

Thalidomide (Thalomid®)

What is thalidomide?

Thalidomide, also known as Thalomid®, belongs to a group of drugs called immunomodulatory drugs (IMiD) which work by modifying the immune system. The immune system is a collection of tissues and organs that help to protect the body from infection and against disease. First prescribed in the 1950s for nausea and insomnia in pregnant women, thalidomide was taken off the market in the 1960s when it was found to cause birth defects. Scientists then discovered it can be used to treat diseases of the immune system such as myeloma. Thalidomide has a similar chemical structure to other next generation immunomodulatory drugs, such as lenalidomide and pomalidomide which are also used to treat myeloma.

How does thalidomide work?

Thalidomide is a more targeted therapy than conventional chemotherapy and is thought to have several mechanisms of action that affect myeloma cell survival. However, the mechanism of action is not fully understood.

Thalidomide is thought to work in the following ways:

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

How is thalidomide given?

Thalidomide comes in tablet form and is taken orally; the tablets should be swallowed whole at least an hour after food. Thalidomide can be taken at any time of the day however it can cause patients to feel drowsy. It is for this reason that it is often recommended that it be taken in the evening just before bed.

Thalidomide is usually taken for 21 days followed by a seven day rest which completes the 28 day cycle. It is commonly given in combination with a chemotherapy tablet and steroid tablet that are prescribed once per week during the 21 day period of the cycle. Most people will continue this regime until it is thought that a deep response has been achieved or the myeloma is showing signs of increasing.

Thalidomide can also be used as maintenance therapy after autologous stem cell transplant. This is a continuous daily dose to help consolidate the effects of the transplant.

When is thalidomide available for use in Australia on the Pharmaceutical Benefits Scheme (PBS)?

In Australia thalidomide is subsidised on the PBS at different stages during the course of the disease. It may be prescribed at diagnosis, at relapse or for maintenance therapy after an autologous stem cell transplant. If thalidomide cannot be tolerated, there are other treatment options available.

How to tell if thalidomide is working?

Patients may observe a reduction in the symptoms caused by the myeloma associated with an improved quality of life. The doctor will also order tests at the start of each treatment cycle to monitor response. These tests may vary from patient to patient but generally include regular blood and/or urine testing and occasional x-rays or bone marrow biopsies.

What are the potential side effects?

As with all drugs, thalidomide has many potential side effects. They can vary considerably from patient to patient and may be mild or more serious. Often the best way to reduce side effects is to lower the dose. It is possible to do this without compromising on efficacy. As side effects can usually be treated or managed, it is very important to highlight them promptly to the doctor or nurse.

Birth defects

Both men and women who are taking thalidomide are educated on the risks to an unborn child and are asked strictly not to reproduce while taking thalidomide. The manufacturer has a pregnancy prevention programme in place to ensure that thalidomide is stored, prescribed, handled and taken safely.



Peripheral neuropathy

Thalidomide can cause damage to the long nerves radiating from the spine, usually starting in the hands and/or feet then progressing up the arms and legs. This can present as feelings of numbness, tingling, increased sensitivity, burning, pain.

The best way to manage peripheral neuropathy is to report any symptoms to the doctor or nurse as soon as possible. They may recommend a dose reduction or taking a break until symptoms subside. The effects of peripheral neuropathy can be irreversible if left unattended for too long.

Cramps

A cramp is an uncontrollable and painful spasm of a muscle and may also be accompanied by twitching. Twitching is an involuntary contraction then relaxation of a muscle which is sometimes caused by nerve damage from thalidomide. Cramps and twitches often occur at night as muscles try to relax. Gentle stretching, massage and ensuring adequate salt balance in the body can help relieve the symptoms of cramps.

For more information about peripheral neuropathy and cramps, please see the *Managing Peripheral Neuropathy Book – A guide for people with myeloma* at www.myeloma.org.au or call head office for a copy.

