

Selinexor (Xpovio®)

Horizons Infosheet Clinical trials and novel drugs

This Horizons Infosheet contains information on selinexor, 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 so-called 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?

Initial results have been published of the large-scale BOSTON trial in which selinexor combined with bortezomib and dexamethasone (SVd) was compared with bortezomib and dexamethasone alone (Vd). 402 patients were included in the trial, of whom 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 median progression-free survival) was

significantly longer than in the Vd group (14 months compared with 9.5 months). Overall response rate was also significantly higher in the SVd group than in the Vd group (76% of the SVd group versus 62% of the Vd group).

This trial supports the results of earlier smaller-scale trials, which indicated that selinexor could be effective in patients who are relapsed and/or refractory to other treatments, and that 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:

- Effects on the blood: low platelet counts and bleeding; anaemia; low white cell counts and infections; and reduced sodium in the blood
- Digestive effects: nausea, vomiting, diarrhoea, loss of appetite and weight loss
- Fatigue

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

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.

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 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).

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 new 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.

Selinexor was approved in the USA in July 2019, for use in combination with dexamethasone in patients with relapsed or refractory myeloma. This was a so-called “accelerated approval” where there is an unmet clinical need for drugs to treat serious medical conditions.

Summary

- Selinexor is a new drug that is 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 that 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, because it has not been licensed and approved for use in myeloma. However, patients may be treated with it as part of a clinical trial

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

We value your feedback about our patient information.

For a short online survey go to myeloma.org.uk/pifeedback or email comments to myelomauk@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

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

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**

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