Lenalidomide Grindeks

Healthcare Professional Educational Material

Pregnancy Prevention Programme

Version 1, Updated August 2024
This document has been approved by HSA as of 02-01-2025

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INTRODUCTION

- Lenalidomide is an immunomodulatory drug.
- Lenalidomide Grindeks has the following indication:

Multiple myeloma

- Lenalidomide Grindeks as monotherapy is indicated for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.

- Lenalidomide Grindeks in combination with dexamethasone, is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.

- Lenalidomide Grindeks in combination with dexamethasone is indicated for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

TERATOGENICITY ASSOCIATED WITH LENALIDOMIDE

- Lenalidomide is structurally related to thalidomide. Thalidomide is a known human teratogenic active substance that causes severe life-threatening birth defects. In monkeys, lenalidomide induced malformations similar to those described with thalidomide. An embryofoetal development study has been conducted in monkeys administered Lenalidomide at doses from 0.5 and up to 4 mg/kg/day. Findings from this study indicate that Lenalidomide produced external malformations including non-patent anus and malformations of upper and lower extremities (bent, shortened, malformed, malrotated and/or absent part of the extremities, oligo and/or polydactyly) in the offspring of female monkeys who received the active substance during pregnancy. Various visceral effects (discoloration, red foci at different organs, small colourless mass above atrio- ventricular valve, small gall bladder, malformed diaphragm) were also observed in single foetuses. If Lenalidomide is taken during pregnancy, a teratogenic effect of Lenalidomide in humans is expected.

- Treatment with Lenalidomide should be supervised by physicians experienced in the use of anticancer therapy.

- Lenalidomide is contraindicated in pregnancy, and in female patients of childbearing potential unless all of the conditions of the PPP are met.

- Lenalidomide can pass into seminal fluid. Male patients must also follow the necessary requirements of the PPP to prevent exposure to a female partner.

SUMMARY OF THE PREGNANCY PREVENTION PROGRAMME REQUIREMENTS

- Prescribing doctors and dispensing pharmacists must complete the "Letter of Undertaking (Physician)" and "Letter of Undertaking (Pharmacist)" respectively.

- Prescribing doctors and dispensing pharmacists must read and understand this material before prescribing or dispensing lenalidomide to their patients.

- At treatment initiation, all male patients and all female patients of childbearing potential should undergo counselling about the need to avoid pregnancy. Prescribing doctors and dispensing pharmacists should follow the "Counselling Checklist" when counselling patients.

- Patients should be provided with a **"Patient Medication Guide".** The "**Patient Medication Guide"** is included in this kit.

- Patients should complete the "Lenalidomide Consent Form".

- All patients must follow the safe use of Lenalidomide and be capable of complying with the requirements for safe use of Lenalidomide.

- Prescriptions for women of childbearing potential can be for a maximum duration of treatment of 4 weeks, and prescriptions for all other patients can be for a maximum duration of treatment of 12 weeks.

- Ideally, for women of childbearing potential, pregnancy testing, issuing a prescription and dispensing should occur on the same day. It is recommended that the dispensing of Lenalidomide to women of childbearing potential should occur within 7 days of the prescription.

