Healthcare Professional Information Pack

Lenalidomide-Teva (Lenalidomide)

PPP- Pregnancy Prevention Program

Contents

For full information, please refer to Lenalidomide-Teva Package Insert as approved by HSA.

SECTION 1: Introduction

This information pack contains safety information for healthcare professionals on the teratogenic risk of lenalidomide as well as the requirements for prescribing and dispensing lenalidomide under the Pregnancy Prevention Program (PPP) to ensure the safe use and handling of the product. Please refer to the Lenalidomide-Teva Package Insert for the full safety and prescribing information.

SECTION 2: About Lenalidomide-Teva

Indication

Lenalidomide-Teva is indicated:

- as monotherapy for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.
- in combination with dexamethasone for the treatment of previously untreated multiple myeloma patients who are not eligible for transplant.
- in combination with dexamethasone for the treatment of multiple myeloma patients who have received at least one prior therapy.

Dosage and administration

- Please refer to Package Insert for dose regimens.

Teratogenicity associated with lenalidomide

- Due to its structural similarity to thalidomide, a known teratogen, lenalidomide is contraindicated in pregnant females or females of childbearing age.
- Females of reproductive potential may be treated with lenalidomide if they take adequate precautions to avoid pregnancy.
- To avoid embryo-foetal exposure, Lenalidomide-Teva is only available under a controlled access program called the Pregnancy Prevention Program (PPP).
- Only registered pharmacies/ dispensing clinics can dispense Lenalidomide-Teva under the PPP.

If lenalidomide is taken during pregnancy, a teratogenic effect of lenalidomide in humans is expected.

SECTION 3: Obligations of the Healthcare Professional regarding Lenalidomide-Teva

Healthcare Professionals must ensure they have read and understood this information pack before prescribing or dispensing Lenalidomide-Teva to their patients.

Comprehensive patient education

Healthcare professionals must ensure that patients receive comprehensive education before taking Lenalidomide-Teva. This must include

- Comprehensive advice and counselling on
  - o Benefits and risks associated with lenalidomide
  - o Potential risk of birth defects and other side effects
  - o Specific arrangements for a lenalidomide prescription to be dispensed

- Safety advice, including
  - o Appropriate advice on pregnancy avoidance (as per PPP)
  - o Risk of venous thromboembolism (predominantly deep vein thrombosis and pulmonary embolism) when taking lenalidomide with dexamethasone
  - o Risk of arterial thromboembolism (predominantly myocardial infarction and cerebrovascular event) when taking lenalidomide with dexamethasone
  - o Risk of second primary malignancies
  - o Disposal of unwanted medicine

