TAPROS® 3M DEPOT 11.25 mg Powder for Injection

LEUPRORELIN ACETATE

DPS

1 NAME OF THE MEDICINAL PRODUCT

TAPROS® 3M DEPOT 11.25 mg Powder for Injection

2 COMPOSITION

TAPROS® 3 Month Depot DPS powder and solvent for prolonged-release suspension for injection in prefilled-syringe 11.25 mg.

Each single-dose syringe contains 11.25 mg of Leuprorelin Acetate. For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

TAPROS® is white powder and clear, colorless solvent in a dual chamber prefilled-syringe.
Reconstituted solution: White suspension which on standing deposits a white sediment which is readily re-suspended on shaking.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of prostatic cancer with metastase.
- Treatment of endometriosis at genital and extragenital localization (from stage I to stage IV).
  The clinical knowledge concerning the endometriosis treatment is limited to women over 18 years old.
  The treatment duration is limited to 6 months.
  It is not recommended to start a second treatment period with TAPROS or with another Gn-RH analogue.
- Breast cancer in pre-menopausal and peri-menopausal women, provided endocrine treatment is indicated.

4.2 Posology and method of administration

- Prostatic cancer and breast cancer
  One subcutaneous or intramuscular injection which will be renewed every 3 months.

- Endometriosis
  The treatment should start during the five first days of the menstrual cycle. One subcutaneous or intramuscular injection will be renewed every 3 months.
  Duration: endometriosis will be treated during no more than 6 months whatever is the stage.

TAPROS® should be used after suspending it completely by transferring the whole quantity of the vehicle into the powder part, by pressing the plunger rod, with the injection needle held upward, with caution against foaming. It becomes impossible to adjust the dosing quantity. Therefore, it should be used only when the patient requires the whole quantity at a time.

4.3 Contraindications

All patient populations

- Hypersensitivity to synthetic Gn-RH, to Gn-RH analogues or to one of the components.

All females

- Vaginal bleedings of non determined origin.
- Pregnancy. Do not use when pregnancy. The non pregnancy must be confirmed before treatment.
- Nursing. Because of the lack of data regarding TAPROS excretion in milk and its potential effects on nursing mothers, TAPROS will not have to be used in this case.

4.4 Special Warnings and Precautions for use PRECAUTION

All patient populations

Since Tapros is a sustained release preparation with its action lasting 12 weeks, administration at an interval exceeding 12 weeks may lead to the recurrence of an increase in the serum level of gonadotropic hormone due to loss of suppression of the pituitary-gonad system, resulting in a transient aggravation of the clinical condition. Therefore, the method of administering once every 12 weeks should be observed.

Seizures:

Postmarketing reports of seizures have been observed in patients treated with leuprorelin acetate and these events have been reported in both children and adults, and in those with or without a history of epilepsy, seizure disorders or risk factors for seizures.

Depression

There is an increased risk of depression in patients undergoing treatment with leuprorelin acetate and patients should be monitored as appropriate.

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) which can be life-threatening or fatal, have been rarely reported with leuprorelin treatment. At the time of prescription patients should be advised of the signs and symptoms and monitored closely for delayed hypersensitivity reactions. If signs and symptoms suggestive of these reactions appear, leuprorelin should be withdrawn immediately and an alternative treatment considered (as appropriate).

All adult populations

Bone mineral loss

Long-term estrogen deprivation by bilateral oophorectomy, ovarian ablation or administration of GnRH analogues or long-term androgen deprivation either by bilateral orchiectomy or administration of GnRH analogues is associated with increased risk of bone mineral loss which, in patients with additional risk factors, may lead to osteoporosis and increased risk of bone fracture (see Undesirable Effects, 4.8).

Metabolic changes and cardiovascular risk

Inhibition of endogenous sex hormone production, such as during androgen deprivation therapy (as identified from epidemiological data) or estrogen deprivation (e.g. in menopausal females), is associated with metabolic changes (e.g. reduction in glucose tolerance or aggravation of pre-existing diabetes) as well as an increased risk for cardiovascular disease (see Undesirable Effects, 4.8). However, prospective data did not confirm a link between treatment with GnRH analogues and an increase in cardiovascular mortality.

Patients at high risk for metabolic or cardiovascular diseases should be appropriately monitored.

