HEALTHCARE PROFESSIONALS GUIDE TO DOMIDE RMP PROGRAM

PREGNANCY PREVENTION PROGRAMME

Prescribing or Dispensing Domide

Healthcare Professionals Guide to DOMIDE RMP Program

A known teratogen, DOMIDE (thalidomide) is available only under a restricted distribution program. This program is called the DOMIDE RMP program.

This guide contains important information for healthcare professionals about:

- The risks of Domide, including a package insert warning for
  - Embryo-fetal toxicity
  - Venous thromboembolism (deep vein thrombosis [DVT] and pulmonary embolism [PE])
- The **Domide** RMP program
  - Prescriber/Pharmacist Letter of Consent
  - Patient Letter of Consent

DOMIDE RMP Resources for Healthcare Professionals Include:

- Healthcare Professionals Guide to **Domide** RMP Program
- Singapore Package Insert for **Domide**

About DOMIDE (thalidomide)

Multiple Myeloma (MM):

Domide in combination with melphalan and prednisone is indicated for the treatment of patients with untreated multiple myeloma ≧65 years or ineligible for high dose chemotherapy.

Domide in combination with dexamethasone is indicated for induction therapy prior to high dose chemotherapy with autologous stem cell rescue, for the treatment of patients with untreated multiple myeloma.

Risks of Domide
Domide has a Boxed Warning for embryo-fetal toxicity

A known teratogen, Domide is contraindicated in pregnant females or females capable of becoming pregnant. Females of reproductive potential may be treated with **Domide** if they take adequate precautions to avoid pregnancy.

The use of thalidomide in MM results in an increased risk of venous thromboembolism, such as deep venous thrombosis and pulmonary embolism. This risk increases significantly when thalidomide is used in combination with standard chemotherapeutic agents including dexamethasone. Patients and physicians should be observant for the signs and symptoms of thromboembolism. Instruct patients to seek medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. Consider thromboprophylaxis based on an assessment of individual patients' underlying risk factors.

This is not a comprehensive description of risks associated with the use of DOMIDE. Please see Singapore package insert, including Boxed WARNINGS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS, for further information regarding the use of Domide.

The DOMIDE RMP program

To avoid embryo-fetal exposure, **Domide** (thalidomide) is only available under a restricted distribution program called **Domide** RMP program. Only certified prescribers can prescribe **Domide** in the **Domide** RMP program.

In order to receive **Domide**, all patients must be enrolled in **Domide** RMP Program and agree to comply with the requirements of the **Domide** RMP program. Information about **Domide** and the **Domide** RMP program can be obtained by calling the Pharm-D Singapore Customer Care Center at 68372122.

Key points of the DOMIDE RMP program

Guide to Prescriber/ Pharmacist/ Nurse

- **Before** starting/counselling first patient on Domide treatment, obtain and complete the **Prescriber/Pharmacist/Nurse Letter of Consent** online. In the event where online completion of the Letter of Consent is not feasible, you may complete the Letter of Consent in hard copy. You should tick **ALL** boxes next to each statement in the Letter of Consent in order to become certified. Submit the signed Letter of Consent to Pharm-D Singapore via fax (6837 2123) or email (regulatory@pharmd.com.sg). You will receive confirmation via fax or email from Pharm-D Singapore once you are certified.
- The certified **Prescriber** is required to enroll each patient by completing Patient Letter of Consent before starting Domide treatment. Obtain and complete **Part 1 of Patient Letter of Consent** online. In the event where online completion of the Letter of Consent is not feasible, you may complete the Letter of Consent in hard copy. Submit the signed Part 1 of Patient Letter of Consent to Pharm-D Singapore via fax (6837 2123) or email (regulatory@pharmd.com.sg). You will receive confirmation via fax or email from Pharm-D Singapore once the patient is enrolled. For Part 2 of Patient Letter of Consent, **ALL** boxes next to each statement under 'For All Patients' AND 'Males Only' (for male patients) OR 'Females of Reproductive Potential Only' (for female patients of reproductive potential) sections should be ticked by the patients in order to be eligible to receive Domide. Do not submit Part 2 of the Patient Letter of Consent to Pharm-D Singapore. It should be stored in the hospital/clinic.
- For **all new patients and each subsequent prescription,** obtain and complete the **Prescription Authorization Form** online. In the event where online completion of the form is not feasible, you may complete the form in hard copy. Submit the signed form to Pharm-D Singapore via fax (6837 2123) or email (regulatory@pharmd.com.sg). **Domide shall only be dispensed after receipt of authorization from Pharm-D Singapore.**

- Provide patient counseling on the benefits and risks of Domide therapy, including risks described in the BOXED WARNINGS in the Singapore package insert for Domide.
- Provide contraception and emergency contraception counseling with each new prescription prior to and during Domide treatment.
- Provide scheduled pregnancy testing for females of reproductive potential and verify negative pregnancy test results prior to writing a new prescription or subsequent prescriptions.
- Provide each patient with Patient Guide to Domide RMP Program.
- Write/ Dispense no more than a 4-week (28-day) supply to females of reproductive potential with no refills.
- Report any pregnancies in female patients or female partners of male patients prescribed Domide immediately to Pharm-D Singapore via email (regulatory@pharmd.com.sg) .