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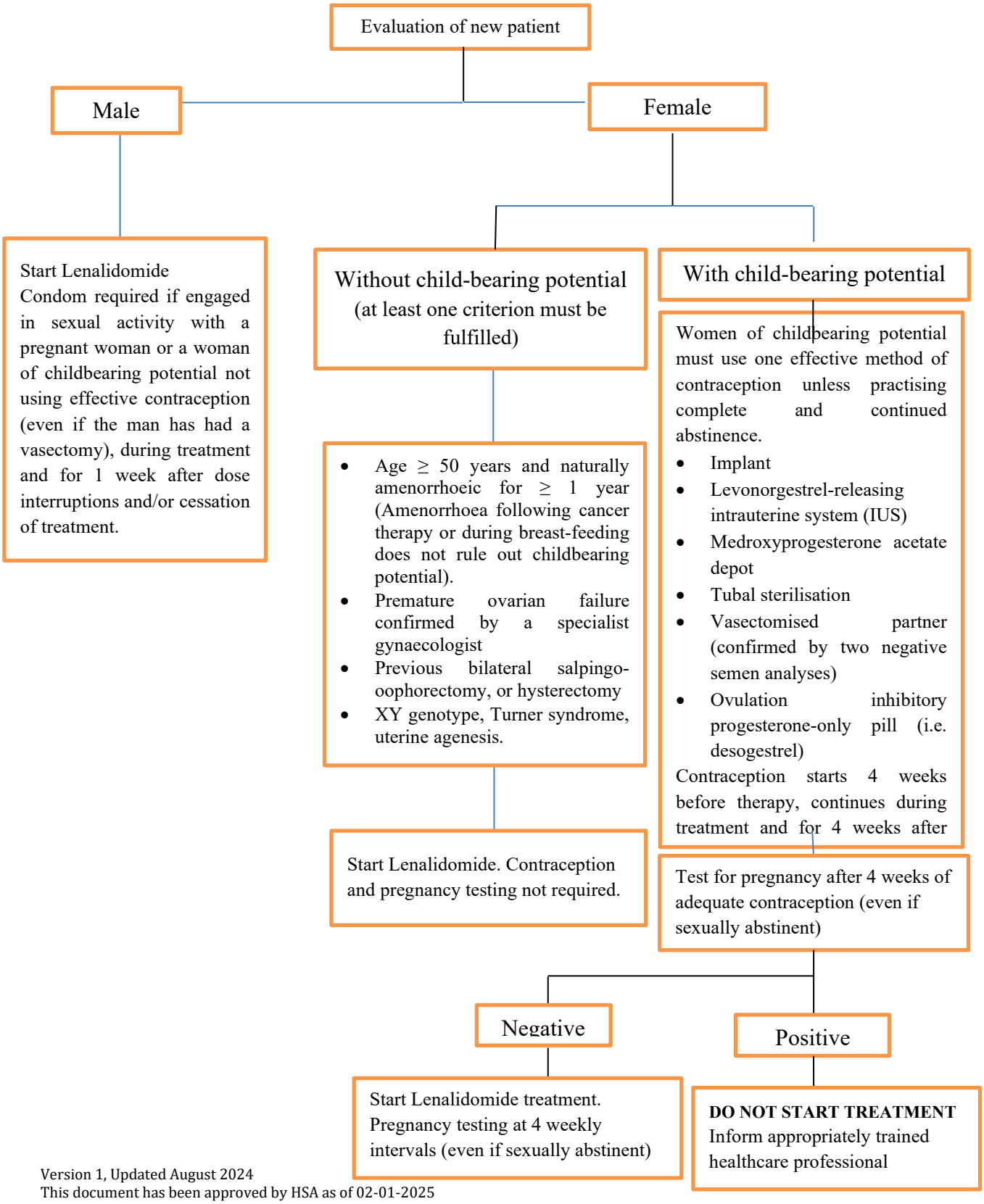
PREGNANCY PREVENTION PROGRAMME

The conditions of the Pregnancy Prevention Programme (PPP) must be fulfilled for all patients unless there is reliable evidence that the patient does not have childbearing potential.

The PPP is designed according to the following algorithm:



A female patient or a female partner of a male patient is considered to have childbearing potential unless she meets at least one of the following criteria:

- Age ≥ 50 years and naturally amenorrhoeic for ≥ 1 year (Amenorrhoea following cancer therapy or during breast-feeding 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.

Healthcare professionals are advised to consult a gynaecologist if there is any doubt whether a female meets the childbearing potential criteria, unless there is reliable evidence that the patient does not have childbearing potential.

The physician should ask in the referral to evaluate the childbearing potential and the need for contraception according to the Lenalidomide PPP. The gynaecologist must substantiate his findings and recommendations for contraceptive use according to the Lenalidomide PPP.

SAFETY ADVICE FOR WOMEN OF CHILDBEARING POTENTIAL

- If Lenalidomide is taken during pregnancy, a teratogenic effect of Lenalidomide in humans is expected. Therefore, Lenalidomide is contraindicated during pregnancy and in women of childbearing potential unless all conditions of the Pregnancy Prevention Programme are met.

- Women of childbearing potential must fulfill the following:
  - To use effective contraception, without interruption, 4 weeks before starting treatment, throughout the entire duration of treatment, and 4 weeks after the end of treatment (even if a woman of childbearing potential has amenorrhea she must follow all the advice on effective contraception);

    OR
  - Commits to absolute and continuous abstinence from heterosexual intercourse, confirmed and documented on a monthly basis by the prescriber.

- Medically supervised pregnancy tests with a minimum sensitivity of 25 mIU/mL must be performed for women of childbearing potential before starting the treatment once the patient had been using effective contraception for at least 4 weeks, every 4 weeks, including at least 4 weeks after the end of treatment, except in the case of confirmed tubal sterilisation. This requirement includes women of childbearing potential who practice absolute and continuous abstinence.

- A medically supervised pregnancy test should be performed during the consultation, when Lenalidomide is prescribed, or in the 3 days prior to the visit to the prescriber

once the patient had been using effective contraception for at least 4 weeks. The test should ensure the patient is not pregnant when she starts treatment with lenalidomide.

