# Prescribers' guide for Myrin® 50 mg and 100 mg tablets (Thalidomide)

Myrin® 50 mg and 100 mg tablets (thalidomide)

Information for Healthcare Professionals Prescribing or Dispensing Myrin® 50 mg and 100 mg tablets (thalidomide)

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# 1 Introduction

## 1.1 Content and aim of the information kit for Healthcare Professionals

The information kit for Healthcare Professionals contains the following key information for Myrin® (thalidomide):

**Information kit for the prescriber:**

a. Prescription guide of Myrin® (Thalidomide) for prescribers
b. Prescriber receipt form (Annex 1)
c. Pharmacist dispensation guide of Myrin® (Thalidomide) and receipt form (Annex 2)
d. Informed consent form for women of childbearing potential (Annex 3)
e. Informed consent form for women of non-childbearing potential (Annex 4)
f. Informed consent form for men (Annex 5)
g. Current product information (Annex 6)
h. Form for reporting of pregnancy (Annex 7)
i. Form for reporting of pregnancy outcome (Annex 8)
j. Form for reporting of adverse events (Annex 9)

This guide is intended for healthcare professionals involved in prescribing Myrin® 50 mg and 100 mg tablets (thalidomide). The aim of this kit is to provide information on:

- Risk management programme to avoid foetal exposure and prevent harm to unborn babies
- Other side effects of Myrin® (Thalidomide)
- Process for reporting adverse events in patients treated with Myrin® (Thalidomide)

This guide will help you understand these problems and make sure you know what to do before prescribing and dispensing Myrin® (Thalidomide).

This risk management programme to avoid foetal exposure is designed to make sure that unborn babies are not exposed to Myrin® (Thalidomide). It will provide you with information about how to follow the programme and explain your responsibilities.

For your patients' health and safety, please read this guide carefully. You must ensure that your patients fully understand what you have told them about Myrin® (Thalidomide) before starting treatment.

These materials must be used for counselling patients on the risks of Myrin® (Thalidomide) and the precautions to be taken (see section 2: *Risk management programme to avoid foetal exposure*). Additional copies can be obtained by using the contact details displayed on the front of this guide.

A scheme of the complete information flow for correct prescription, ordering and dispensation of Myrin® (Thalidomide) and the respective role of the doctor, the pharmacist, Cherubino as the distributor is described in Section 6.

All educational material has been approved by the Medicines Authorities and will be conditional for the Marketing Authorisation.

## 1.2 Product information

Please refer to the current product information included in the information kit.

# 2 Risk management programme to avoid foetal exposure

| Myrin® (thalidomide) warning: |
|---|

Teratogenic effects: Thalidomide is a powerful human teratogen, inducing a high frequency of severe and life-threatening birth defects. Thalidomide must never be used by patients unless all the conditions of the risk management plan are met.

Myrin® (Thalidomide) must be prescribed and dispensed according to the Myrin® (Thalidomide) risk management programme to avoid foetal exposure. This is necessary because thalidomide is known to cause severe birth defects and foetal death.

In the 1950s and 1960s, approximately 12,000 children were born with severe birth defects caused by thalidomide, and approximately 5,000 are alive today.

The conditions of the Myrin® (thalidomide) risk management programme to avoid foetal exposure must be fulfilled for all male and female patients.

## 2.1 Prescriber registration

It is a requirement of the risk management programme to avoid foetal exposure that all healthcare professionals confirm that they have received, read and understood this information kit before prescribing or dispensing Myrin® (Thalidomide).

Prior to the first prescription of Myrin® (Thalidomide) and thereafter every 2 years, you have to complete the following form and send it to Cherubino Ltd:

- Prescription receipt form (Annex 1)

This form must be sent to: Cherubino Ltd

Phone: 21343270

Fax: 21330916

**Pharmacy registration**
In your kit you have also received a dispensation guide of Myrin® (Thalidomide) and a receipt form for Pharmacists (Annex 2). You need to add this document unfilled to the prescription for the pharmacy (see section 3). The pharmacist will have to sign this document and send it together with the order of Myrin® (Thalidomide) to Cherubino.