Adult females (Endometriosis, breast cancer)

- Before starting treatment with leuprorelin acetate, pregnancy must be excluded (see Contraindications, 4.3).
- During the period of the treatment, the patient should be instructed to prevent conception with the use of non-hormonal methods.
- In the early period after first administration of this medicinal product, transient aggravation of the clinical condition may occur. However, this may disappear in the course of continued administration.
- Prior to administration of leuprorelin acetate, undiagnosed abnormal vaginal bleeding must be investigated, diagnosis confirmed and relevant management initiated.

Endometriosis indication

- The incidence of adverse reactions generally tends to increase with an increase in dose. Thus, in setting the dose, careful attention should be paid to the body weight.
- In administration of TAPROS, care should be taken to differentiate a similar disease (malignant tumor, etc) from endometriosis. If during administration of TAPROS, any growing phyma is found or no improvement is seen in the clinical symptom, the administration should be discontinued.
- The duration of administration of leuprorelin acetate should be limited to 6 months, as its use is associated with an increased risk of bone mineral loss (see Bone Mineral loss, 4.4). If it is necessary to resume administration of leuprorelin acetate, changes in bone parameters should be closely followed.

Breast cancer indication

- When starting treatment with TAPROS, absence/presence of hormone receptor expression should be confirmed as a rule. When hormone receptor expression is confirmed to be negative, TAPROS should not be used.
- Since TAPROS is an agent for endocrine therapy, use of this drug for premenopausal breast cancer should be limited to patients for whom treatment with TAPROS is considered appropriate under the supervision of a physician who has adequate knowledge and experience in medication for cancer.
- If antitumor effect is not obtained with TAPROS and any progression of the tumor is observed, the administration should be discontinued.

Adult males (Prostate cancer)

- Since Tapros is an agent for endocrine therapy, use of this drug for prostate cancer should be limited to patients for whom treatment with TAPROS is considered appropriate under the supervision of a physician who has adequate knowledge and experience in medication for cancer.
- ***Flare phenomenon***

  Aggravation of the signs and symptoms of prostate cancer may occur following a transient increase in serum testosterone level in the early period after initiation of treatment, for example urinary tract obstruction and hematuria (as urinary symptoms). In patients with spinal cord compression due to metastasis to the spine, bone pain, weakness of lower extremities and paresthesia (as neurologic symptoms) may also occur (see Undesirable Effects, 4.8).

  Therefore, particular care should be taken in patients with metastasis to the spine and those with urinary tract obstruction. Careful observation should be made during the first several weeks after initiation of the treatment.
- **QT prolongation:**

  Androgen deprivation therapy may prolong the QT interval.

  In patients with a history of or risk factors for QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval (see Section 4.5) physicians

should assess the risk and benefits risk ratio including the potential for Torsade de pointes prior to initiating leuprorelin acetate.

CAREFUL ADMINISTRATION
TAPROS should be administered with care in the following patients:

Endometriosis and Breast cancer
Patients with submucous myoma, bleeding symptom may be aggravated. Therefore, close observations should be made. The patient should be instructed to contact the attending physician in case of any aggravation of the bleeding symptom.

Breast cancer
In the early period after the first administration of TAPROS, a transient elevation of the serum level of estrogen may occur owing to the stimulating effect of TAPROS, as a highly active LH-RH derivative, on the pituitary-gonad system, resulting in a transient aggravation of bone pain, etc. In such a case, symptomatic treatment should be given.

PRECAUTION CONCERNING USE
- Route of administration
  Tapros should be used only by the subcutaneous or intramuscular route. [Intravenous injection of Tapros may induce thrombosis].
- Preparation:
  - Use immediately after mixing as the suspension settles out very quickly following reconstitution.
  - If any sedimentation is noticed in the suspension of vial product, such suspension should be used after swirling gently, avoiding formation of bubbles, to resuspend the particles uniformly.
- Use immediately after reconstitution.
- Method of administration, see Instruction for Use/ Handling, 6.5.

Other Precautions
<u>For all indications</u>
It has been reported that the benign pituitary adenoma was observed in rats in a study in which this drug was administered subcutaneously in doses of 0.8, 3.6 and 16 mg (as leuprorelin acetate)/kg at 4- week intervals for 1 year and another study in which an aqueous injectable solution of Leuprorelin Acetate was similarly administered in doses of 0.6, 1.5 and 4 mg/kg/day for 2 years.

<u>Endometriosis and breast cancer</u>
It has been reported that the administration of TAPROS brought about venous thrombosis or pulmonary embolism.

<u>Prostate cancer</u>
It has been reported that the administration of TAPROS brought about cerebral infarction, venous thrombosis or pulmonary embolism.