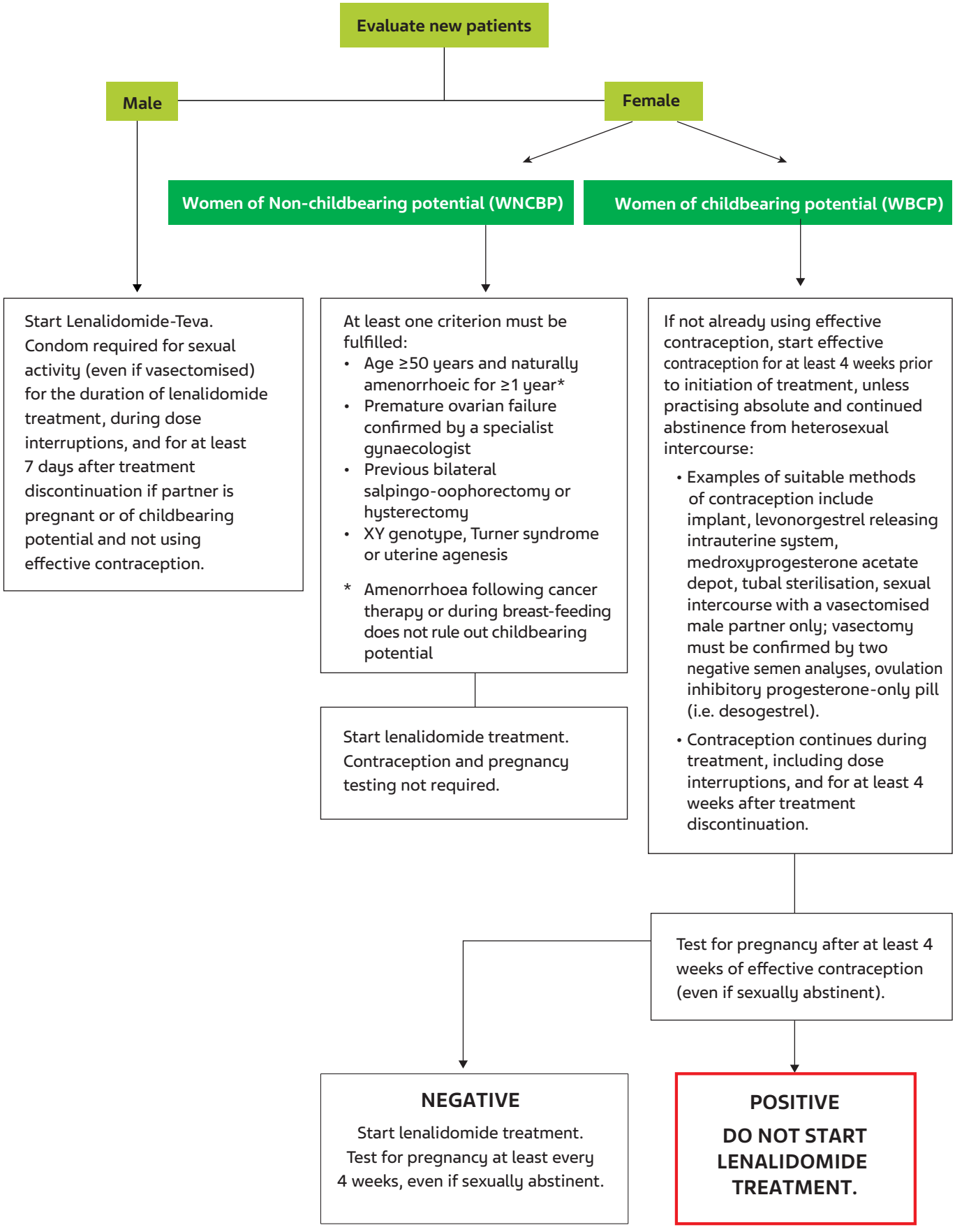
- Confirmation that the patient is able to comply with the requirements for the safe use of Lenalidomide-Teva

The prescriber should provide comprehensive safety information for patients with patient educational brochures and patient cards.

Maximum duration of prescription

- 4 weeks for women of childbearing potential
- 12 weeks for men and women without childbearing potential

SECTION 4: Lenalidomide-Teva Pregnancy Prevention Program and Patient Risk Categorisation Algorithm



Section 5: Information for Healthcare Professional

Categorisation of patients based on gender and childbearing potential
- Women of Non-Childbearing Potential
- Women of Childbearing Potential
- Men

To minimise the risk of a pregnancy occurring under the treatment of Lenalidomide-Teva, there are different requirements for each of these risk categories.

The prescriber must provide individual counselling for patients before they receive Lenalidomide-Teva to ensure that the associated risks of lenalidomide, particularly the risks of foetal exposure, are understood. Refer to the Risk Awareness Form for counselling patients receiving Lenalidomide-Teva which guides HCPs through the fulfillment of the PPP requirements. Please ensure that the patients are fully informed of and understand the risk of teratogenicity associated with the use of lenalidomide, including ensuring the patient declaration section is completed by the patient.

Other risks of venous and arterial thromboembolic events, and second primary malignancies in patients taking lenalidomide should be evaluated (refer to section 4.4 'Special warnings and precautions for use' of Package Insert). In addition, patient counselling should include general information (for example safety advice and side effects) about lenalidomide therapy as described in the Package Insert.