## 2.2 Patient information and informed consent

All patients should be given the Myrin® (Thalidomide) patient information and be informed about the risks and benefits of the product. You must ensure that your patients fully understand what you have told them about Myrin® (Thalidomide). As the conditions of the Myrin® (Thalidomide) risk management programme to avoid foetal exposure must be fulfilled for all male as well as female patients and both must follow pregnancy prevention measures, all patients must sign the appropriate informed consent form before starting treatment.

In order to provide appropriate information to your female patients about the precautions they must follow when using Myrin® (Thalidomide), it is important to determine whether your patient is or is not of childbearing potential. Based on the age of the patient you must carefully consider how to proceed with education and counselling regarding pregnancy prevention measures, and evaluate when to involve the patient's parent or guardian. The possibility of female patients becoming pregnant from the age of 8 years (the accepted lower age of menarche) should be considered.

## 2.3 Women of childbearing potential

Thalidomide is absolutely contraindicated in pregnancy and must never be used by women who are pregnant.

Women of child bearing potential should not use thalidomide unless adequate contraceptive methods as outlined in the risk management program are used to prevent pregnancy.

Thalidomide is known to cause teratogenic effects resulting in severe birth defects and foetal death. A single dose taken by a pregnant woman can cause severe birth defects. Severe birth defects affect about 30% of exposed pregnancies with defects such as: ectromelia (amelia, phocomelia, hemimelia) of the upper and/or lower extremities, microtia with abnormality of the external acoustic meatus (blind or absent), middle and internal ear lesions (less frequent), ocular lesions (anophthalmia, microphthalmia), congenital heart disease, renal abnormalities. Other less frequent abnormalities have also been described.

The development of pregnancy during treatment with thalidomide despite contraceptive measures carries a high risk of serious malformations or death of the unborn baby.

Your female patient must be counselled on the risks and benefits of Myrin® (Thalidomide) therapy, including the risk of birth defects, other side effects and important precautions associated with Myrin® (Thalidomide) therapy.

In particular women of childbearing potential receiving thalidomide must be informed:

- About the need to avoid pregnancy. These patients must be adequately counselled regarding the use of pregnancy prevention measures every time a prescription is issued. If your patient is not established on an effective method of pregnancy prevention, they must be referred preferably to an appropriately trained health care professional for advice in order that a pregnancy prevention method can be initiated.
- that contraceptive measures should be started at least 4 weeks prior to initiation of the drug therapy, continued throughout the entire period of treatment (even in the case of dose interruptions) and at least for 12 weeks after cessation of treatment with Myrin® (Thalidomide). This must be followed even if the patient commits to absolute and continuous abstinence confirmed to her physician.
- That before starting treatment, she should have a pregnancy test (sensitivity of a least 25mIU/mL). The test should be performed within 24 hours prior to beginning the therapy. A prescription for thalidomide for a woman of child-bearing age must not be issued by the prescriber until a written report of a negative pregnancy test has been obtained by the prescriber.
- to take Myrin® (Thalidomide) only as prescribed
- not to donate blood whilst or within 12 weeks of stopping taking MYRIN®
- not to take alcoholic drinks throughout Myrin® (Thalidomide) treatment
- that if they discontinue therapy, they must return any unused Myrin® (Thalidomide) to the pharmacy.
- that their Myrin® (thalidomide) is only for them, and it must not be shared with anyone else, even if they have similar symptoms. Myrin® must be stored away safely so no one else could take the tablets by accident. It must be kept out of reach and sight of children.
- to inform her doctor immediately, if she misses, or is suspected to have missed her period or there is any abnormality in menstrual bleeding, or suspects she is pregnant.
- that if she has sexual contact without using a pregnancy prevention method while taking Myrin® (Thalidomide) or believes for any reason that she may be pregnant, she must stop treatment and consult her doctor immediately.

**Pregnancy testing**

This may be embarrassing for some patients and may need to be handled sensitively. Special consideration must be given when communicating such advice to female women. The test must be performed by a healthcare professional, and the result must be negative before Myrin® (Thalidomide) treatment can begin or continue.