Prescription requirements

All patients

- Provide comprehensive counseling on the benefits and risks of therapy with Domide.
- Patients must be counseled on the risks of birth defects, venous thromboembolism, other side effects, and important precautions associated with Domide.
- Provide counseling not to share Domide capsules, and not to donate blood during treatment (including dose interruptions) and for 4 weeks after receiving their last dose of Domide as well as counseling on appropriate contraceptive use, including emergency contraception.
- Provide each patient with Patient Guide to Domide RMP Program.
- Patients should be instructed to not extensively handle or open Domide capsules and to maintain storage of capsules in blister packs until ingestion.
- Instruct patients to return unused Domide capsules for disposal to their Domide prescriber, or to the pharmacy that dispensed the Domide to them.

Female patients

Determine if female patient is of reproductive potential

Two categories:
1. Females of Reproductive Potential ● All females who are menstruating, amenorrheic from previous medical treatments, under 50 years of age, and/or perimenopausal, and do not qualify for the females not of reproductive potential category. **2. Females Not of Reproductive Potential** ● 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's syndrome, uterine agenesis

1. Females of Reproductive Potential

Pregnancy test requirements

- Prior to starting treatment:
  - Obtain a negative pregnancy test during consultation, when Domide 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.
- Follow-up and end of treatment:
  - A medically supervised pregnancy test should be repeated every 4 weeks, including 4 weeks after the end of treatment, except in the case of confirmed tubal sterilisation. These pregnancy tests should be performed on the day of the prescribing visit or in the 3 days prior to the visit to the prescriber.
  - If a patient misses her period or if there is any abnormality in menstrual bleeding, Domide should be discontinued immediately. Obtain a pregnancy test and counsel the patient.
- If pregnancy does occur during treatment, Domide must be immediately discontinued. Any suspected embryo-fetal exposure to Domide must be reported immediately to Pharm-D Singapore via email (regulatory@pharmd.com.sg). The

patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling.

- The patient must not breastfeed a baby while being treated with Domide.

Patient Counseling on Contraception Requirements

Contraception requirements

- Female patients of reproductive potential must either completely abstain from heterosexual sexual contact or must use 2 effective methods of contraception (at least one highly effective method and one effective method) at the same time.
- The 2 effective contraceptive methods include using at the same time at least 1 highly effective method and at least 1 additional method of birth control every time they have sex with a male.
- The 2 effective contraceptive methods must be started at least 4 weeks before Domide therapy, during therapy (including dose interruptions), and for at least 4 weeks following discontinuation of therapy.

Effective Methods of Birth Control Used at the Same Time

Highly effective birth control methods	**Additional effective birth control methods**
Birth control pill Contraceptive Injection (done 4 times a year) Intrauterine Device (IUD) Female sterilisation (permanent)	Male latex or synthetic condom Spermicide Diaphragm (to be used with spermicide) Cervical cap (to be used with spermicide) Female condom Vaginal ring

Remind all patients that not having any sexual intercourse is the only birth control method that is 100% effective.

- **Unacceptable forms of contraception:**
  - Natural family planning (rhythm method) or breastfeeding
  - Fertility awareness
  - Withdrawal
  - Cervical shield*

- Patients should be counseled that concomitant use of certain prescription drugs and/or dietary supplements can decrease the effects of hormonal contraception. If hormonal or IUD contraception is medically contraindicated, 2 other contraceptive methods may be used simultaneously during periods of concomitant use and for 4 weeks after stopping therapy.

*A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception.

2. Females Not of Reproductive Potential

- The patient must confirm that she is currently not pregnant, nor of reproductive potential as she has been in natural menopause for at least 12 months, or had a hysterectomy and/or bilateral oophorectomy.

- The parent or guardian must confirm that a prepubertal female child is not now pregnant, nor is of reproductive potential as menstruation has not yet begun, and/or the child will not be engaging in heterosexual sexual contact for at least 4 weeks before Domide therapy, during therapy, during dose interruptions, and for at least 4 weeks after stopping therapy.

Male patients

- Male patients must be instructed to use a latex or synthetic condom every time they have sexual intercourse with a female of reproductive potential during treatment and for 4 weeks after their last dose of Domide, even if they have undergone a successful vasectomy. The risk to the developing baby from the semen of male patients taking Domide is unknown.
- Male patients must be instructed not to donate sperm during treatment (including dose interruptions) and for 4 weeks after their last dose of Domide.

<u>Subsequent prescription requirements</u>

Female patients

- Provide counseling as outlined in the "Female patients" section on page 5.
- Follow pregnancy test requirements as outlined in "Pregnancy test requirements" section on page 5.

Male patients

- Provide patient counseling as outlined in the "Male patients" section on page 7.