

# Selinexor (Xpovio®)

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## Horizons Infosheet Clinical trials and novel drugs

**This Horizons Infosheet contains information on selinexor, also known as Xpovio®, 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 novel 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 selinexor?

Selinexor is the first in a new family of drugs known as Selective Inhibitor of Nuclear Export (SINE™) compounds. Selinexor works by blocking the action of a protein called XPO1 within the nucleus (centre compartment) of myeloma cells.

### What is XPO1?

XPO1 (also known as Exportin 1) is a protein responsible for moving other proteins between different parts of the cell.

Cells are made up of two compartments called the cytoplasm and the nucleus, which are separated by a plasma membrane. Some proteins involved in the life cycle of the cell, for example tumour suppressor proteins, are active only when located within the nucleus. Other proteins must be moved from the nucleus into the cytoplasm to become active. The compartment in which different proteins are located can therefore affect the growth and survival of the cell.

XPO1 is a transport protein responsible for moving proteins out of the nucleus of a cell into the cytoplasm. One of the characteristics of myeloma cells that makes them different from healthy cells is their high level of XPO1, which has been found to be essential for myeloma cell survival. Myeloma cells use XPO1 to move tumour suppressor proteins from the nucleus into the cytoplasm. This deactivates them and allows the myeloma cells to multiply uninhibited.

### **How does selinexor work?**

Selinexor is the first myeloma drug developed to block the action of XPO1. By blocking XPO1, selinexor prevents myeloma cells from moving tumour suppressor proteins out of the nucleus and into the cytoplasm.

The tumour suppressor proteins are then activated as normal within the nucleus of the myeloma cell, leading to controlled death of the myeloma cells.

### **How is selinexor given?**

Selinexor is given in tablet form. It can be given on its own as a monotherapy but it has shown to be most effective when used in combination with other myeloma treatments such as dexamethasone.

The dose of selinexor may be 80mg twice a week or 100mg once a week.

### **What evidence exists to support the use of selinexor?**

In the large-scale BOSTON trial, selinexor combined with bortezomib and dexamethasone (SVd) was compared with bortezomib and dexamethasone alone (Vd). This trial included 402 patients. Half were given SVd weekly, and the other half were given Vd twice weekly. The patients had relapsed and refractory myeloma, with between one and three previous treatment lines. In the SVd group, the average time before the myeloma came back (called progression-free survival) was significantly longer than in the Vd group (14 months compared with 9.5 months). The overall response rate (a partial response or better

to treatment) was also significantly higher in the SVd group than in the Vd group (76% of the SVd group versus 62% of the Vd group).

In the STORM trial, 123 patients were included who had triple-class refractory myeloma (not responsive to at least three previous treatment lines including one proteasome inhibitor, one immunomodulatory agent and monoclonal antibodies). The patients were given selinexor and dexamethasone twice weekly. The percentage of patients who experienced a partial response or better to treatment was 26%, with a progression-free survival median of 3.7 months and an overall survival median of 8.6 months.

These trials support the results of earlier smaller-scale trials, which indicated selinexor could be effective in patients who are relapsed and/or refractory to other treatments, and selinexor is more effective in combination with other drugs than on its own.

## What are the possible known side effects of selinexor?

Selinexor is a new treatment which can cause serious side effects. Side effects which have been reported so far include:

- Thrombocytopenia (low level of platelets in the blood, which increases risk of bleeding)
- Anaemia (low level of red blood cells, which can cause fatigue)
- Low level of white blood cells which can increase risk of infections
- Reduced sodium in the blood
- Digestive effects: nausea, vomiting, diarrhoea, loss of appetite and weight loss
- Fatigue
- Cataracts (developing or new)

In a number of patients in trials, side effects have been severe enough to require reduction of the drug dose or stopping treatment. Because selinexor is not yet in widespread use, new side effects may emerge which have not yet been reported.

## Is selinexor currently available in any UK clinical trials?

Most selinexor clinical trials are being done in patients who have had multiple relapses and treatments, and for whom existing treatment options are limited, rather than patients at earlier stages of their treatment pathway.