If a female patient misses, or is suspected to have missed her period or there is any abnormality in menstrual bleeding, or suspects she is pregnant then a pregnancy test and counselling must be performed immediately.

If pregnancy occurs in a patient during thalidomide treatment, see section 2.6. *Actions in case of actual or suspected foetal exposure to Myrin® (Thalidomide)*.

Thalidomide is contraindicated during breast-feeding. It is not known whether thalidomide is excreted in human milk.

Further pregnancy tests should be performed during Myrin® (Thalidomide) treatment, and a final test conducted after treatment ends.

### 2.3.1 Effective methods of pregnancy prevention

Please advise your patients for her/his most adapt and recognised effective contraceptive method.

If your patient needs to change or stop her pregnancy prevention method during her Myrin® (Thalidomide) therapy, she must understand the need to discuss this first with:

• The physician prescribing her pregnancy prevention method

• The physician prescribing her Myrin® (Thalidomide)

Please note that the concomitant use of HIV-protease inhibitors, griseofulvin, rifampicin, rifabutin, phenytoin, carbamazepine with hormonal contraceptives may reduce their efficacy. Therefore, throughout thalidomide treatment more reliable contraception should be used.

## 2.4 Women of non-childbearing potential

Your female patient must be counselled on the risks and benefits of Myrin® (Thalidomide) therapy, including the risk of birth defects, other side effects and important precautions associated with Myrin® (Thalidomide) therapy.

In particular women of non-childbearing potential receiving thalidomide must be informed:

- to take Myrin® (Thalidomide) only as prescribed
- not to donate blood whilst or within 12 weeks of stopping taking Myrin® (Thalidomide)
- not to take alcoholic drinks throughout MYRIN® treatment
- If they discontinue therapy, they must return any unused Myrin® (Thalidomide) to the pharmacy.
- that their Myrin® (Thalidomide) is only for them, and it must not be shared with anyone else, even if they have similar symptoms. Myrin® must be stored away safely so no one else could take the tablets by accident. It must be kept out of reach and sight of children.

Women that are considered not to have childbearing potential and do not need to undergo pregnancy testing or receive contraceptive advice:

- Age ≥50 years and naturally amenorrhoeic for ≥1 year. Please note amenorrhoea following cancer therapy does not rule out childbearing potential
- Premature ovarian failure confirmed by a specialist gynaecologist
- Previous bilateral salpingo-oophorectomy, or hysterectomy
- XY genotype, Turner syndrome, uterine agenesis.

Women of childbearing potential are all other women who are menstruating or premenopausal, even those who abstain from sexual intercourse.

Prescribers are advised to refer their patient for a gynaecological opinion if they are unsure if their patient meets the criteria for being of non-childbearing potential.

## 2.5 Men

Your male patients must be counselled on the risks and benefits of Myrin® (Thalidomide) therapy including the risk of birth defects, other side effects and important precautions associated with Myrin® (Thalidomide) therapy.

Because thalidomide is present in the semen of patients receiving the medicinal product, males receiving thalidomide must be informed:

- to take Myrin® only as prescribed
- to always use a condom during any sexual contact with women of child bearing potential. As thalidomide is found in semen, male patients must use condoms during treatment and for 1 week after dose interruption and/or cessation of treatment if their partner is pregnant or is of childbearing potential and not using an effective pregnancy prevention method.
- to inform his doctor immediately, if the female partner misses, or is suspected to have missed her period or there is any abnormality in menstrual bleeding, or suspects she is pregnant
- not to donate semen whilst or within 12 weeks of stopping taking Myrin® (thalidomide)
- not to donate blood whilst or within 12 weeks of stopping taking Myrin® (thalidomide)
- not to take alcoholic drinks throughout MYRIN® treatment
- that if they discontinue therapy, they must return any unused Myrin® (thalidomide) to the pharmacy.
- that their Myrin® (thalidomide) is only for them, and it must not be shared with anyone else, even if they have similar symptoms. Myrin® must be stored away safely so no one else could take the tablets by accident. It must be kept out of reach and sight of children.

