL (25 mg/mL) multiple-dose vials.