Myeloma Patients Europe

FACTSHEET

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SELINEXOR (NEXPOVIO®)

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Myeloma Patients Europe (MPE) has developed a series of factsheets for patients and patient advocates, providing an overview of available treatment options for myeloma and covering some topics related to the disease.

The factsheets cover important issues around the treatment, so that patients can feel safe and informed when asking their doctor specific questions.

For each of the available therapies, the following topics will be addressed:

- What is myeloma?
- What is the particular treatment?
- How does the treatment work?
- What are the benefits?
- What are the side effects?
- How and when is the treatment given?

Myeloma treatment is constantly evolving and the factsheets will be updated regularly to reflect the latest developments.

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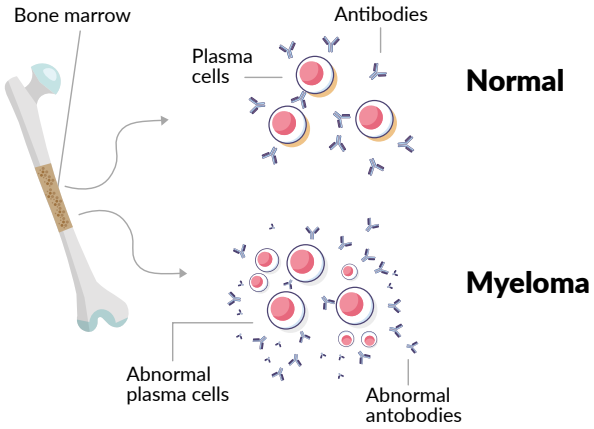
Myeloma Patients Europe AISBL
Avenue Louise 143/4
1050 Brussels
Belgium
www.mpeurope.org
info@mpeurope.org

What is myeloma?

Myeloma is a rare cancer of the bone marrow. It causes the formation of abnormal plasma cells, also called myeloma cells, which divide uncontrollably. Usually, plasma cells help the body to fight infections by making antibodies that recognise and attack viruses, bacteria and fungi. Myeloma affects multiple places in the body (this is why it is sometimes referred to as 'multiple myeloma') where bone marrow is normally active, such as the bones of the spine, pelvis, rib cage and the areas around the shoulders and hips.

Myeloma causes pain, anaemia (low red blood cells), fatigue, fractures, recurring infection, bruising and high blood calcium (hypercalcaemia). These symptoms usually require treatment and could be followed by a period of remission where symptoms subside and may not require any treatment. This cycle of remission and recurrence (relapse) often occurs several times. Many patients, particularly in relapse setting, will receive treatment for a long period of time to ensure that their myeloma is kept at bay.

Treatment may involve taking a combination of drugs that have been found to be more effective than single drugs. Myeloma generally cannot be cured, but survival rates are increasing, due to the availability of new treatments and many patients are able to enjoy a good quality of life. A number of other new treatments have recently been approved or are under consideration for use following relapse, or for refractory myeloma.



What is Selinexor (Nexpovio®)?

Selinexor is a first-in-class selective inhibitor of nuclear export (SINE) drug that was granted conditional marketing authorisation from the European Commission in March 2021[1]. It has since obtained full market approval in July 2022[2] after the company provided additional information to the European Medicines Agency (EMA).

Selinexor is indicated in combination with bortezomib and dexamethasone for the treatment of myeloma in patients who have received at least one prior line of therapy. It is also indicated in combination with dexamethasone in patients who have received at least four prior lines of therapy and are refractory to at least two proteasome inhibitors, two immunomodulatory agents (IMiDs) and an anti-CD38 monoclonal antibody with evidence of progressed disease after their last treatment[2,3].

How does selinexor work?

Selinexor binds to a protein called exportin 1 (XPO1). This protein is involved in the transport of proteins out of the cell nucleus. Thus, selinexor blocks the transport of several proteins involved in cancer cell growth from the cell nucleus to the rest of the cell. This may lead to cancerous myeloma cells being unable to grow and divide, therefore leading to death of the cancer cells[1,3].

What are the benefits of selinexor?

Selinexor has been evaluated in several clinical studies, known as the STORM, STOMP and BOSTON trials. The STOMP trial is still ongoing, while the STORM and BOSTON trials are complete and their results are available.

The phase 2 STORM clinical trial[4] led to the initial approval of selinexor in combination with dexamethasone for use in Europe. This trial assessed a combination of selinexor and dexamethasone in 123 patients with relapsed/refractory myeloma, who received 80mg of selinexor plus 20mg of dexamethasone, twice weekly in four-week cycles. A total of 26% of patients saw an improvement in their myeloma and had 3.7 months without displaying signs of disease progression. Half of the patients in the study were still alive after 8.6 months. Patients who had achieved at least a partial response to treatment (more than a 50% reduction in myeloma markers in the blood), were still alive after 15.6 months[1].