If pregnancy occurs in a partner during thalidomide treatment, see section 2.6. Actions in case of actual or suspected foetal exposure to Myrin® (thalidomide).

### 2.6 Actions in case of actual or suspected foetal exposure to Myrin® (Thalidomide)

In the instance of any positive pregnancy test or suspected foetal exposure to Myrin® (thalidomide) you must:

- stop the treatment immediately
- refer the patient or female pregnant partner of the patient to an obstetrician or gynaecologist experienced in teratology for further evaluation and counselling.
- notify Cherubino Ltd (Tel: 21343270).
- Please also complete the Pregnancy Reporting Form included in this pack and send it to Cherubino Ltd (Annex 7).
- Cherubino Ltd will wish to follow-up with you the progress of all pregnancies and report about the new born baby with the Pregnancy Outcome Reporting Form also included in this pack (Annex 8).
- Report the event the local pharmacovigilance as required by the applicable national law and guidelines

## 3 Prescribers obligations

Healthcare professionals have specific obligations that must be followed when prescribing or dispensing Myrin® (Thalidomide), which are described in the following sections.

As the prescribing physician, you play a central role in ensuring that Myrin® (Thalidomide) is used safely and correctly.

Most importantly, you will be helping to ensure that your patients understand the risks involved in taking Myrin® and that they are aware of their responsibilities in preventing foetal exposure to the drug.

Myrin® (Thalidomide) treatment must be initiated and monitored under the supervision of physicians with expertise in managing immunomodulatory or chemotherapeutic agents and a full understanding of the risks of thalidomide therapy and monitoring requirements.

Before first prescription of Myrin® (Thalidomide) (or every 2 years thereafter) you must ensure that:

- You have received, read and understood the information kit for the prescriber that was sent to you by Cherubino Ltd.
- You have sent the receipt form (Annex 1) to Cherubino Ltd.

Before issuing the initial prescription for Myrin® (Thalidomide) to a specific patient you must ensure that:

- Your patient understands the information and the precautions to be taken. He confirms this by completing the appropriate 'informed consent form' (either Annex 3, 4 or 5 depending on the patient)
- For women of childbearing potential, a written report of a negative pregnancy test (performed within 24 hours prior to beginning the therapy) has been obtained.

At each first and subsequent Myrin® (thalidomide) prescription to a specific patient you must ensure that:

- Your patient is fully educated and counselled on the risks of Myrin® (Thalidomide)
- You provide the patient with a prescription for Myrin® (thalidomide) that contains the treatment regimen (dosage and therapy duration). The maximum prescription length is of 30 days' supply.
- Your patient is using the appropriate pregnancy prevention measures
- Female patients of childbearing potential receive a pregnancy test, which must be negative, before every prescription that you issue
- You prescribe Myrin® (Thalidomide) in accordance with the measures described in this guide and the current product information which is included in the information kit.

At each prescription you will have to provide to the patient the following:

- Their prescription of Myrin® (Thalidomide)
- a copy of their signed informed consent (either Annex 3, 4 or 5 depending on the patient)
- Dispensation guide of Myrin® (Thalidomide) and receipt form for Pharmacists (Annex 2), that the pharmacist will have to sign

### 3.1 Repeat of subsequent prescriptions

The patient must return to the initial prescriber for every repeat prescription of Myrin®. If a patient is transferred or consulted by another prescriber, the initial prescriber must remind them to contact Cherubino Ltd to be sure that they received the information kit.

# 4 Safety management advice

In addition to the information about the risk management programme to avoid foetal exposure, this kit contains important advice for healthcare professionals about how to minimise the risk of adverse events during treatment with Myrin® (Thalidomide).

For further information about the appropriate use and safety profile of Myrin® (Thalidomide) please refer to the current product information which is included in the information kit.

Patients must be counselled on the risks and benefits of Myrin® (Thalidomide) therapy, including the risk of birth defects, other side effects and important precautions associated with Myrin® (Thalidomide) therapy.

