

## PRESS RELEASE

### Scotland first in the UK to make VENCLYXTO® ▼ (venetoclax) routinely available for patients with most common form of adult leukaemia<sup>1</sup>

*Scottish Medicines Consortium accepts AbbVie's venetoclax for routine prescribing across NHS Scotland, offering a new therapy option for patients with certain types of difficult-to-treat chronic lymphocytic Leukemia (CLL).<sup>1</sup>*

**EMBARGOED UNTIL 14.00 Monday 07 August, 2017** — Today, the Scottish Medicines Consortium (SMC) has announced acceptance of AbbVie's VENCLYXTO® (venetoclax) for use across NHS Scotland in the treatment of chronic lymphocytic leukaemia (CLL) in adult patients in the absence of 17p deletion or TP53 mutation who have failed both chemo-immunotherapy and a B-cell receptor (BCR) inhibitor. Venetoclax has also been accepted for the treatment of adult CLL patients in the presence of 17p deletion or TP53 mutation who are either unsuitable for or have failed a BCR inhibitor.<sup>2</sup> This acceptance marks AbbVie's first oncology reimbursement decision in the UK with eligible Scottish CLL patients being the first in the UK to benefit from routine access to venetoclax.

Venetoclax is a first-in-class, oral, once-daily medicine that selectively inhibits the function of the BCL-2 protein, restoring the body's ability to trigger cancer cell self-destruction.<sup>2</sup> Despite treatment, the majority of people living with CLL will eventually have their disease recur,<sup>3</sup> with one in two patients failing current treatments facing survival as short as three months.<sup>4,5</sup> Venetoclax is being developed by AbbVie and Roche. It is commercialized by AbbVie outside of the U.S. and jointly by AbbVie and Genentech, a member of the Roche Group, in the U.S.

Dr Mike Leach, Consultant Haematologist at the Beatson West of Scotland Cancer Centre, commented, *"The SMC approval of venetoclax is an important decision for patients with difficult-to-treat forms of CLL, particularly in cases where existing treatments such as BCR inhibitors have failed and patients have limited options left. The data and our clinical experience show that patients respond well to treatment with a number achieving complete remission justifying not only today's acceptance by the SMC but also its inclusion in the latest treatment guidelines from ESMO.<sup>6</sup> Today's positive decision has the potential to make a difference to the lives of this patient population."*

CLL affects the blood and immune system and is the most common form of adult leukaemia with almost 3,500 people affected in the UK each year, with an estimated 168 new cases in Scotland per year.<sup>7,8</sup> For people who develop or harbour gene mutations, such as 17p deletion or TP53 mutation, treatment is particularly challenging and these are associated with poorer quality of life and a median life expectancy of less than two to three years with current standard-of-care regimens.<sup>9,10</sup>

In a Phase 2 study (M13-982) of 158 patients with relapsed and/or refractory CLL with a 17p deletion, the overall response rate was 77.2% (122/158) according to an investigator assessment.<sup>11,12</sup>

Job bag number: AXONC171062  
Date of prep: August 2017

AbbVie Ltd  
AbbVie House  
Vanwall Business Park  
Vanwall Road  
Maidenhead, Berkshire SL6 4UB

OFFICE +44 (0)1628 561090  
[www.abbvie.co.uk](http://www.abbvie.co.uk)

Registered Number: 08004972  
Registered Office: AbbVie House, Vanwall Business Park,  
Vanwall Road, Maidenhead, Berkshire SL6 4UB

Based on Kaplan-Meier estimations, 86.7% of patients were estimated to be alive following 12 months of treatment.<sup>12</sup> In a separate Phase 2 two arm study (M14-032) of venetoclax in 64 CLL patients who relapsed or were refractory to BCR inhibitors (ibrutinib or idelalisib), the primary endpoint, overall response rate was 67% and 57% respectively, according to investigator assessment.<sup>12</sup>

A recent study supports the use of Minimal Residual Disease (MRD) negativity as a prognostic marker for long-term progression-free survival and as a potential therapeutic goal in CLL. MRD negativity describes the presence of a small number of leukaemic cells that remain following treatment and is defined as <1 CLL cell detectable per 10, 000 leukocytes.<sup>13</sup> In the M14-032 Phase 2 trial where MRD was used as an exploratory endpoint, 25% (16/64) of patients treated with venetoclax achieved MRD negativity in the peripheral blood, including 1 patient who was also MRD negative in the bone marrow.<sup>2</sup>

