# THALIDOMIDE

## What are the aims of this leaflet?

This leaflet has been written to help you understand more about thalidomide. It tells you what it is, how it works, how it is used to treat skin conditions, and where you can find out more about it. Please note that some of the treatment options in this leaflet may not be available on the NHS.

## What is thalidomide and how does it work?

Thalidomide was first introduced in 1957 as a sedative tablet that could also control severe morning sickness in pregnant women. When taken in pregnancy, it was associated with severe birth defects from which many babies died across the world. This did not result in any action for several years and it was withdrawn from the UK in 1961. After this tragedy, stronger rules were introduced to improve the safety of medicines.

Thalidomide re-emerged as a therapeutic agent and in 1998 was approved in the USA for treatment of multiple myeloma, a haematological (blood) condition. How exactly thalidomide works is not clear. It appears that thalidomide acts on a part of the immune system and plays a role in wound healing and reduces inflammation.

## What skin conditions are treated with thalidomide?

It is used by dermatologists **as an off-license medication** (this means that it is used in a way that is different to that described in the license) for a number of treatment-resistant skin conditions, including some types of leprosy (response rates greater than 90%). Other skin diseases treated with thalidomide are HIV associated aphthous ulceration, nodular prurigo, Behçet's disease, discoid and systemic lupus erythematosus, pyoderma gangrenosum, actinic prurigo, graft versus host disease, polymorphic light eruption, lichen planus, bullous pemphigoid and cutaneous sarcoidosis. It has also been used

in palliative medicine as a sedative and antiemetic (preventing vomiting) with some pain relief properties. Thalidomide is usually only considered when other treatments have failed.

**What does "off-license" mean in relation to a drug?**

An unlicensed drug is one that has not been awarded a market authorisation (MA) by the UK Medicines Healthcare Products Regulatory Agency (MHRA). The reasons a drug has not been awarded MA by a country are because the company producing it has not applied for a license in a specific condition, or because safety and efficacy data are insufficient. Thalidomide is licensed (so has an MA) for use in multiple myeloma in the UK so safety and efficacy in that condition has been evaluated and therefore approval granted. However, it does not have a license for use in skin conditions so is an "off-license" drug. This means that your dermatologists will only recommend it if they consider that it is in your best interest and that any alternative licensed drugs are not suitable.

**Will thalidomide cure my skin condition?**

Thalidomide does not work for everybody, but it may improve and control certain skin diseases. It is not a cure and the condition can recur when treatment is stopped.

**How should I take thalidomide?**

For skin conditions, thalidomide is available as 50mg hard capsules. It is best taken on an empty stomach, at least 1 hour after eating a meal. Thalidomide causes drowsiness, so it should be taken at bedtime. Do not drive or operate machinery if you feel drowsy. Alcohol should be avoided as it may increase the possibility of drowsiness.

**What dose of thalidomide should I take?**

The dose of thalidomide will depend on your skin disease and whether you have other medical conditions. The dose may be adjusted depending on how well it works and any side effects. In adults the usual dose is 50 to 200mg per day.

**When should thalidomide be avoided?**

- Anybody planning a pregnancy **must not** take thalidomide. Women must not take thalidomide, if they think they may be pregnant. Thalidomide is present in milk in animal studies and must not therefore be taken during breastfeeding. Men must not father children or donate semen. (See below for more details).
- Peripheral neuropathy (a condition in which the nerves in hands and/or feet are not working correctly) may be made worse by thalidomide.

**Thalidomide and pregnancy**

Thalidomide causes severe birth defects affecting the arms, legs, eyes, ears, face and heart. There is even a risk of foetal death. It must **never** be taken during pregnancy.

All women of childbearing potential should be counselled about this risk and entered into a **pregnancy prevention programme** before starting thalidomide to minimise the risk of pregnancy. Even if you do not have regular menstrual bleeding, you may become pregnant.

Women with fertility problems are also required to use birth control while taking thalidomide.

Women who are beyond the menopause or who have been sterilised may be excluded from the pregnancy prevention programme.

For women of childbearing potential:

Your doctor will make sure that you have negative pregnancy tests
- before treatment
- every 4 weeks during treatment
- 4 weeks after stopping treatment

You must use one, and preferably two, forms of effective contraception:
- for 4 weeks before starting treatment
- during treatment
- until 4 weeks after stopping treatment

For the best type of contraception you should discuss this with your primary care doctor.

**For men taking Thalidomide**

Always use a condom **(even if you have had a vasectomy).** Thalidomide is present in semen. Pregnancy and any exposure during pregnancy **must** be avoided

- during treatment
- for 1 week after stopping treatment

- You must not donate semen:

  - during treatment
  - for 1 week after stopping treatment

**Pregnancy prevention programme**

• Women will need to sign a form stating that they understand the harmful effects of thalidomide on an unborn baby and that they agree to take part in the pregnancy prevention programme.

• Thalidomide should be started on day 2 or 3 of the menstrual cycle.

- The maximum supply of medication is for 30 days and the prescription is only valid for 7 days after being signed. A negative pregnancy test is required before each prescription.

- The birth control method must be proven highly effective, such as birth control pills, an intrauterine device (IUD), intrauterine coil, depot injections (slow release medication), subcutaneous implant, tubal ligation or a sexual partner's vasectomy. The latter should be confirmed by two negative semen tests.