## 4.1 Reporting of any other adverse events

In the instance of any adverse event suspected to be related to the treatment with Myrin® (Thalidomide) you must also report it to the Malta Medicines Authority by post or e-mail: ADR reporting/ Sir Temi Zammit Building, Malta Life Sciences Park, San Gwann or on www.medicinesauthority.gov.mt/adrportal using the adverse drug reaction form of the Medicines Authority (download see www.maltamedicinesauthority (gov.mt))

and must also report it to Cherubino Ltd

- Notify Cherubino Ltd immediately (see contact details in section 5)
- Please use the adverse event form included in this pack (Annex 9).
- Report the event to the competent authority as required by the applicable national law and guidelines.

### 4.2 Other special warnings and precautions for use

For extensive safety considerations and for the full list of undesirable effects, please read carefully the current product information included in the information kit.

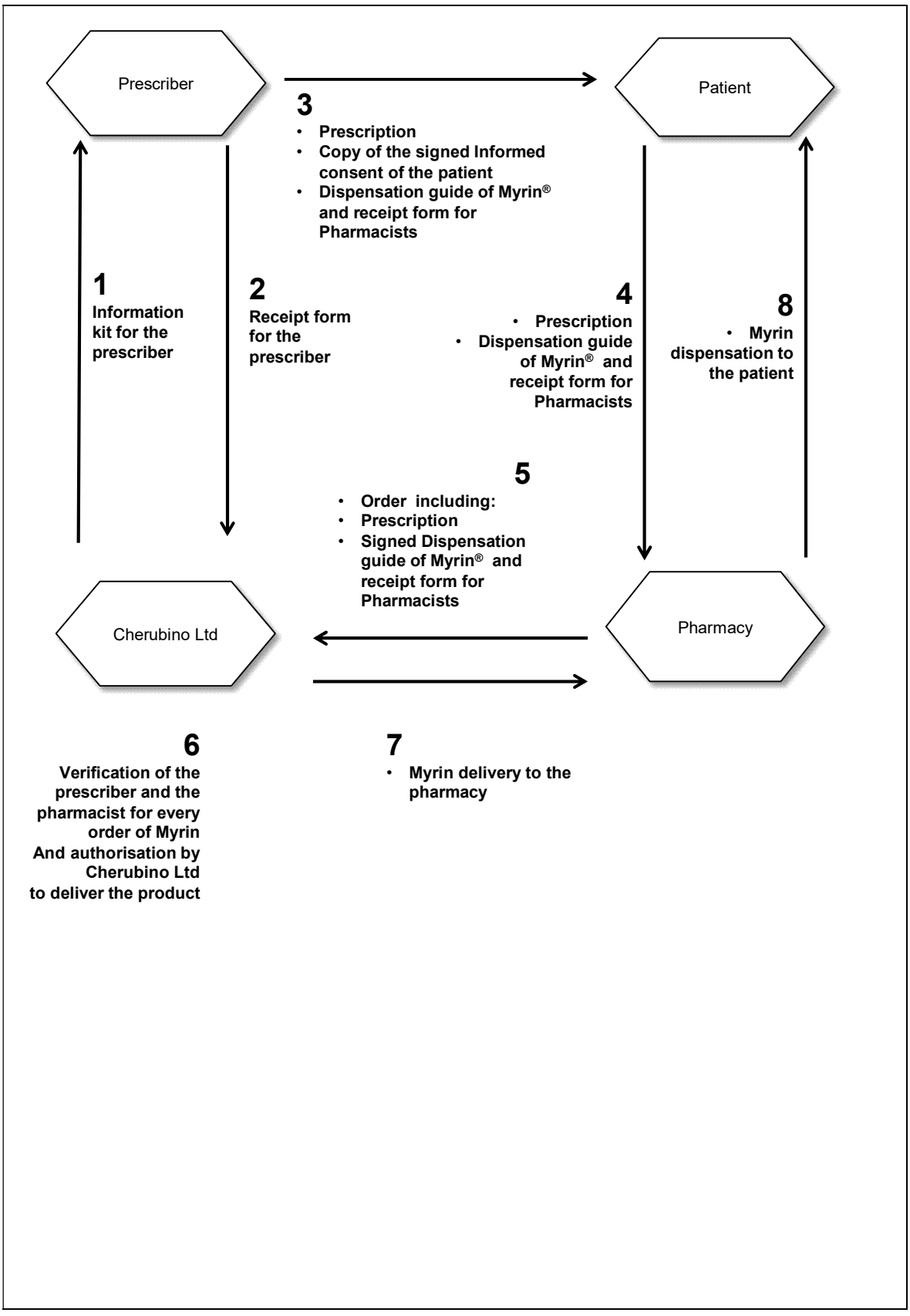
In case of undesirable effects, dose reduction or discontinuation may be required.