Prior to treatment initiation, Patients and Prescribers must complete the following:
• Risk Awareness Form for Counselling Patients Receiving Lenalidomide.

Patients should be provided with a copy of the following
• Risk Awareness Form for Counselling Patients Receiving Lenalidomide,
• Patient brochure,
• Patient Card.

These materials will provide the relevant information, including explaining the safe use of Lenalidomide-Teva, to patients receiving treatment with Lenalidomide-Teva.

General Advice for All Patients

- Lenalidomide is teratogenic in animals and expected to be teratogenic in humans.
- Inform of general precautions associated with the use of Lenalidomide-Teva.
- Inform patients on specific arrangements for a Lenalidomide-Teva prescription to be dispensed.
- Inform patient not to share medication and must return unused capsules at the end of treatment to their pharmacist for safe disposal.
- Inform patient to store the medication away safely so that no one else can take the medication by accident.
- Inform patient that the medication must be kept out of reach of children.
- Inform patient not to donate blood whilst taking Lenalidomide-Teva (including during dose interruptions) or for at least 7 days after stopping treatment.
- Inform female patient not to breastfeed during therapy with Lenalidomide-Teva as it is not known whether lenalidomide is excreted in human milk.
- Inform patients to tell their doctor about any adverse events.
- Inform patient why it is necessary to carry a patient card.

Handling Precautions

- The capsules should not be opened, crushed or overly handled.
- If powder from Lenalidomide-Teva makes contact with the skin, the skin should be washed immediately and thoroughly with soap and water.
- If powder from Lenalidomide-Teva 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.

For more information on safe handling of lenalidomide, please refer to the Lenalidomide-Teva Package Insert.

Criteria for women of non-childbearing potential

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. They do not need to undergo pregnancy testing nor receive contraceptive advice.

- Age ≥ 50 years and naturally amenorrhoeic for ≥ 1 year*
- Premature ovarian failure confirmed by a specialist gynaecologist.
- Previous bilateral salpingo-oophorectomy, or hysterectomy.
- XY genotype, Turner syndrome, uterine agenesis.

* *Amenorrhoea following cancer therapy or during breast-feeding does not rule out childbearing potential.*

Treating physicians are advised to refer their patient for a gynaecological opinion if there is any uncertainty whether a woman meets the criteria of non-childbearing potential.

A female patient must never take lenalidomide if she is pregnant.

5.1 Counselling

Safety advice for women of childbearing potential

For women of childbearing potential, **Lenalidomide-Teva is contraindicated unless all of the following are met:**

- She understands the expected teratogenic risk to the unborn child.
- She understands the need to use at least one effective method of contraception, without interruption, at least 4 weeks before starting treatment, throughout the entire duration of treatment, and at least 4 weeks after the end of treatment, and even in case of dose interruption.

OR

- She can commit to absolute and continuous abstinence from heterosexual intercourse during the entire period of risk associated with lenalidomide. The reliability of sexual abstinence needs to be evaluated in relation to the duration of use of treatment with lenalidomide and the preferred and usual lifestyle of the patient and be confirmed on a monthly basis. The prescriber should document this each month in the patient's medical records.

AND

- She must have a medically supervised negative pregnancy test (with a minimum sensitivity of 25_mIU/mL) prior to starting treatment (during the consultation when Lenalidomide-Teva is prescribed, or in the 3 days prior to the visit to the prescriber once contraception has been established for at least 4 weeks prior to treatment initiation), at least every 4 weeks during treatment (this includes dose interruptions), and at least 4 weeks after the end of treatment (unless confirmed tubal sterilization). This includes female patients of childbearing potential who confirm absolute and continuous abstinence from heterosexual intercourse during the entire period of teratogenic risk associated with Lenalidomide.