*“The positive recommendation by the SMC is very welcome news for CLL patients in Scotland.”* commented David Innes, Chair of the CLL Support Association. *“There is a clear unmet need for patients with this type of cancer, and the evidence clearly demonstrates the potential impact of venetoclax as a new therapy option that may increase survival and improve the quality of life for someone with CLL, providing an important new option for both patients and their families.”*

Last year venetoclax was granted a Promising Innovation in Medicine (PIM) designation by the UK’s Medicines and Healthcare products Regulatory Agency (MHRA). Also, in August 2016, the UK’s MHRA granted venetoclax a positive scientific opinion through the Early Access to Medicines Scheme (EAMS), a first in any blood cancer for the scheme.<sup>14</sup> Prior to today’s announcement, 7 Scottish patients with certain types of relapsed/refractory CLL have already been able to benefit from venetoclax through EAMS and AbbVie’s commitment to providing the treatment free of charge until reimbursement.

– Ends –

▼ Adverse events should be reported. Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). Adverse events should also be reported to AbbVie UK Ltd. Please contact [ukadverseevents@abbvie.com](mailto:ukadverseevents@abbvie.com).

**For further information:**

Joanna Jones  
AbbVie  
+44 (0)7795 590 344  
[joanna.jones@abbvie.com](mailto:joanna.jones@abbvie.com)

Jessica Smith  
Virgo Health  
+44 (0)20 8939 1294 / 07749 628280  
[jessica.smith@virgohealth.com](mailto:jessica.smith@virgohealth.com)

Job bag number: AXONC171062  
Date of prep: August 2017

AbbVie Ltd  
AbbVie House  
Vanwall Business Park  
Vanwall Road  
Maidenhead, Berkshire SL6 4UB

OFFICE +44 (0)1628 561090  
[www.abbvie.co.uk](http://www.abbvie.co.uk)

Registered Number: 08004972  
Registered Office: AbbVie House, Vanwall Business Park,  
Vanwall Road, Maidenhead, Berkshire SL6 4UB

**Editors Notes****About VENCLYXTO® (venetoclax)**

Venetoclax is an oral B-cell lymphoma-2 (BCL-2) inhibitor. The BCL-2 protein prevents apoptosis (programmed cell death) of some cells, including lymphocytes, and can be overexpressed in some cancer types. Venetoclax, which is given once daily, is designed to selectively inhibit the function of the BCL-2 protein.<sup>2</sup>

Venetoclax is being developed by AbbVie and Genentech, a member of the Roche Group. It is jointly commercialised by the companies in the U.S. and by AbbVie outside of the U.S. Together, the companies are committed to further BCL-2 research with venetoclax.

The safety of venetoclax is based on pooled data of 296 patients treated with venetoclax in two Phase 2 studies and one Phase 1 study.<sup>2</sup> In all, the studies enrolled patients with previously treated CLL, including 188 patients with 17p deletion and 92 patients who had failed a BCR inhibitor.<sup>2</sup> Patients were treated with venetoclax 400mg monotherapy once daily following a dose-titration schedule. The most commonly occurring adverse reactions (≥20 per cent) of any grade in patients receiving venetoclax were neutropenia/neutrophil count decreased, diarrhoea, nausea, anaemia, upper respiratory tract infection, fatigue, hyperphosphataemia, vomiting and constipation.<sup>2</sup> The most frequently reported serious adverse reactions (≥2 per cent) were pneumonia, febrile neutropenia and tumor lysis syndrome (TLS).<sup>2</sup> Discontinuations due to adverse reactions occurred in 9.1 per cent of patients. Dosage adjustments due to adverse reactions occurred in 11.8 per cent of patients.<sup>2</sup>

TLS is an important identified risk when initiating venetoclax. TLS is caused by rapid killing of cancer cells. In 122 patients with CLL with a 20mg daily starting dose, the rate of TLS was three per cent. No TLS with clinical consequences such as acute renal failure, cardiac arrhythmias or sudden death and/or seizures was observed in these patients.<sup>2</sup> This rate of TLS reflects the use of a dose ramp up, starting with a daily dose of 20mg and increasing over five weeks to a daily dose of 400mg, as well as implementation of specific prophylaxis and monitoring measures during the ramp up phase.

