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LEVACT[®]/RIBOMUSTIN[®]/RIBOVACT[®] (BENDAMUSTINE) BACKGROUNDER

THE 50-YEAR JOURNEY OF A NOVEL CHEMOTHERAPY AGENT

- Bendamustine was developed by East German pharmacologists in the 1960s. It has been used as an anti-cancer therapy for over 40 years in Germany, but has only been more widely available across Europe since 2010.
- Bendamustine was developed at the Institute for Microbiology and Experimental Therapy in Jena, East Germany. Following German reunification, there was renewed interest in its potential in haematological malignancies and clinical studies were undertaken in the US and Europe, exploring its potential in indolent non-Hodgkin lymphoma (iNHL), chronic lymphocytic leukaemia (CLL) and multiple myeloma (MM).
- In 2008, the US Food and Drug Administration (FDA) approved bendamustine for the treatment of indolent B-cell NHL and CLL. It was approved by the EMA (European Medicines Agency) in 2010 for specific patient populations with indolent B-cell NHL, CLL and MM.
- Since 1994, an estimated 191,488 patients have been treated with bendamustine across the US, Asia and Europe¹.
- Bendamustine is marketed across Europe under several brand names, including Levact[®], Ribomustin[®] and Ribovact[®]. Bendamustine is currently approved in 24 European countries: Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the UK.

EFFICACY AND TOLERABILITY

- In clinical trials, combination therapy with bendamustine and rituximab (BR) has demonstrated superior efficacy to a standard rituximab-containing chemotherapy regimen in patients with previously untreated iNHL², and is currently being compared against the standard first-line regimen in CLL: fludarabine, cyclophosphamide, and rituximab (FCR).
- Bendamustine has been shown to have a superior toxicity profile to conventional alkylating agents³.

FIRST-LINE TREATMENT OF CLL

- The European indication for bendamustine's use as a first-line treatment for CLL (Binet stage B or C) in patients for whom fludarabine combination chemotherapy is not appropriate was based on an open-label, phase III study comparing it with chlorambucil.
- The prospective, multi-centre, randomised study involved 319 previously untreated patients with CLL (Binet stage B or C) and found that first-line treatment with bendamustine resulted in

significantly longer median progression-free survival (PFS) compared to treatment with chlorambucil (21.6 vs 8.3 months, $p < 0.0001$).^{4,5,6}

BENDAMUSTINE IN OTHER HAEMATOLOGICAL MALIGNANCIES

- In Europe, bendamustine is licensed to treat some of the most common white blood cell malignancies:
 - As monotherapy for iNHL patients who have experienced a relapse during, or within six months following, treatment with a rituximab-containing regimen. In 2012, a Type II variation to extend the indication was submitted to the BfArM and the twenty two concerned member states. The proposed indication is first-line treatment of indolent non-Hodgkin's lymphoma and mantle cell lymphoma in combination with rituximab.
 - First-line treatment of MM (Durie-Salmon stage II with progress or stage III) in combination with prednisone for patients older than 65 years who are not eligible for autologous stem cell transplantation (a medical procedure in which stem cells are removed, stored, and later given back to the same person), and who have clinical neuropathy (a functional disturbance or pathological change in the peripheral nervous system) at time of diagnosis, preventing the use of thalidomide or bortezomib-containing treatment regimens⁶.

References

¹ Mundipharma International Ltd. Data on file.

² Rummel MJ, et al. Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial. *The Lancet* 2013

³ Bruce D. Cheson, MD Bendamustine: Mechanism of Action and Clinical Data. *Clinical Advances in Hematology Oncology* August 2011 Volume 9 Supplement 19.

⁴ Knauf WU, et al. Phase III randomized study of bendamustine versus chlorambucil in previously untreated patients with chronic lymphocytic leukaemia. *J Clin Oncol* 2009;27(26):4378-84.

⁵ Knauf WU, et al. Bendamustine in the treatment of chronic lymphocytic leukaemia - consistent superiority over chlorambucil in elderly patients and across clinically defined risk groups. *American Society of Hematology, 51st Annual Meeting, New Orleans, Louisiana, 5 – 8 December 2009* [poster 2367].

⁶ Napp Summary of Product Characteristics *Levact*[®] (bendamustine hydrochloride) 2.5 mg/ml powder for concentrate for solution for infusion, 2010, 5.1. Available at:

<http://www.medicines.org.uk/emc/document.aspx?documentid=23469> Accessed November 2013

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