For an up-to-date list of UK clinical trials involving selinexor, visit the Myeloma Trial Finder on [myeloma.org.uk](http://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.

If you are considering taking part in a clinical trial your doctor will discuss in detail the risks and benefits for you. They will give you detailed information to enable you to make an informed decision about whether to take part.

## Availability of selinexor in the UK

Selinexor is not currently available for use in myeloma in the UK, and is only accessible to patients as part of a clinical trial, or as part of an expanded access programme which the manufacturer has put in place.

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.

Selinexor has been licensed under conditional marketing authorisation by the European Medicines Agency (EMA) and by the UK's Medicine and Healthcare Products Regulatory Agency (MHRA) for use in relapsed and refractory myeloma. These licenses are for use of selinexor in combination with dexamethasone. Conditional marketing authorisation is given when initial evidence shows the benefits outweigh the risks for the treatment but more evidence is required to be reviewed. In the UK, conditional marketing authorisations are valid for one year and are reviewed and renewed each year. A drug licensed under conditional marketing authorisation can follow the UK drug appraisal process.

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 looks at how effective the newly-licensed drug is compared with existing drugs

already in use on the NHS, and decides whether the drug 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).

Selinexor has not been appraised by NICE or the SMC for use in myeloma. Therefore, it is not approved for use on the NHS in the UK.



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

## Future directions

Selinexor continues to be studied in combination with steroids and various other anti-myeloma drugs. These trials will combine to provide better information about the best way to use selinexor in myeloma.

A trial developed with Myeloma UK started in 2018. It is looking at the combination of selinexor, cyclophosphamide and prednisolone, compared

with cyclophosphamide and prednisolone alone, in patients who have relapsed after two or more previous drug treatments.

In December 2020, the US Food and Drug Administration (FDA) approved selinexor for use in combination with bortezomib and dexamethasone, in myeloma patients who have had one or more previous treatments. This approval was based on the results of the BOSTON trial. The FDA previously approved selinexor with dexamethasone in 2019, for myeloma patients after multiple relapses.

## Key points

- Selinexor is a new drug being investigated for the treatment of myeloma
- Selinexor is the first in a new class of drugs called SINE™ compounds. It works by blocking the movement of particular proteins within cells. The aim is to use this to stop myeloma cells from multiplying out of control
- Clinical trials with selinexor have so far been promising, indicating selinexor in combination with other drugs is a potential treatment option in patients with relapsed and refractory myeloma. Trials are continuing

to provide further information about selinexor's effectiveness and side effects, and to compare it with existing myeloma treatments

- Selinexor can cause serious side effects, which have so far included effects on blood cell counts, digestive effects, and fatigue
- Selinexor is not yet widely available in the UK, because it has not been approved for use in myeloma. However, patients may be treated with it as part of a clinical trial or an expanded access programme

### About this Infosheet

The information in this 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 [myeloma.org.uk/references](https://myeloma.org.uk/references)

We value your feedback about our patient information.

For a short online survey go to [myeloma.org.uk/pifeedback](https://myeloma.org.uk/pifeedback) or email comments to [patientinfo@myeloma.org.uk](mailto:patientinfo@myeloma.org.uk)

### Other information available from Myeloma UK

Myeloma UK has a range of publications available covering all aspects of myeloma, its treatment and management. Download or order them from [myeloma.org.uk/publications](https://myeloma.org.uk/publications)

To talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma 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 [myeloma.org.uk](https://myeloma.org.uk)

# Notes

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## We're here for everything a diagnosis of myeloma brings

Get in touch to find out more about how we can support you

Call the Myeloma Infoline on

 **0800 980 3332**

Email Ask the Nurse at

 **[AskTheNurse@myeloma.org.uk](mailto:AskTheNurse@myeloma.org.uk)**

Visit our website at

 **[myeloma.org.uk](http://myeloma.org.uk)**



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Registered Charity No: SC026116

Published by:	Myeloma UK
Publication date:	November 2016
Last updated:	October 2021
Review date:	October 2022

**Myeloma Awareness Week • 21–27 June**