**About AbbVie in Oncology**

At AbbVie, we strive to discover and develop medicines that deliver transformational improvements in cancer treatment by uniquely combining our deep knowledge in core areas of biology with cutting-edge technologies, and by working together with our partners – scientists, clinical experts, industry peers, advocates, and patients. We remain focused on delivering these transformative advances in treatment across some of the most debilitating and widespread cancers. We are also committed to exploring solutions to help patients obtain access to our cancer medicines. With the acquisitions of Pharmacyclics in 2015 and Stemcentrx in 2016, our research and development efforts, and through collaborations, AbbVie's oncology portfolio now consists of marketed medicines

Job bag number: AXONC171062

Date of prep: August 2017

AbbVie Ltd  
AbbVie House  
Vanwall Business Park  
Vanwall Road  
Maidenhead, Berkshire SL6 4UB

OFFICE +44 (0)1628 561090  
[www.abbvie.co.uk](http://www.abbvie.co.uk)

Registered Number: 08004972  
Registered Office: AbbVie House, Vanwall Business Park,  
Vanwall Road, Maidenhead, Berkshire SL6 4UB

and a pipeline containing multiple new molecules being evaluated worldwide in more than 200 clinical trials and more than 20 different tumour types.

### About AbbVie

AbbVie is a global, research-driven biopharmaceutical company committed to developing innovative advanced therapies for some of the world's most complex and critical conditions. The company's mission is to use its expertise, dedicated people and unique approach to innovation to markedly improve treatments across four primary therapeutic areas: immunology, oncology, virology and neuroscience. In more than 75 countries, AbbVie employees are working every day to advance health solutions for people around the world. For more information about AbbVie, please visit us at [www.abbvie.co.uk](http://www.abbvie.co.uk).

### REFERENCES

- <sup>1</sup> Scottish Medicines Consortium (correspondence with AbbVie UK) July 2017
- <sup>2</sup> VENClyxTO summary of product characteristics.
- <sup>3</sup> American Cancer Society. (2013) Leukemia – Chronic Lymphocytic. Available at: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003111-pdf.pdf>. Last accessed July 2017.
- <sup>4</sup> Jain PW et al. Outcomes of patients with chronic lymphocytic leukemia after discontinuing ibrutinib. *Blood*. 2015; 125: 2062-2067.
- <sup>5</sup> NCCN clinical practice guidelines in oncology. Non-Hodgkin's Lymphoma. Available at: <https://www.nccn.org/about/nhl.pdf>. Last accessed July 2017.
- <sup>6</sup> Eichhorst B et al. eUpdate June 2017- Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2015; 26 (Suppl 5): v78-v84. Available at: <http://www.esmo.org/Guidelines/Haematological-Malignancies/Chronic-Lymphocytic-Leukaemia/eUpdate-Treatment-Recommendations> Last accessed July 2017
- <sup>7</sup> Macmillan. What is Chronic Lymphocytic Leukaemia. Available at: <http://www.macmillan.org.uk/information-and-support/leukaemia/chronic-lymphocytic/understanding-cancer/about-cll.html>. Last accessed July 2017.
- <sup>8</sup> Cancer Research UK. Chronic lymphocytic leukaemia (CLL) statistics. Available at: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/leukaemia-cll/incidence#heading-Zero>. Last accessed July 2017.
- <sup>9</sup> Schnaiter A, et al. 17p deletion in chronic lymphocytic leukemia: risk stratification and therapeutic approach. *Hematol Oncol Clin N Am*. 2013; 27:289-301
- <sup>10</sup> Stilgenbauer S, et al. Understanding and managing ultra high-risk chronic lymphocytic leukemia. *Hematology Am Soc Hematol Educ Program*. 2010; 1:481-488.
- <sup>11</sup> Stilgenbauer S, et al. Venetoclax in relapsed/refractory chronic lymphocytic leukemia (CLL) with 17p deletion: outcome and minimal residual disease from the full population of the pivotal M13-982 trial. Presented at the 2017 European Hematology Association Congress, June 23, 2017.
- <sup>12</sup> Committee for Medicinal Products for Human Use (CHMP). Assessment report: Venclyxto. European Medicines Agency. EMA/725631, 2016.
- <sup>13</sup> Kwok M et al. Minimal residual disease is an independent predictor for 10-year survival in CLL. *Blood Journal*. 2016;128 (24): 2770-2774
- <sup>14</sup> MHRA. Early Access to Medicines Scientific Opinion - Public Assessment Report on venetoclax. Available at: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/547406/EAMS\\_Public\\_Assessment\\_Report\\_-\\_Venetoclax.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/547406/EAMS_Public_Assessment_Report_-_Venetoclax.pdf). Last accessed July 2017.

Job bag number: AXONC171062

Date of prep: August 2017

AbbVie Ltd  
AbbVie House  
Vanwall Business Park  
Vanwall Road  
Maidenhead, Berkshire SL6 4UB

OFFICE +44 (0)1628 561090  
[www.abbvie.co.uk](http://www.abbvie.co.uk)

Registered Number: 08004972  
Registered Office: AbbVie House, Vanwall Business Park,  
Vanwall Road, Maidenhead, Berkshire SL6 4UB