- The extra form of birth control should be the barrier method such as a condom, diaphragm, cervical cap, or contraceptive sponge.

If a pregnancy occurs or is suspected whilst taking thalidomide, the drug must be stopped immediately. Contact your primary care doctor and dermatologist, for further advice.

**Will thalidomide affect fertility or future pregnancies?**

Thalidomide does not affect fertility and there is no long-lasting effect on future pregnancies. As stated above however, pregnancy must be avoided for a

month after completing treatment to avoid exposing an unborn baby to any medication that might still be present in the woman or man's body.

**What are the common side effects of thalidomide?**

Thalidomide commonly causes sedation, constipation and itching. Other common side effects include a dry mouth, dizziness, breathing difficulty, rash and tremor. Thalidomide can lower your white and red blood cells. If you develop mouth ulcers, a sore throat or a fever, you need to inform your doctor immediately. Thalidomide can also reduce the number of platelets in your blood (thrombocytopaenia), which may result in an increased chance of excessive bruising or bleeding.
Thalidomide can cause peripheral neuropathy, which means damage to the nerve endings of the hands and feet. You may experience numbness, tingling, weakness, abnormal coordination, pain and/or weakness in the hands, arms, legs and feet. Any of these symptoms should be reported as soon as possible to your doctor.

**What are the rarer side effects of thalidomide?**

Thalidomide can cause damage to the liver, which may not cause symptoms, so it is important to have regular blood tests as advised by your doctor. Another rare side effect is an underactive thyroid.

Thalidomide can lead to the formation of blood clots (thromboembolism). Sudden breathlessness or chest pain, or unexplained pain and swelling of an arm or leg, may be a sign of a blood clot. If you develop any of these symptoms you must seek urgent medical advice. Smokers are at increased risk of blood clots and should make every effort to stop smoking.

Thalidomide can slow the heart rate causing dizziness and fainting, so the pulse and blood pressure should be checked regularly. It may also increase the risk of a heart attack and stroke.

Very rarely, thalidomide can cause a severe allergic rash with skin blistering. It should be stopped immediately if a new widespread rash appears.

**How will I be monitored for the side-effects of thalidomide treatment?**

Before starting treatment, a clinical examination should be performed including a neurological examination. Other tests before starting treatment

include a pregnancy test, full blood count, kidney and liver tests, HIV and sometimes nerve conduction studies.

While on treatment, regular blood tests (usually every 3 months) to check the kidneys, liver, white blood cell count and platelets are required. Monthly pregnancy tests are required if you are on the pregnancy prevention programme. A neurological examination is recommended monthly for the first 3 months and then every 6 months. Some hospitals repeat nerve conduction studies twice yearly or if the dose is increased. If symptoms develop such as numbness or strange sensation in the hands or feet, difficulties with coordination, or weakness, examination of the nervous system and nerve conduction studies may be needed. In HIV positive patients, the HIV viral load will need to be repeated at 1 month, 3 months and every 3 months thereafter.

**Can I give blood if I am taking thalidomide?**

Patients on thalidomide must **not** give blood.

**What happens if I miss a dose of thalidomide?**

Take the medicine as soon as you can, but skip the missed dose if it is almost time for your next dose. Do not take two doses at one time.

**What should I avoid while taking thalidomide?**

- You must not donate blood or sperm while you are using thalidomide, and for at least 4 weeks after your last dose.
- Avoid exposing another person to your blood or semen through casual or sexual contact.
- Avoid driving or hazardous activity until you know how this medicine will affect you.
- Your reactions could be impaired. Avoid getting up too fast from a sitting or lying position, or you may feel dizzy.
- Drinking alcohol should be avoided (details as under).

**May I drink alcohol while taking thalidomide?**

Drinking alcohol will increase the sedating effects of thalidomide and will increase tiredness. It will impair thinking and reactions and therefore decrease the ability to drive or operate machinery.

Because of the risk of liver damage, alcohol intake should be limited to the Chief Medical Officer's recommended alcohol guidelines (currently 14 units per week for men and women) whilst taking thalidomide.

**Can I take other medications at the same time as thalidomide?**

Any other medicine that may cause drowsiness may make a person more sleepy when taken with thalidomide. This includes some over-the-counter cold or hay fever medications, sleeping tablets, some anti-depressants, muscle relaxants, seizure treatment and pain killers. (Please ask your pharmacist or doctor if in doubt).

Thalidomide may aggravate the side effect of a slow heartbeat caused by some drugs for blood pressure and by tricyclic antidepressants. This may lead to dizziness or fainting.

Many drugs may interact with thalidomide. Always discuss this with your doctor before starting any new medication.

**Where can I get more information about thalidomide?**

*Web links to detailed leaflets:*

https://www.medicines.org.uk/emc/medicine/21005

https://www.medicines.org.uk/emc/PIL.22442.latest.pdf

http://dermnetnz.org/treatments/thalidomide.html

http://www.emedicinehealth.com/drug-thalidomide/article_em.htm

For details of source materials used please contact the Clinical Standards Unit (clinicalstandards@bad.org.uk).

**This leaflet aims to provide accurate information about the subject and is a consensus of the views held by representatives of the British Association of Dermatologists: individual patient circumstances may**

**differ, which might alter both the advice and course of therapy given to you by your doctor.**

*This leaflet has been assessed for readability by the British Association of Dermatologists' Patient Information Lay Review Panel*

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