Drowsiness

Drowsiness is a common and expected side effect because thalidomide's original use was as a sedative. Drowsiness usually decreases over time while on the same dose, but the doctor may reduce the dose if severe drowsiness occurs. It is recommended to take thalidomide before bed (at least one hour after food) to lessen the effects of drowsiness during the day. If drowsiness is still a problem upon waking, take the dose a little earlier each night until the effects have worn off by morning.

It is also helpful to avoid alcohol. If affected by drowsiness, do not operate machinery or drive a car. Drowsiness can exacerbate problems associated with fatigue, a common symptom for many people with myeloma. A balanced diet, adequate fluid intake, regular exercise and adequate sleep can help minimise the effects of fatigue.

Constipation

A decrease in the normal frequency of bowel movements can occur whilst taking thalidomide. It may be accompanied by gas, pain, or pressure in the stomach. Constipation is usually easier to prevent than to treat.

To help relieve the symptoms of constipation, patients can eat a healthy diet which is high in fibre. Fibre absorbs water making stools softer, bulkier and easier to eliminate. Drinking plenty of fluids (aim for about 8 glasses of water a day) helps the fibre work. Pear or prune juice may also help. Regular gentle exercise keeps the bowels more active to help move things along. Gentle laxatives (consult a nurse or pharmacist) may be needed but if constipation continues to be a problem, talk with the doctor.

Dizziness

Sometimes dizziness occurs just after standing. Sitting upright for a minute or two before standing will help the blood pressure adjust, especially if patients have been lying for a while. If patients are also taking blood pressure, fluid or heart medication, their doctor must be informed.

Blood clots or venous thromboembolic events

Developing a blood clot in deep veins is a potentially serious side effect of treatment with thalidomide. The condition is called deep vein thrombosis (DVT). Symptoms include redness, swelling, tenderness and pain. If patients develop any of these symptoms, the doctor must be informed immediately. Sometimes a piece of the clot breaks off and travels to the lung. This can be life threatening and is called pulmonary embolism (PE). Symptoms of PE include anxiety, shortness of breath with or without exertion and chest pain/tightness. Patients must seek medical assistance urgently if these symptoms occur.

Each person is assessed for their risk of VTE and may be prescribed an anticoagulant drug such as aspirin or low-dose heparin to prevent (prophylaxis) or to treat VTE.

Low blood counts

Thalidomide can sometimes cause a decrease in the number of white blood cells and platelets in the blood. A low white blood cell count will increase the risk of infection and extra precautions will be required such as diligent hand washing and avoidance of people with infections. A sign of infection is a fever or temperature of 38°C or above.

If a patient's temperature is 38°C or above, medical attention must be sought immediately

If the white cell count is consistently low, it may be necessary to have an injection of granulocyte-colony stimulating factor (G-CSF), to increase the white blood cell count.

A low platelet count (thrombocytopenia) increases the risk of bruising and bleeding. If the platelet count is too low a platelet transfusion may be required.

The blood counts will be measured regularly to monitor for changes. In some cases, treatment may be delayed until blood counts have improved.

Skin rashes

Thalidomide can sometimes cause a rash which may begin on the trunk (body) and spread to the arms and legs. This can occur within the first few weeks of starting treatment but usually clears up by itself. Sometimes the rash may need treatment. If the rash continues and is problematic, the dose of thalidomide may be reduced or stopped temporarily. Rarely, rashes may be a more serious side effect of thalidomide where skin can turn red, blister and peel (Steven Johnson syndrome or toxic epidermal necrolysis). If this happens, you should inform your doctor immediately and thalidomide should be stopped straightaway.

Special precautions

Patients receiving Thalidomide under this PBS listing must be registered in the i-access risk management program, run by the manufacturer, Celgene. This is an information and consent process, to ensure safety recommendations are adhered to.

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For further information please contact our Myeloma Support Nurses on our toll free Support Line:

1800 MYELOMA (1800 693 566)
or visit our website: **www.myeloma.org.au**