European Medicines Agency

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QUESTIONS AND ANSWERS ON THE POSITIVE OPINION
for
REVLIMID

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

On 22 March 2007, the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion recommending that a marketing authorisation for Revlimid be granted. Because Revlimid contains an active substance that has a chemical structure that resembles thalidomide, a number of measures have been taken to minimise any risk of damage to unborn children of patients taking the medicine.

What is Revlimid?
Revlimid is a medicine containing the active substance lenalidomide. It is to be used with dexamethasone (an anti-inflammatory medicine) to treat multiple myeloma in patients who have already been treated at least once for this disease. Multiple myeloma is a rare type of bone marrow cancer that is very difficult to treat.

What is lenalidomide?
Lenalidomide is a new substance. In multiple myeloma, it works by blocking the development of tumour cells and by stimulating some of the specialised cells of the immune system (the body's defence mechanism) to attack the cancerous cells. Clinical studies have shown that Revlimid can prolong the time until multiple myeloma gets worse.

Lenalidomide has a chemical structure that resembles that of thalidomide, a substance that was used in medicines in the late 1950s and early 1960s. Thalidomide is 'teratogenic', meaning that it has a harmful effect on the unborn child. Its use during the first three months of pregnancy, mostly as a treatment for morning sickness, led to the birth of babies with malformed, short or absent limbs, and other severe, life-threatening deformities.

How was the safety of Revlimid assessed during its development?
During the development of Revlimid, extensive tests were carried out to find out whether lenalidomide is teratogenic in animals. These studies showed that lenalidomide had some effect on the developing animals, but did not affect the development of the limbs. Although lenalidomide's effect was limited in comparison with that of thalidomide, the studies were not sufficient to allow the CHMP to rule out a risk of lenalidomide also being teratogenic.

What measures were taken during the assessment of Revlimid?
During the assessment of Revlimid by the CHMP, associations of thalidomide victims and of 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) and to the development of the plan put in place to manage the risks associated with the use of the medicine.

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The groups were consulted twice:

- The first consultation occurred just before day 120 of the assessment procedure, when the committee issues a list of questions to be answered by the company that makes the medicine.
- The groups were also consulted as the committee was reaching the final phase of the opinion-making process.

What measures are being put in place to minimise the risks associated with Revlimid when it is available on the market?

As part of the marketing authorisation for Revlimid, the CHMP has requested that a number of measures be put in place, to ensure that healthcare workers and patients are fully aware of the risks associated with the medicine and that unborn children are not exposed to lenalidomide.

Before the medicine can be marketed, the company will put a programme in place to inform doctors and pharmacists about the special measures they will need to take when prescribing and dispensing Revlimid. This will include an information pack for doctors who will be prescribing Revlimid. These doctors must have experience in the treatment of multiple myeloma.

Education brochures will also be prepared for patients who are prescribed Revlimid, with different brochures for men and for women. In addition, there will be a clear warning printed on the boxes containing the medicine, indicating that Revlimid may harm unborn children.

There will also be very strict measures to ensure that pregnant women do not take Revlimid, and that women do not become pregnant while taking the medicine. Women who are able to become pregnant must:

- have a negative pregnancy test before they are prescribed Revlimid. Ideally, the test should be carried out on the same day that the medicine is prescribed and dispensed.
- agree to have a pregnancy test every four weeks during treatment, and at least once after treatment is stopped. Women who become pregnant should stop taking Revlimid and speak to their doctor immediately.
- use an effective form of contraception before, during and for up to 4 weeks after treatment with Revlimid. Most oral contraceptives are not suitable, because of an elevated risk of blood clots in the veins when they are taken with Revlimid and dexamethasone. Dexamethasone may also reduce the activity of oral contraceptives.