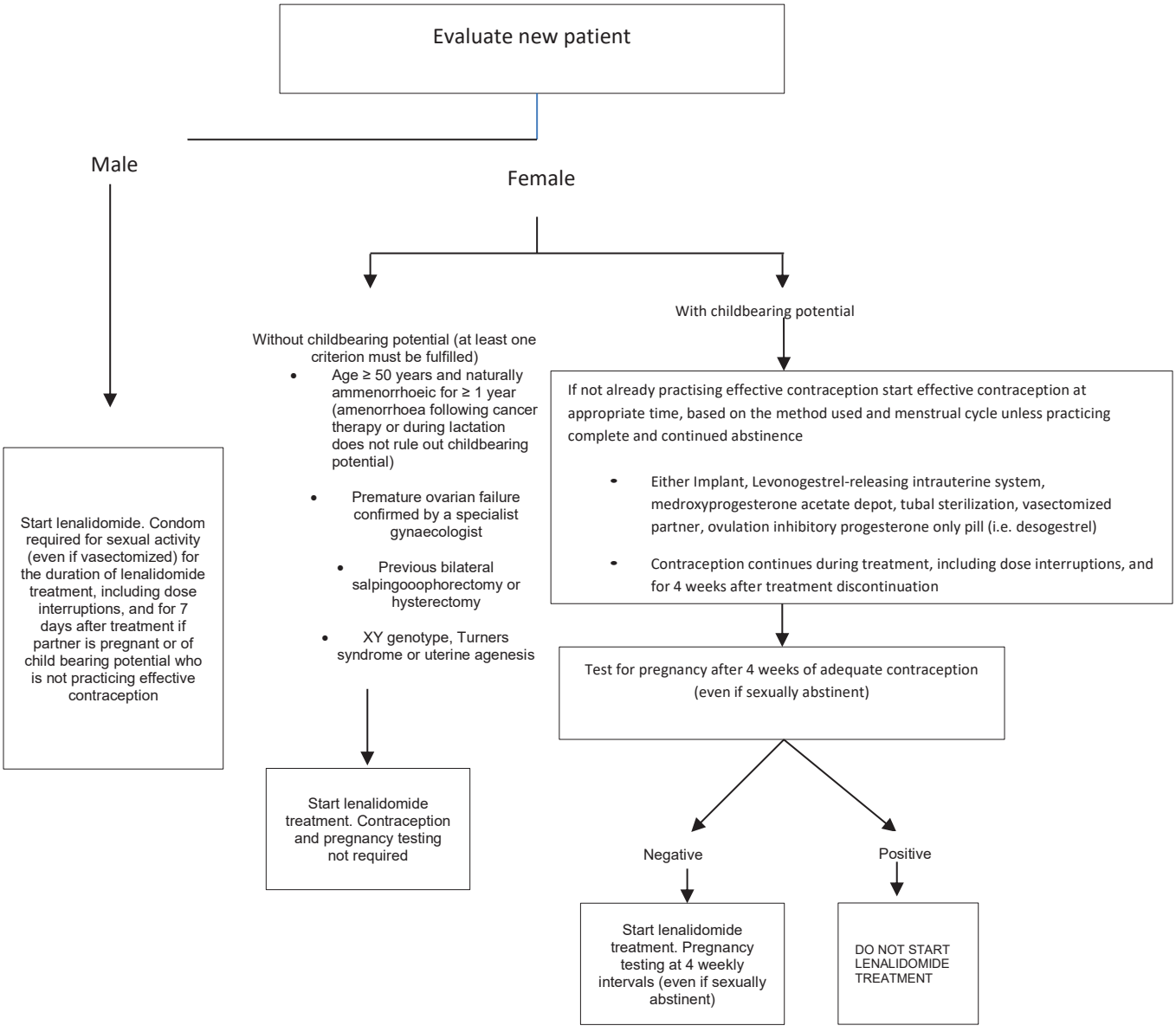
Lenalidomide Te Arai Restricted Access Programme

• Lenalidomide is structurally related to thalidomide. Thalidomide is a known human teratogenic active substance. Lenalidomide induced malformations in monkeys similar to those described for thalidomide. If lenalidomide is taken in pregnancy, a teratogenic effect in humans is expected.