- A physician informs and agrees with the patient on the procedure for carrying out the pregnancy test on a specific patient.

- The pregnancy test should be performed according to the pregnancy test instruction.

- Patients should be asked to inform their physician who prescribes contraception about treatment with Lenalidomide.

- Patient should be asked to inform their physician if there is a need to change contraception or stop using it.

- If not established on effective contraception, the patient must be referred to an appropriately trained healthcare professional for contraceptive advice so that contraception can be initiated.

- The following can be considered to be examples of suitable 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
    - Ovulation inhibitory progesterone-only pills (i.e. desogestrel)

    - Because of the increased risk of venous thromboembolism in patients with multiple myeloma taking Lenalidomide in combination therapy, combined oral contraceptive pills are not recommended. If a patient is currently using combined oral contraception the patient should switch to one of the effective methods listed above. The risk of venous thromboembolism continues for 4−6 weeks after discontinuing combined oral contraception. The efficacy of contraceptive steroids may be reduced during co-treatment with dexamethasone.
    - Implants and levonorgestrel-releasing intrauterine systems are associated with an increased risk of infection at the time of insertion and irregular vaginal bleeding. Prophylactic antibiotics should be considered particularly in patients with neutropenia.
    - Copper-releasing intrauterine devices are generally not recommended due to the potential risks of infection at the time of insertion and menstrual blood loss which may compromise patients with neutropenia or thrombocytopenia.

- Patients should be advised to inform their physician of a missed menstrual period, any unusual menstrual bleeding, or if she believes that she may be pregnant. If a pregnancy does occur while receiving treatment with lenalidomide, treatment must be discontinued, and the physician be informed immediately. Refer the patient to a healthcare professional specialised in teratology for evaluation and advice.

SAFETY ADVICE FOR MEN

- Due to the expected teratogenic risk of Lenalidomide, exposure to the unborn child should be avoided.

- Lenalidomide is present in human semen. Therefore, all men must use a condom if they are engaged in sexual activity with a pregnant woman or a woman of childbearing potential not using effective contraception (even if the man has had a vasectomy), throughout treatment duration, during dose interruption and for at least 7 days after cessation of treatment.

- Patient must be informed if his female partner becomes pregnant whilst he is taking Lenalidomide or within 7 days after he has stopped taking Lenalidomide, he should inform his treating physician immediately and that it is recommended to refer the female partner to a physician specialised or experienced in teratology for evaluation and advice.

- Patient should not donate semen or sperm during treatment, including during dose interruptions, and for at least 7 days following discontinuation of lenalidomide.

DEMANDS IN CASE OF PREGNANCY

- If pregnancy occurs in a woman treated with Lenalidomide, treatment must be stopped.

- If pregnancy occurs in a female partner of male patient, the healthcare professional must be informed.

- Pregnant woman must be refered to a physician specialised or experienced in teratology for evaluation and advice.

- All such cases must be reported by filling in the **"Pregnancy Reporting Form"** which is included in the educational kit for the healthcare professional and sending it to Goldplus Universal Pte Ltd via email (productfeedback@goldplusuniversal.com.sg).

- The patient or the female partner of male patient must be monitored throughout pregnancy.

SAFETY ADVICE RELEVANT TO ALL PATIENTS

- The capsules should not be opened, broken or overly handled. If powder from Lenalidomide makes contact with the skin, the skin should be washed immediately and thoroughly with soap and water. If Lenalidomide makes contact with the mucous membranes, they should be thoroughly flushed with water.

- Healthcare professionals and caregivers should wear disposable gloves when handling the blister or capsule. Gloves should then be removed carefully to prevent skin exposure, placed in a sealable plastic polyethylene bag and disposed of in accordance with local requirements. Hands should then be washed thoroughly with soap and water. Women who are pregnant or suspect they may be pregnant should not handle the blister or capsule.

- Patients should be instructed never to give this product to another person and to return any unused capsules to their pharmacist at the end of treatment for safe disposal.

- Patients should not donate blood during therapy or for at least 7 days following discontinuation of Lenalidomide.

REPORTING OF ADVERSE REACTIONS

- The safe use of lenalidomide is of paramount importance.
- All adverse events should be reported.
- Adverse events should be reported to Goldplus Universal Pte Ltd via email (productfeedback@goldplusuniversal.com.sg)
- You are also encouraged to report any suspected adverse reactions to the Vigilance &
- Compliance Branch, Health Products Regulation Group, Health Sciences Authority at https://www.hsa.gov.sg/adverse-events

ANNEX

- Letter of Undertaking (Physician)
- Letter of Undertaking (Pharmacist)
- Counselling Checklist
- Lenalidomide Consent Form
- Pregnancy Reporting Form
- Patient Medication Guide