Imnovid® (pomalidomide)

This Horizons Infosheet contains information on Imnovid® (also known as pomalidomide), a drug being investigated for the treatment of myeloma.

The Horizons Infosheet series provides information relating to novel drugs 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 drug development.

The drugs 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 Imnovid?

Imnovid is a drug that is being used to treat myeloma and belongs to a group of drugs known as immunomodulatory drugs (IMiDs).

Imnovid is the third type of IMiD to be used to treat myeloma

after thalidomide and Revlimid® (lenalidomide). Imnovid is a chemical derivative of thalidomide.

How does Imnovid work?

Imnovid works in a similar manner to thalidomide and Revlimid and is likely to have several mechanisms of action against myeloma cells.

It acts mainly by encouraging the patient's immune system to attack and destroy myeloma cells. It also prevents the growth of new blood vessels, thereby reducing the supply of oxygen and nutrients to the myeloma cells.

The fact that Imnovid works in many ways is thought to be why it is so active against myeloma.

Its possible mechanisms of action are shown in Figure 1.

Imnovid is thought to work in the following ways:

1. Stimulating the immune system to attack the myeloma cells
2. Blocking the growth of new blood vessels that supply the myeloma cells with oxygen and nutrition (anti-angiogenesis)
3. Directly killing and/or preventing the growth of myeloma cells
4. Preventing the myeloma cells from sticking to the bone marrow
5. Altering the production of chemical messages involved in the growth and survival of myeloma cells

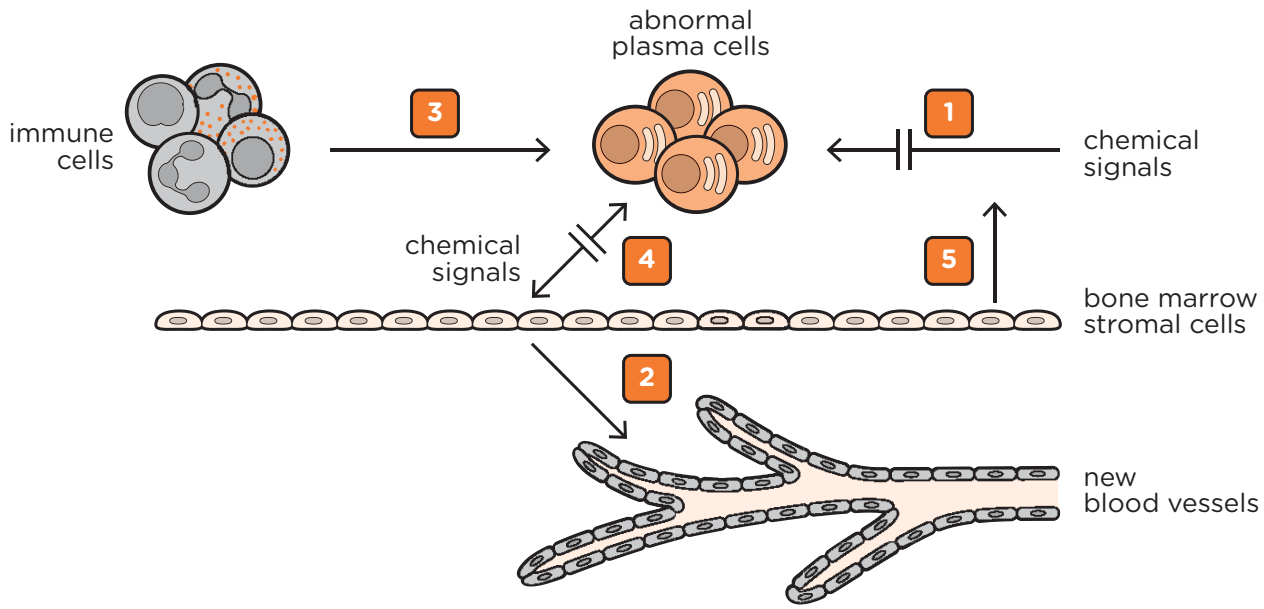

Figure 1. Imnovid's mechanisms of action

How is Imnovid given?

Imnovid is given orally, as a capsule. The recommended starting dose of Imnovid is 4mg taken once daily on days 1 – 21 of repeated 28-day cycles until disease progression.

Imnovid can be given as a monotherapy (i.e. used on its own and not in combination with other drugs) but it has been shown to be most effective when used in combination with other anti-myeloma treatments such as dexamethasone.

What evidence exists to support the use of Imnovid?

A large-scale Phase III clinical trial (known as the Nimbus trial), involving 455 patients, compared the effectiveness of Imnovid in combination with low-dose dexamethasone to high-dose dexamethasone alone, in relapsed and refractory myeloma patients who had previously been treated with both Revlimid and Velcade. The results of the trial showed that Imnovid in combination with low-dose dexamethasone significantly improved progression free survival (the length of time following treatment before the myeloma starts to come back) and overall survival compared to high-dose dexamethasone alone. These results led to a European licence for Imnovid (see section on 'UK availability of Imnovid').

No trials have yet investigated the use of Imnovid in newly diagnosed myeloma patients.

What are the possible known side-effects of Imnovid?

Some of the more common side-effects of Imnovid that have been reported include: low red blood counts (which may cause fatigue and weakness), loss of appetite, shortness of breath (dyspnoea) and constipation, diarrhoea or nausea.

Imnovid can also cause heart problems (or worsen pre-existing heart conditions), and also lung and liver problems. Patients receiving Imnovid will therefore be monitored carefully during treatment.

Is Imnovid currently available in any UK clinical trials?

For an up-to-date list of UK clinical trials involving Imnovid, 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.

UK availability of Imnovid

Before a drug can be widely used, it must first be licensed as a safe and effective treatment. This is usually done by the European licensing body, the European Medicines Agency (EMA) and involves a review of evidence from large-scale clinical trials.

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). However, in Wales they also have their own appraisal body known as the All Wales Medicines Strategy Group (AWMSG). NICE recommendations are usually adopted in Northern Ireland. Scotland's drug appraisal body is the Scottish Medicines Consortium (SMC).

Imnovid was granted a licence for use in myeloma patients across Europe by the EMA in August 2013. It has been licensed for myeloma patients who have received at least two prior treatments, including Revlimid and Velcade, and whose myeloma has progressed within 60 days of taking the last treatment.

Both the SMC and the AWMSG approved Imnovid for use in Scotland and Wales in the licensed setting.

NICE issued negative guidance on Imnovid in England in February 2015. This was because NICE believed there to be too much uncertainty over whether the clinical benefits of Imnovid justified the costs of the drug to the NHS.

The drug company and Myeloma UK are continuing to pursue all avenues to seek routine funding in England for Imnovid.

Future directions

Imnovid is being studied in clinical trials around the world in combination with established treatments suh as dexamethasone, cyclophosphamide, and Velcade, but also with more experimental drugs such as the newer proteasome inhibitors Ninlaro® (ixazomib) and marizomib.

Current clinical trials are designed to provide information about the safest and most effective way to use Imnovid in myeloma. Trials investigating Imnovid as a treatment for newly diagnosed myeloma patients are expected to follow soon.

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. All Myeloma UK publications are extensively reviewed by patients and healthcare professionals prior to publication.

Other information available from Myeloma UK

Myeloma UK has a range of Essential Guides, Infoguides and Infosheets available covering many 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 the **Myeloma Infoline: 0800 980 3332** or **1800 937 773** from Ireland.

The Myeloma Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland. From outside the UK and Ireland, call **0131 557 9988** (charged at normal rate).

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

Notes

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