• Lenalidomide is therefore contraindicated in pregnancy. It is also contraindicated in women of childbearing potential unless all the conditions of the Lenalidomide Te Arai Restricted Access Programme are met.

• The Lenalidomide Te Arai Restricted Access Programme is set out in the following Algorithm



• The following are considered to not have childbearing potential.

- ✓ Age ≥ 50 years and naturally amenorrhoeic for 1 year or more (amenorrhoea following cancer therapy or during lactation does not rule out childbearing potential).
- ✓ Confirmed premature ovarian failure if confirmed by specialist gynaecologist.
- ✓ Previous bilateral salpingo-oophorectomy, or hysterectomy
- ✓ XY genotype, Turner syndrome, uterine agenesis.

You are advised to refer your patient for a gynaecological opinion if you are unsure whether or not she meets these criteria.

Safety Advice for Women of Childbearing Potential

• In view of the expected teratogenic risk of lenalidomide, foetal exposure should be avoided

• Women of childbearing potential (even if they have amenorrhoea) must:

- ✓ use one effective method of contraception for 4 weeks before therapy, during therapy, and until 4 weeks after lenalidomide therapy, and even in case of dose interruption or,
- ✓ commit to absolute and continuous sexual abstinence

AND

- ✓ Have a medically supervised negative pregnancy test (with a minimum sensitivity of 25 mIU/mL) once she has been established on contraception for 4 weeks, at 4 weekly intervals during therapy (this includes dose interruptions) and 4 weeks after the end of therapy (unless confirmed tubal sterilisation). This includes those women of childbearing potential who confirm absolute and continued sexual abstinence.

• Patients should be advised to inform the physician prescribing her contraception about the lenalidomide treatment.

• Patients should be advised to inform you if a change or stop of method of contraception is needed.

If not established on effective contraception, the patient must be referred to an appropriately trained health care professional for contraceptive advice in order 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, and to a lesser extent in patients with multiple myeloma taking lenalidomide monotherapy, 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.

- Your patient should be advised that if a pregnancy does occur whilst she is receiving lenalidomide, she must stop treatment immediately and inform her physician immediately.

Safety Advice for Men

- In view of the expected teratogenic risk of lenalidomide, foetal exposure should be avoided.

- Lenalidomide is present in semen. Therefore, all male patients should use condoms throughout treatment duration, during dose interruption and for 7 days after cessation of treatment if their partner is pregnant or of child bearing potential who is not using effective contraception and even if the male patient has undergone vasectomy.

- Patients should be instructed that if their partner becomes pregnant whilst he is taking lenalidomide or shortly after he has stopped taking lenalidomide he should inform his treating doctor immediately. TI1e partner should inform her physician immediately. It is recommended that she be referred to a physician specialised in teratology for evaluation and advice

Lenalidomide Te Arai Restricted Access Programme Reporting

The requirements of the Lenalidomide Te Arai Restricted Access Programme are recorded online at www.lenalidomide.co.nz.

Requirements in the event of a suspected pregnancy

- ✓ Stop treatment if female patient.
- ✓ Refer patient to a physician specialised or experienced in teratology for evaluation and advice.
- ✓ Notify Te Arai BioFarma of all such occurrences by using the Pregnancy Report Form found at www.lenalidomide.co.nz or by emailing lenalidomide@tearaibiofarma.com.
- ✓ Te Arai BioFarma will follow-up with you the progress of all pregnancies.

Reporting of Adverse Reactions

The safe use of lenalidomide is of paramount importance. As part of Te Arai BioFarma's ongoing safety monitoring, the company seeks to learn of Adverse Reactions that have occurred during the use of lenalidomide. Adverse Reaction report forms are included in this Health Care Professional Kit.

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

Contact Details

For information and questions on the risk management of Te Arai BioFarma's products, and the Lenalidomide Te Arai Restricted Access Programme, please visit www.lenalidomide.co.nz or email lenalidomide@tearaibiofarma.com.