Direct Healthcare Professional Communication

We wish to inform you about important aspects in the clinical use of Imnovid® (pomalidomide) which has now received market authorisation in combination with dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma (MM) who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.

The content of this communication has been agreed with the Committee for Medicinal Products for Human Use (CHMP) and the Malta Medicines Authority.

Pregnancy Prevention Programme

- Pomalidomide is structurally related to thalidomide. Thalidomide is a known human teratogen that causes severe life-threatening birth defects. Pomalidomide was found to be teratogenic in both rats and rabbits when administered during the period of major organogenesis. If pomalidomide is taken during pregnancy, a tetratogenic effect in humans is expected.

- Pomalidomide is contraindicated for use in pregnancy. It is also contraindicated in women of childbearing potential unless all the conditions of the pomalidomide Pregnancy Prevention Programme are met.

Multiple Myeloma is a disease of a predominantly elderly population. However, women of childbearing potential could be part of the patient population. We wish to draw your attention to the conditions of the Pregnancy Prevention Programme that must be complied with in this small specific patient population.

Further information on the Pregnancy Prevention Programme and recommendations

The Educational Healthcare Professionals Kit contains the following documents:

- Imnovid® Summary of Product Characteristics (SmPC)
- Imnovid® Educational Healthcare Professionals Brochure
- Imnovid® Patient Brochure (Male, Women of Childbearing Potential, Women Not of Childbearing Potential)
- Imnovid® Treatment Initiation Form (Male, Women of Childbearing Potential, Women Not of Childbearing Potential)
- Imnovid® Patient Card
- Adverse Event Reporting Form
- Pregnancy Capture Form

- Imnovid® Order Form (also used to enrol patients into the Pregnancy Prevention Programme)

Prescribing and dispensing Healthcare Professionals are enrolled in the Pregnancy Prevention Programme after undergoing local training.

All purchase orders for Imnovid® must be prescribed by enrolled specialists for enrolled patients and dispensed by enrolled Healthcare Professionals.

Women of childbearing potential

All women of childbearing potential must:

- Receive counselling regarding the expected teratogenic risk of pomalidomide to the unborn child and the need to avoid pregnancy
- Use one effective method of contraception for 4 weeks before therapy, during therapy, during dose interruptions and 4 weeks after therapy has finished, unless the woman commits to absolute and continued abstinence confirmed on a monthly basis.
- Have a medically supervised negative pregnancy test once she has been established on contraception for 4 weeks, at 4 weekly intervals during therapy and 4 weeks after the end of therapy, except in the case of confirmed tubal sterilisation. This pregnancy test requirement includes women of childbearing potential who practice absolute and continued abstinence.
- The following can be considered to be examples of effective methods of contraception:
    - Implant
    - Levonorgestrel-releasing intrauterine system (IUS)
    - Medroxyprogesterone acetate depot
    - Tubal sterilisation
    - Sexual intercourse with a vasectomised male partner only; vasectomy must be confirmed by two negative semen analyses
    - Ovulatory inhibitory progesterone-only pills (i.e., desogestrel).

Because of the increased risk of venous thromboembolism in patients with multiple myeloma taking pomalidomide and dexamethasone, combined oral contraceptive pills are not recommended.

Ideally pregnancy testing, issuing a prescription and dispensing should occur on the same day. Dispensing of pomalidomide should occur within a maximum of 7 days of the prescription.

Section 4.4 of the enclosed SmPC provides further guidance on the definition of a woman of childbearing potential, counselling, effective contraception and pregnancy testing.

If pregnancy does occur in your patient whilst she is receiving pomalidomide, treatment must be stopped and the patient be referred to a physician specialised or experienced in

teratology for evaluation and advice. If pregnancy occurs in a partner of a male patient while he is taking pomalidomide or 1 week after he has stopped taking pomalidomide, he should inform his treating physician immediately and it is recommended to refer the female partner to a physician specialised or experienced in teratology for evaluation and advice.
You are also requested to notify AM Mangion Ltd. of all such occurrences.

Pregnancy Capture Forms are available in the Educational Healthcare Professionals Kit and may be requested by email to pv@ammangion.com.mt.

Men
Pomalidomide is present in semen during treatment. Therefore, all male patients should use condoms throughout treatment duration, during dose interruption and for 1 week after cessation of treatment if their partner is pregnant or of childbearing potential and is not using effective contraception.
Patients should not donate sperm during treatment (including during dose interruptions) or for 1 week following discontinuation of pomalidomide

All patients
Patients should be instructed never to give pomalidomide to another person and to return any unused capsules to their pharmacist at the end of treatment.

Patients should not donate blood during therapy (including during dose interruptions) and for 1 week following the discontinuation of pomalidomide.

Controlled Distribution
A controlled distribution system has been implemented in order to ensure prevention of foetal exposure to pomalidomide. Prior to treating a patient with pomalidomide, it is required that the treating physician and the patient sign a Treatment Initiation Form to confirm that the benefits and risks of pomalidomide therapy have been explained and understood and that the requirements of the Pregnancy Prevention Programme will be complied with. One copy of this form should be given to the patient and the other should be retained in the patient file. In addition, patients should be provided with the relevant Patient Brochure.

Patient Cards to document childbearing status of the patient and to confirm counselling are contained within the Educational Healthcare Professionals Kit. For Women of Childbearing Potential, the Patient Card will also document the date and results of the monthly pregnancy test. The Patient Card must be completed and a copy provided to the patient. The pharmacist will be required to check the Patient Card for each female patient and verify the correct completion of the Patient Card for each Woman of Childbearing Potential prior to each dispense of pomalidomide.

Call for reporting

Any ADRs should be reported to the Pharmacovigilance department at AM Mangion Ltd. "Mangion Building", New Street off Valletta Road, Luqa, LQA6000 or via email on pv@ammangion.com.mt. Alternatively, you may use the 24 hour PV line on +356 23976333 or fax +356 23976123.

You may also report ADRs to Malta Medicines Authority on their website http://www.medicinesauthority.gov.mt/adrportal or by post at Medicines Authority 203, Level 3, Rue D'Argens, Gzira GZR 1368, Malta.

Company Contact Point

If you have any further questions, require further information or would like to request an Educational Healthcare Professional Kit for *Imnovid*®, please contact your local Celgene representative at AM Mangion Ltd. "Mangion Building", New Street off Valletta Road, Luqa, LQA6000 or via email on pv@ammangion.com.mt. Alternatively, you may use the 24 hour PV line on +356 23976333 or fax +356 23976123.

Annexes

Summary of Product Characteristics