- She should be capable of complying with effective contraceptive measures.
- She understands the need to commence the treatment as soon as Lenalidomide-Teva is dispensed following a negative pregnancy test.
- She acknowledges that she understands the hazards and necessary precautions associated with the use of Lenalidomide-Teva.
- If she becomes pregnant whilst taking Lenalidomide-Teva, she should stop therapy and inform her treating physician immediately.
- She should be advised to inform the HCP prescribing her contraception about her treatment with lenalidomide.
- She should be advised to inform the HCP prescribing her treatment with lenalidomide if a change or cessation in method of contraception is needed.

Women of childbearing potential must acknowledge that they understand the risks and necessary precautions associated with the use of Lenalidomide-Teva. They must follow all the advice on effective contraception, even if the patient has amenorrhea. A patient not established on effective contraception must be referred to an appropriately trained HCP for contraceptive advice in order that contraception can be initiated.

Safety advice for men

Clinical data has demonstrated the presence of lenalidomide in human semen. As a precaution, **all male patients taking Lenalidomide-Teva must meet the following conditions:**

- He understands the expected teratogenic risk if engaged in sexual activity with a pregnant woman or a woman of childbearing potential.
- He understands and complies with the need to use condom if engaged in sexual activity with a pregnant woman or a woman of childbearing potential not using effective contraception (even if he has had a vasectomy) throughout the duration of treatment, during dose interruption and for at least 7 days after cessation of treatment.
- He must not donate semen or sperm during therapy (including during dose interruptions) and for at least 7 days following the discontinuation of Lenalidomide-Teva.
- He should be instructed that if his female partner becomes pregnant whilst he is taking Lenalidomide-Teva or 7 days after he has stopped taking Lenalidomide-Teva, he should inform his treating physician immediately. His partner should inform her HCP immediately. It is recommended that she be referred to an HCP specialized in teratology for evaluation and advice.

SECTION 6: Contraception

Women of childbearing potential must use at least one effective method of contraception for at least 4 weeks before therapy, during therapy, and until at least 4 weeks after ceasing Lenalidomide-Teva therapy and even in case of dose interruption unless the patient commits to absolute and continuous abstinence confirmed on a monthly basis. If not established on effective contraception, the patient must be referred to an appropriately trained healthcare professional for contraceptive advice in order that contraception can be initiated.

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)
- Ovulation inhibitory progesterone-only pills (i.e. desogestrel)

Because of the increased risk of venous thromboembolism in patients with multiple myeloma taking lenalidomide, combined oral contraceptive pills are not recommended (please refer to Package Insert for further details).

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.

Patients should be advised to inform their HCP 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-Teva agents, treatment must be discontinued, and the HCP informed immediately. Refer the patient to an HCP specialized in teratology for evaluation and advice.

SECTION 7: Pregnancy Testing

To confirm the absence of a pregnancy, women of childbearing potential patient must have medically supervised negative pregnancy tests with a minimum sensitivity of 25 mIU/mL before starting, during and after treatment with Lenalidomide-Teva.

Prior to starting treatment
A medically supervised pregnancy test should be performed during the consultation, when Lenalidomide-Teva 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-Teva.

During treatment and end of treatment
A medically supervised pregnancy test should be repeated at least every 4 weeks, including at least 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.

Requirements in the event of pregnancy
In the event of pregnancy (confirmed or suspected) whilst on treatment (or within 4 weeks from stopping treatment), the prescriber should:

- For women of childbearing potential, stop Lenalidomide-Teva immediately.
- For male patients, inform treating HCP immediately if female partner becomes pregnant while he is on Lenalidomide-Teva, or within 7 days after he has stopped receiving treatment with Lenalidomide-Teva.
- Refer the patient (or partner of a male patient) to a physician specialised or experienced in teratology for evaluation and advice.
- Notify Teva immediately by contacting Teva Drug Safety (contact details in section 8) and completing the Pregnancy Reporting Form. Teva will follow up with the HCP regarding the progress of all suspected pregnancies in female patients or female partners of male patients.
- Report the event to the Health Sciences Authority as per guidelines.

