European Medicines Agency

London, 24 January 2008
Doc. Ref. EMEA/543524/2007

QUESTIONS AND ANSWERS ON THE POSITIVE OPINION
for
THALIDOMIDE PHARMION

International non-proprietary name (INN): ***thalidomide***

On 24 January 2008, the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion recommending that a marketing authorisation for Thalidomide Pharmion be granted. Because thalidomide is known to cause birth defects, a number of measures have been put in place to minimise the risk of exposure of unborn children to the medicine.

What is Thalidomide Pharmion?
Thalidomide Pharmion is a medicine containing the active substance thalidomide. It is to be used to treat multiple myeloma in combination with other medicines (melphalan and prednisone). Multiple myeloma is a rare type of bone marrow cancer that usually occurs in older people and that is very difficult to treat.

Thalidomide Pharmion is to be used in patients who cannot be treated with high-dose chemotherapy (anticancer treatments), or in patients aged over 65 years who have not been treated for multiple myeloma before.

What is thalidomide?
Thalidomide is a substance that is thought to work in multiple myeloma by blocking the development of cancer cells, and by stimulating some of the specialised cells of the immune system (the body's defence mechanism) to attack the cancer cells. Clinical studies have shown that adding thalidomide to melphalan and prednisone can prolong survival time in patients with multiple myeloma.

Thalidomide is 'teratogenic', meaning that it has a harmful effect on the unborn child. This was not known when thalidomide was first used in medicines in the late 1950s and early 1960s. At that time, it was available without a prescription, mostly for use as a sedative but also as a treatment for morning sickness. The use of thalidomide during the first three months of pregnancy led to the birth of babies with malformed, short or absent limbs, and other severe, life-threatening deformities. This led to its withdrawal from the market worldwide in the mid-1960s.

Why has thalidomide been granted a positive opinion?
As studies have shown that thalidomide has significant activity against multiple myeloma, Pharmion applied for a marketing authorisation for the medicine in Europe. On the basis of the information supplied by the company, the CHMP has concluded that the medicine's benefits outweigh its risks for the treatment of multiple myeloma, provided that strict measures are put in place to avoid exposure of unborn children to thalidomide.

Thalidomide is already authorised for multiple myeloma in other countries outside the European Union[1]. Thalidomide has also been used in Europe for a number of years under very strict conditions, through compassionate use or named-patient programmes, which allow certain patients to access medicines before they are licensed.

[1] Thalidomide is authorised for the treatment of multiple myeloma in Australia, Israel, New Zealand, South Africa, South Korea, Thailand, Turkey and the United States of America.

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Have the views of thalidomide victims and of patients been considered?
During the assessment of Thalidomide Pharmion by the CHMP, associations of thalidomide victims and of myeloma patients were consulted, so that their views could be taken into account. The associations contributed to the contents of the Package Leaflet (the information sheet given to the patient with the medicine), the information printed on the medicine's packaging, and the development of the plan put in place to manage the risks associated with the use of Thalidomide Pharmion.

The CHMP will continue to inform these groups about the monitoring of Thalidomide Pharmion's safety once it is on the market. It will also tell them if any changes are made to the ways in which the medicine can be used.

What measures are being put in place to minimise the risks associated with Thalidomide Pharmion when it is available on the market?
The CHMP has requested that a number of measures be put in place in all Member States, to ensure that doctors, nurses, pharmacists and patients are fully aware of the risks associated with the medicine and that unborn children are not exposed to thalidomide.

Before the medicine can be marketed, the company will put a programme in place, including educational kits, to inform health care professionals about the special measures they will need to take when prescribing and dispensing it.

Thalidomide Pharmion will only be available with a prescription, and treatment will be initiated and monitored by a doctor who has experience in the treatment of multiple myeloma. Each prescription will be limited to four weeks in women who are able to become pregnant, and to 12 weeks in all other patients.

There will be information booklets for patients, with different booklets available for men, for women who are able to become pregnant, and for women who are unable to become pregnant. Each patient will also be counselled on the safe use of the product before each prescription. In addition, there will be a clear warning printed on the boxes containing the medicine, indicating that Thalidomide Pharmion causes birth defects and death in unborn children.

There will be very strict measures put in place to ensure that:

- **Pregnant women do not take Thalidomide Pharmion:**
  Women who are able to become pregnant must have a negative pregnancy test before they are prescribed Thalidomide Pharmion. Ideally, the test should be carried out on the same day that the medicine is prescribed and dispensed.
- **Women do not become pregnant while taking the medicine:**
  Women who are able to become pregnant must use an effective form of contraception as recommended by their doctor, for four weeks before, during and for four weeks after treatment with Thalidomide Pharmion. Most oral contraceptives are not suitable, because of an elevated risk of blood clots in the veins when they are taken by patients with multiple myeloma.
  They must agree to have a pregnancy test every four weeks during treatment, and at least once more, four weeks after treatment is stopped. Women who become pregnant should stop taking Thalidomide Pharmion and inform their doctor straight away.
- **The exposure of unborn children to thalidomide is avoided:**
  Men taking Thalidomide Pharmion should not donate semen and should not have unprotected intercourse. These measures are intended to avoid any thalidomide reaching an unborn child in the womb and to avoid pregnancies.
  All patients taking Thalidomide Pharmion should also not donate blood.

The effectiveness of the measures put in place to minimise the risks associated with Thalidomide Pharmion will be evaluated by the CHMP at regular intervals, and may be adapted accordingly.