Annex related to the Art. 127a

Conditions or restrictions with regard to the safe and effective use of the medicinal product to be implemented by the member states

Conditions or restrictions with regard to the safe and effective use of medicinal product to be implemented by the member states

The Member States should ensure that all conditions or restrictions with regard to the safe and effective use of the medicinal product described below are implemented:

1. The Member state shall agree the details of a controlled distribution system with the Marketing authorisation holder (MAH) according to national regulations and healthcare system and must implement such programme nationally to ensure that:

Prior to prescribing (and where appropriate, and in agreement with MAH, prior to dispensing) all healthcare professionals who intend to prescribe (and dispense) Lenalidomide Krka d.d. are provided with a physician information pack containing the following:

- Educational Health Care Professional's kit
- Educational brochures for Patients
- Patient cards
- Summary of Product Characteristics (SmPC) and Package Leaflet and Labelling.

2. The Member State shall ensure that the MAH implements a pregnancy prevention programme (PPP) within their territory. Details of the PPP including the set-up of national measures to assess the effectiveness of and compliance with the PPP should be agreed with the National Competent Authorities in each Member State and put in place prior to the marketing of the product.

3. The Member state should agree the final text of the healthcare professional's information pack contents with the MAH and ensure that the materials contain the key elements as described below.

4. The Member state should agree on the implementation of the patient card system in each Member State.

Key elements to be included

The Educational Healthcare Professional's Kit

The Educational Health Care Professional's Kit shall contain the following elements:

- Brief background on lenalidomide and its licensed indication
- Posology
- Maximum duration of treatment prescribed
    - 4 weeks treatment for women with childbearing potential
    - 12 weeks treatment for men and women without childbearing potential
- The need to avoid foetal exposure due to teratogenicity of lenalidomide in animals and the expected teratogenic effect of lenalidomide in humans including a summary of the results of study CC-5013-TOX-004
- Guidance on handling the blister or capsule of Lenalidomide Krka d.d. for healthcare professionals and caregivers

- Obligations of the health care professional in relation to the prescribing of Lenalidomide Krka d.d.
    - Need to provide comprehensive advice and counselling to patients
    - That patients should be capable of complying with the requirements for the safe use of Lenalidomide Krka d.d.
    - Need to provide patients with appropriate patient educational brochure and patient card
- Safety advice relevant to all patients
    - Disposal of unwanted medicine
    - Local country specific arrangements for a prescription for Lenalidomide Krka d.d. to be dispensed
    - Description of risk of tumour flare reaction
    - Description of the risk of progression to AML in MDS patients including incidence rates from clinical trials
    - Description of risk of SPM
- Description of the PPP and categorisation of patients based on sex and childbearing potential
    - Algorithm for implementation of PPP
    - Definition of women of childbearing potential (WCBP) and actions the physician should take if unsure
- Safety advice for women of childbearing potential
    - The need to avoid foetal exposure
    - Description of the PPP
    - Need for adequate contraception (even if woman has amenorrhoea) and definition of adequate contraception
    - Pregnancy test regime
        - Advice on suitable tests
        - Before commencing treatment
        - During treatment based on method of contraception
        - After finishing treatment
    - Need to stop Lenalidomide Krka d.d. immediately upon suspicion of pregnancy
    - Need to tell treating doctor immediately upon suspicion of pregnancy
- Safety advice for men
    - The need to avoid foetal exposure
    - The need to use condoms if sexual partner is pregnant or a WCBP not using effective contraception (even if man has had a vasectomy)
        - During Lenalidomide Krka d.d. treatment
        - For at least 7 days following final dose.
    - That if his partner becomes pregnant whilst he is taking Lenalidomide Krka d.d. or shortly after he has stopped taking Lenalidomide Krka d.d. he should inform his treating doctor immediately
- Requirements in the event of pregnancy
    - Instructions to stop Lenalidomide Krka d.d. immediately upon suspicion of pregnancy, if female patient
    - Need to refer to physician specialised or experienced in dealing with teratology and its diagnosis for evaluation and advice

    - Local contact details for reporting of any suspected pregnancy
    - Pregnancy reporting form
- Check list for physicians ensuring that patients receive the appropriate counselling concerning the treatment, contraceptive methods and pregnancy prevention appropriate for their sex and childbearing status at treatment initiation.
- Adverse event reporting forms

Educational Brochures for patients

The Educational brochures for patients should be of 3 types:

- Brochure for women patients of childbearing potential
- Brochure for women patients who are not of childbearing potential
- Brochure for male patients

All patient brochures should contain the following elements:

- That lenalidomide is teratogenic in animals and is expected to be teratogenic in humans
- Description of the patient card and its necessity
- Disposal of unwanted medicine
- Guidance on handling lenalidomide for patients, caregivers and family members
- National or other applicable specific arrangements for a prescription for Lenalidomide Krka d.d. to be dispensed
- That the patient should not give Lenalidomide Krka d.d. to any other person
- That the patient should not donate blood during therapy (including during dose interruptions) and for at least 7 days after discontinuation of Lenalidomide Krka d.d. treatment
- That the patient should tell their doctor about any adverse events

The following information should also be provided in the appropriate brochure:

Brochure for women patients with childbearing potential

- The need to avoid foetal exposure
- Description of the PPP
- Need for adequate contraception and definition of adequate contraception
- Pregnancy test regime
    - Before commencing treatment
    - During treatment, at least every 4 weeks except in case of confirmed tubal sterilisation
    - After finishing treatment
- The need to stop Lenalidomide Krka d.d. immediately upon suspicion of pregnancy
- The need to contact their doctor immediately upon suspicion of pregnancy

Brochure for male patients

- The need to avoid foetal exposure
- The need to use condoms if sexual partner is pregnant or a WCBP not using effective contraception (even if man has had vasectomy)
    - During Lenalidomide Krka d.d. treatment
    - For at least 7 days following final dose
- That if his partner becomes pregnant, he should inform his treating doctor immediately
- That he should not donate semen or sperm during therapy (including during dose interruptions) and at least for 7 days after discontinuation of Lenalidomide Krka d.d. treatment

Patient Card

The patient card shall contain the following elements:

- Verification that appropriate counselling has taken place
- Documentation of childbearing status potential
- Pregnancy test dates and results