SECTION 8: Reporting of Adverse Events and Pregnancy

The safe use of Lenalidomide-Teva is of paramount importance. As part of the ongoing safety monitoring, Teva wishes to be informed of all adverse events, including pregnancy events, which have occurred during the use of Lenalidomide-Teva. Please report all adverse events to Teva Drug Safety within 1 business day.

In the event of pregnancy report, it is important that Teva should be notified immediately together with the completed Pregnancy Reporting form. The Pregnancy Reporting form is included in this pack.

Adverse events should be reported to the Vigilance and Compliance Branch, Health Products Regulation Group, Health Sciences Authority (HSA) via their online reporting portal (https://www.hsa.gov.sg/adverse-events). Please also email a copy of the submitted HSA adverse event reporting form to Teva.

Drug Safety Contact Details
Teva Pharmaceutical Investments Singapore Pte. Ltd.:
By Email: Safety.Singapore@teva.sg

SECTION 9: Other Risks Associated With Lenalidomide-Teva

The following section contains advice about how to minimize the other risks associated with the use of Lenalidomide-Teva.

Thrombocytopenia
Thrombocytopenia is one of the most commonly reported blood and lymphatic system disorders with Lenalidomide-Teva. It is recommended to monitor complete blood counts, including platelet count at baseline, weekly for the first 8 weeks and monthly thereafter. Patients should be monitored for signs of bleeding such as epistaxis, especially with use of concomitant medicinal products known to increase the risk of bleeding. The management of thrombocytopenia may require dose modification, use of blood product support and/or growth factors.

Please refer to the package insert on the recommended dose modifications during treatment and restart of treatment following an event of thrombocytopenia.

Second primary malignancies
The risk of occurrence of second primary malignancies (SPM) with Lenalidomide-Teva must be considered before initiating treatment with Lenalidomide-Teva. Physicians should carefully evaluate patients before and during treatment using standard cancer screening for occurrence of SPM and institute treatment as indicated.
Please refer to the package insert for further information regarding this adverse reaction.

Cardiac Dysfunction (Failure)
Cardiac dysfunction (failure) may occur during the treatment with Lenalidomide-Teva.

Please refer to the package insert for further information about these adverse reactions and the recommended precautions.

Tumor flare reaction and Tumor lysis syndrome
Cases of tumor flare reaction (TFR) and tumor lysis syndrome (TLS), including fatal cases, have been reported with the use of Lenalidomide-Teva. Cases of TLS have also been reported in clinical trials and post-marketing use of Lenalidomide-Teva. The patients at risk of TFR and TLS are those with high tumor burden prior to treatment. Caution should be practiced when introducing these patients to Lenalidomide-Teva. These patients should be monitored closely, and appropriate precautions taken where necessary.

Information for physicians, the treatment staff, patients and pharmacists about the use of personal information – Pregnancy Prevention Program relating to the administration of the drug Lenalidomide-Teva

Teva Pharmaceutical Investments Singapore Pte. Ltd. (hereinafter: "**Teva**" or "**we**") respects your right to privacy. Your ability to make informed decisions about the use of information belonging to you is important to us. In this document, we specify the information that we collect from you, how we protect it and what uses we make of the information.

Information that we collect

"Personal information" is information that can be attributed to a person or entity, such as a name, address or medical information. The personal information that we collect is collected through the completion of a paper or online registration form for the Pregnancy Prevention Program (the form is completed by the patient, the treating physician or the pharmacist), which includes, inter alia, name, identity card number (or other identification number), date of birth, membership in any private or public health insurance plan or cooperative, medical condition and diagnosis, state of pregnancy and/or fertility, the type of treatment and medicines, language preferences, details about parents and/or guardians and/or participation in instructional sessions. The personal information that we collect from physicians, the treatment staff and/or from pharmacists through their completion of the program registration form includes name, institutional affiliation, occupation, license number, telephone number and e-mail address. We may also collect any additional personal information that may be provided by patients, physicians, treatment staff and pharmacists in the future within the framework of the Pregnancy Prevention Program. We may also collect any additional personal information that you may provide to us now or in the future. It is your voluntary decision whether or not to provide us with particular information, and in doing so, you have consented to our collection of your personal information for any one or more of the above-mentioned purposes, including the collection and retention of some of the information in order to comply with the statutory and regulatory requirements.