The BOSTON trial led to the full approval of selinexor in combination with bortezomib and dexamethasone, and assessed 402 patients with relapsed/refractory myeloma who had received one to three prior lines of therapy. Patients received either a combination of selinexor, bortezomib and dexamethasone (SVd), or bortezomib and dexamethasone alone (Vd). The BOSTON study showed that patients who received selinexor as part of the treatment took longer to show signs of disease progression, had a higher rate of survival and also a higher rate of response to therapy[4]. Patients who received selinexor and had received one prior line of therapy took 21 months to first show signs of disease progression compared to 10.7 months in patients who did not receive selinexor. Patients who had never had prior exposure to a proteasome inhibitor or bortezomib took 29.5 months to first show signs of disease progression when taking selinexor compared to 9.7 months for patients who did not receive selinexor[4].

The phase 1b/2 STOMP trial is still ongoing and is assessing the use of a combination of selinexor and dexamethasone with various myeloma medications, including pomalidomide, bortezomib, lenalidomide, daratumumab, carfilzomib, ixazomib, elotuzumab and belantamab mafodotin in patients who had progressed disease. So far, of 42 patients who received a combination of selinexor, bortezomib and dexamethasone, 58% have shown a response to treatment. This study has also shown that patients who are not refractory to a proteasome inhibitor have an even higher response rate, at 84%, and first show signs of disease progression after 17.8 months, compared to nine months in other treatment groups[5]. In 11 patients who had previously received an anti-BCMA therapy, half of these patients survived for 14.8 months or more[6].

What are the side effects of selinexor?

The most common side effects of selinexor, in combination with bortezomib and dexamethasone, affecting 30% or more of patients, include[3,7]:

- Nausea, affecting 75% of patients
- Thrombocytopenia (low levels of platelets, a component of blood important for clotting), affecting 62% of patients
- Fatigue, affecting 66% of patients
- Anaemia (low red blood cell count)
- Decreased appetite, affecting 35% of patients
- Decreased weight
- Diarrhoea
- Vomiting

- Hyponatraemia (low blood sodium level)
- Neutropenia (low levels of neutrophils, a type of white blood cell)
- Leukopenia (low white blood cell count)
- Peripheral neuropathy (nerve damage, especially in the arms and legs)
- Back pain

In the STORM trial, 118 of the 123 patients discontinued treatment due to adverse events, with the majority of events occurring in the first two treatment cycles. The most common reasons for discontinuation of treatment were thrombocytopenia/low platelets (in 43% of the patients), fatigue (in 16%), and neutropenia/low white blood cells (in 11%). To manage the occurrence of adverse events, supportive care was provided in the form of medicines to stimulate bone marrow to make new blood cells and platelets, as well as appropriate fluid and caloric intake, appetite stimulants and antinausea agents. During the study, 12 patients died due to adverse events. In two of these cases, the cause of death could be directly linked to pneumonia as a result of the treatment[1].

To manage adverse events, the manufacturer recommends maintaining adequate fluid and caloric intake, as well as the use of intravenous hydration. Anti-nausea medicines (5-HT3 receptor antagonists) are also recommended prior to treatment with selinexor. For more serious adverse events such as thrombocytopenia and neutropenia, frequent monitoring is recommended e.g., blood tests, especially in the first three months, for signs of infection or changes in the amounts of blood cells. Medications that can stimulate bone marrow or platelet infusions can be provided if necessary. The dose of selinexor can also be decreased in 20mg intervals from the starting dose to reduce the emergence and severity of adverse events[8].

In the BOSTON trial, reducing the dose of selinexor from 100mg to a median dose of 80mg per week was found to reduce adverse events and improve quality of life[9]. This trial also demonstrated that the occurrence of nausea decreased with longer duration of treatment, with more than 90% of patients not experiencing nausea after their first two treatment cycles[10].

How and when is selinexor given?

Selinexor is orally administered in the form of 20mg film coated tablets[3]. The recommended dose when used in combination with bortezomib and dexamethasone is 100mg once weekly. When used with dexamethasone alone, the dose is 80mg on days one and three on a weekly basis[8].

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MPE is a network of European myeloma patient organisations. It supports national patient organisations to improve treatment and access for patients in their countries and helps inform and raise awareness at a European level through its educational programmes. Please note, this information does not replace the information provided by your doctor. If there is anything that is not clear to you, please always ask your clinical team.

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mpeurope
@mpeurope
info.@mpeurope.org
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