

Venetoclax (Venclyxto™)

This Horizons Infosheet contains information on venetoclax, a drug being investigated for the treatment of myeloma.

The Horizons Infosheet series provides information relating to novel drugs and treatment strategies that are currently being investigated for the treatment of myeloma. The series also aims to highlight the considerable amount of research currently taking place in the field of myeloma.

The drugs and treatment strategies described in the Horizons Infosheets may not be licensed and/or approved for use in myeloma. You

may, however, be able to access them as part of a clinical trial.

What is venetoclax and how does it work?

Venetoclax (also known as Venclyxto™) is a new type of drug being investigated for the treatment of myeloma.

It belongs to a class of drugs known as pro-survival inhibitors, which work by accelerating cancer cell death.

Venetoclax targets a protein called

BCL-2, which is found in higher amounts in myeloma cells than in healthy cells. The BCL-2 protein prevents apoptosis (programmed cell death) of some cells.

Myeloma cells exploit the BCL-2 protein to promote their survival, allowing them to keep growing and multiplying. Venetoclax inhibits the action of BCL-2. This then causes myeloma cells to die.

Myeloma is associated with multiple genetic abnormalities. BCL-2 has been found to be present in higher amounts in the myeloma cells of patients with a specific chromosomal abnormality (abnormality in the structures in which DNA is packaged within the cell) called t(11;14). Correspondingly, venetoclax has been shown to work especially well in patients with the t(11;14) genetic subtype.

For more information see the [Genetics and myeloma Infoguide](#) from Myeloma UK

How is venetoclax given?

Venetoclax is an oral drug, given as a tablet. It is currently being investigated in Phase III clinical trials as a once-daily treatment of 800mg in myeloma.

Though venetoclax has been shown to work on its own (as a monotherapy), its effects have been

shown to be enhanced when given in combination with other myeloma treatments such as dexamethasone and bortezomib (Velcade®).

What evidence exists to support the use of venetoclax?

Venetoclax is currently being studied in a number of different blood cancers, including myeloma.

In a Phase I clinical trial, 14 of 66 (21%) of the relapsed and/or refractory myeloma patients taking part in the trial responded to venetoclax monotherapy. This rose to 12 out of 30 (40%) patients with the t(11;14) abnormality.

When venetoclax was combined with bortezomib and dexamethasone, the response rate increased to 44 out of 66 (67%) patients. Additionally, in patients with the t(11;14) abnormality there was a particularly high response rate of 17 out of 18 (94%).

What are the possible known side effects of venetoclax?

The most commonly seen side effects of venetoclax in myeloma trials include diarrhoea, constipation, nausea, anaemia, fatigue, neutropenia (low level of neutrophils, a type of white blood cell) and thrombocytopenia (low level of platelets).

Is venetoclax currently available in any UK clinical trials?

For an up-to-date list of UK clinical trials involving venetoclax, visit the **Myeloma Trial Finder** on www.myeloma.org.uk

To be enrolled on a clinical trial, patients have to meet certain conditions known as eligibility criteria. You should speak to your doctor in the first instance if you are interested in taking part in a trial.

Availability of venetoclax in the UK

Before a drug can be widely used, it must first be licensed as a safe and effective treatment. This is usually done by the regulatory authorities at a European level and involves a review of evidence from large-scale clinical studies.

Normally, the licensed drug must then be approved by a UK drug appraisal body before it can be routinely prescribed by NHS doctors. The drug appraisal process differs from licensing - it compares how effective the newly-licensed drug is to existing drugs already in use on the NHS and decides whether it offers the NHS good value for money.

The main body responsible for carrying out drug appraisals in England and Wales is the

National Institute for Health and Care Excellence (NICE). NICE recommendations are usually adopted in Northern Ireland. Scotland's drug appraisal body is the Scottish Medicines Consortium (SMC).

For more information see the **Health Technology Assessment (HTA) Infosheet from Myeloma UK**

In 2016 venetoclax was granted "orphan drug designation" by the European Medicines Agency (EMA) for myeloma. This means that the EMA will offer the drug company certain financial incentives throughout the development and licensing process in order to enable venetoclax to become available to patients sooner.

Therefore, venetoclax is not currently licensed for use in myeloma in the UK and is only accessible to patients as part of a clinical trial.

Future directions

Venetoclax continues to be studied in different patient groups and in different combinations, having recently entered Phase III trials in the UK in combination with bortezomib and dexamethasone in relapsed and/or refractory myeloma patients. It is also being studied in a Phase II

trial in combination with carfilzomib (Kyprolis®) and dexamethasone.

These trials will provide information about the safest and most effective way to use venetoclax in myeloma.

Due to an increased understanding of the genetic changes in myeloma and the development of new diagnostic tools to detect them, clinical trials are looking at new approaches, such as stratified medicine, for treating myeloma. Stratified medicine is a treatment approach that aims to tailor treatment to an individual patient, for example based on their genetic subtype of myeloma. The increased overall response rate of venetoclax in patients with the t(11;14) genetic abnormality means that it may, in the future, be used specifically for patients with this subtype of myeloma.

About this Horizons Infosheet

The information in this Horizons Infosheet is not meant to replace the advice of your medical team. They are the people to ask if you have questions about your individual situation.

For a list of references used to develop our resources, visit www.myeloma.org.uk/references

To provide feedback about this publication, email myelomauk@myeloma.org.uk

Other information available from Myeloma UK

Myeloma UK has a range of publications available covering all areas of myeloma, its treatment and management.

To order your free copies or to talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma UK Infoline on **0800 980 3332** or **1800 937 773** from Ireland.

The Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland.

Information and support about myeloma is also available around the clock at **www.myeloma.org.uk**

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Published by: Myeloma UK
Publication date: July 2017
Last updated: July 2018
Review date: January 2019



Myeloma UK 22 Logie Mill, Beaverbank Business Park, Edinburgh EH7 4HG
T: 0131 557 3332 **E: myelomauk@myeloma.org.uk** Charity No: SC 026116

Myeloma Infoline: 0800 980 3332 or
1800 937 773 from Ireland
www.myeloma.org.uk

Myeloma Awareness Week 21 - 27 June