How we protect the information

We employ commercially reasonable and accepted information-security measures to protect the information furnished to us, but there are no electronic transfer or storage methods that are absolutely secure. Therefore, although we try to employ maximum measures to protect your information, we cannot guarantee the absolute security of the information.

How we use the information

We will not share your information with any other parties without your express consent, apart from in ways explicitly referred to here, unless we will be required to do so pursuant to any law, regulation or court order or for the purpose of cooperating with an investigation by the law enforcement authorities. The main purposes for collecting and saving the information about you are for the participation in Pregnancy Prevention Program as is required by law and regulation, for the operation of this program and for the controlled dispensing of the medicine within its framework. We will share the information with the authorized authorities for the purpose of complying with these requirements. We may also use or share your personal information in order to provide or carry out services that may be ancillary to but necessary for your participation in the Pregnancy Prevention Program or any other services that you may have requested from us.

We use external companies as our subcontractors in order to provide us with services relating to the personal information, including in order to participate in the Pregnancy Prevention Program, and in order to store the personal information on their servers, which will be operated on our behalf. All of the subcontractors that will operate on our behalf will be subject to obligations regarding the use of information and to the obligations by law. We might transfer our databases, which contain your information, if we sell our business or a portion thereof, including while negotiating the sale and including during liquidation but, in such instance, the recipients of the information will undertake to safeguard confidentiality and to act in compliance with the relevant provisions specified in this document and to afford your personal data a standard of care and protection that is at least comparable to that required under the Personal Data Protection Act 2012.

Right to peruse and amend

You have a right to demand to peruse your information or to update or correct it in particular instances. If you wish to do so, please contact us at [IL_Privacy.Tevail@teva.co.il]. If you have any questions about this privacy policy, or if you do not agree to that stated therein or if you wish to contact us about any other matter, please contact us at [IL_Privacy.Tevail@teva.co.il]. While we will try our best to accommodate your request, we reserve the right to impose certain restrictions and requirements on such access requests, if allowed or required by applicable laws, such as, without limitation, where providing access could reasonably be expected to cause immediate or grave harm to the safety or to the physical or mental health of the individual who made the request.

Where you have withdrawn your consent, we will only retain such minimum necessary information pursuant to the applicable laws or any legal requirements. We may also decide for statistical analysis reasons or for business improvement purposes to keep track of your activity data on an aggregated or anonymous basis. Please note that we may not be able to provide the requested services or fulfil the purposes for which your personal information had been collected if you withdraw your consent.

Retention of personal data

We will retain your personal information for as long as the purposes for which you had provided such information to us requires it or as required by applicable law. We may also retain your personal information in a form that can no longer be associated with a particular individual (i.e., anonymised form), once said personal information is no longer required for the purpose for which it was collected, and retention is no longer necessary for legal or business purposes.

Modifications to this policy

For Healthcare Providers:

We reserve the right to change this privacy policy for any reason at any time without prior notice to you other than by either posting such revisions in a manner accessible to you, or / and on our website or via email notification. Such changes will be effective upon notice being given to you in either of the above-mentioned ways. The provisions contained herein supersede all previous notices or policies regarding our privacy practices.

For Patients:

We reserve the right to change this privacy policy for any reason at any time without notice to you other than by making such revisions accessible to you via your Healthcare Provider. If the revisions or changes to this privacy policy result in any collection, use or disclosure of your personal information in a manner not contemplated by this privacy policy, we may seek your consent again.

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