Patients must be advised never to give Myrin® (Thalidomide) to another person and to return any unused tablets to their pharmacist at the end of the treatment

## 5 Contact details

For information and questions on the risk management programme to avoid foetal exposure, medical information, product deliveries and adverse events (including suspected or confirmed pregnancy or foetal exposure) please contact: Cherubino Ltd. On 21343270 or on email: elaine@cherubino.com.mt

## 6 Information flow for correct prescription, dispensation and reporting of pregnancy



Information flow:

**STEP 1**

Cherubino Ltd sends to the prescriber the information kit for the prescriber containing:

a. **Prescription guide of Myrin® (Thalidomide) for prescribers**
**b. Prescriber receipt form**
**c. Dispensation guide of Myrin® (Thalidomide) and receipt form for Pharmacists**
**d. Informed consent form for women of childbearing potential**
**e. Informed consent form for women of non-childbearing potential**
**f. Informed consent form for men**
**g. Current product information**
**h. Form for reporting of pregnancy**
**i. Form for reporting of pregnancy outcome**
**j. Form for reporting of adverse events**

**STEP 2**

The prescriber sends back the **Prescriber receipt form** to Cherubino Ltd.

Cherubino Ltd keeps a record of all prescribers that have received the information kit and confirmed the reception by sending back the receipt form

**STEP 3**

You prescribe Myrin® (Thalidomide). At each prescription you will have to provide the patient with the following:

- Their **prescription of Myrin® (Thalidomide)**
- a copy of their signed **informed consent**
- **Dispensation guide of Myrin® (Thalidomide) and receipt form for Pharmacists**, that the pharmacist will have to sign.

**STEP 4**

The patient will present the pharmacy with:

- Their **prescription of Myrin® (Thalidomide)**
- Dispensation guide of Myrin® (Thalidomide) and receipt form for Pharmacists, that the pharmacist will have to sign.

**STEP 5**

The pharmacy will order: Myrin® (Thalidomide) to Cherubino by providing:

- The **prescription of Myrin® (Thalidomide**)
- Copy of the **dispensation guide of Myrin® (Thalidomide) and receipt form for Pharmacists**, signed by the pharmacist

**STEP 6**

Cherubino Ltd will meet regularly to verify that for every order:

- the prescriber is in the list of doctors that have received and confirmed the reception of the information kit
- The pharmacist has signed the **dispensation guide of Myrin® (Thalidomide) and receipt form for Pharmacists**

If this information is correct and complete Cherubino Ltd will authorise to deliver the product for the specific prescription

If this information is not correct of incomplete the delivery of the product is denied and contact is taken with the pharmacy and/or the prescriber.

**STEP 7**

Myrin is delivered to the pharmacy for the specific prescription

**STEP 8**

Myrin is dispensed to the patient

## Reporting of pregnancy and adverse events

In the instance of any suspect of pregnancy or adverse even suspected to be related to the treatment with Myrin® (thalidomide), these have to be reported to Cherubino Ltd by using the appropriate forms which are part of the information kit for prescribers.

- Form for reporting of Pregnancy
- Form for reporting of Pregnancy outcome
- Form for reporting of adverse events

Pharmacies are not provided with these forms by default, but they can request them any time to Cherubino Ltd.