4.5 Interaction with other medicaments and other forms of interaction
TAPROS should be administered with care when coadministered with sex hormone preparations. There is no specific data described in each data sheet.

Prostate cancer Indication
Since androgen deprivation treatment may prolong the QT interval, the concomitant use of leuprorelin acetate with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes such as Class IA (e.g. quinidine, disopyramide) or Class III (e.g. amiodarone,

sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, should be carefully evaluated (see Section 4.4).

4.6 Pregnancy and lactation

This drug should not be administered to pregnant females or nursing mothers.

4.7 Effects on ability to drive and use machines

TAPROS can influence the ability to drive and use machines due to visual disturbances and dizziness.

4.8 Undesirable effects

Adverse reactions

Clinically significant adverse reaction:

- Since **interstitial lung disease**, accompanied by fever, coughing, dyspnea, abnormal chest X-ray, etc. may occur (<0.1%), the patient's condition should be closely observed. If any abnormality is observed, appropriate measures, such as treatment with adrenal cortical hormones, should be taken.
- Since anaphylactoid symptoms may occur (<0.1%), careful inquiry should be made, and close observation should be made after the administration of Tapros. If any abnormality is observed, appropriate measures should be taken.
- **Hepatic dysfunction or jaundice**, with increased AST(GOT), ALT(GPT) etc., may occur (frequency unknown). Therefore, close observation should be made, and if any abnormality is observed, appropriate measures should be taken.
- **Metabolic syndrome (including hypertension, dyslipidemia, Development or aggravation of diabetes** may occur (frequency unknown). If any abnormality is observed, appropriate measures should be taken.
- **Pituitary apoplexy** has been reported in patients with pituitary adenoma (frequency unknown). Therefore, if headache, vision impairment, visual field disorder, etc. are observed immediately after the first dose of Tapros, appropriate measures, such as surgical treatment, should be taken after conducting examination.
- **Thromboembolic event, such as myocardial infarction, cerebral infarction, venous thrombosis, pulmonary embolism**, may occur (frequency unknown). Therefore, close observation should be made, and if any abnormality is observed, appropriate measures, such as discontinuation of administration, should be taken.
- For all patient populations, **metabolic disorders (hepatic steatosis)**, **skin and subcutaneous tissue disorders (Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, Erythema multiforme, Bullous dermatitis, Exfoliative dermatitis, Acute generalized exanthematous pustulosis, Toxic skin eruption), and psychiatric disorders (suicidal ideation, suicidal behaviour, suicide attempt)** may occur (frequency unknown).

<u>Prostatic cancer</u>

- Since a depressed state may occur (<0.1%)/ mood changes, the patient's condition should be closely observed.
- Elevation of serum testosterone level due to the stimulation effect of Tapros on the pituitary-gonad system may bring about a transient aggravation of bone pain, ureteral obstruction or spinal cord compression (≥ 5%). If any of such symptoms occurs, appropriate measures, such, as pertinent symptomatic treatment, should be taken.
- Since cardiac failure may occur (0.1 - <5%), close observation should be made. If any abnormality is observed, appropriate measures, such as discontinuation of administration, should be taken.

	≥5%	0.1% - < 5%	< 0.1%	Frequency unknown
1) Hepatic Close observation should be made	Increased LDH	Jaundice, or increased AST(GOT), ALT(GPT), γ-GTP or ALP		
2) Endocrine	Hot flushes, feeling of warmth	Headache, insomnia, facial hot flushes, dizziness, diaphoresis, decreased libido, erectile dysfunction, gynecomastia, testicular atrophy or discomfort in the perineal region		
3) Musculoskeletal		Arthralgia, bone pain, pain in the shoulder, low back or limbs, or difficulty in walking, or stiffness of fingers or other joints	Muscle ache or decreased bone mass	Osteoporosis (including vertebral body fractures)
4) Dermatologic		Dermatitis, or hair growth on the head		
5) Urinary		Pollakiuria, hematuria or increased BUN		
6) Cardiovascular		ECG abnormalities or increased cardiothoracic ratio		
7) Hematologic		Anemia or platelet count decreased		White blood cell decreased
8) Gastrointestinal		Nausea, vomiting, anorexia or constipation	Diarrhea	
9) Hypersensitivity		Rash or pruritus		
10) Administration site		Pain, induration and redness		Reactions at the injection site such as abscess, swelling, ulcer, pruritus, granuloma, mass, warmth, and necrosis
11) Others	Fatigue	Edema, pressure sensation of chest, rigor, malaise, numbness of lips	Weakness	Seizures, visual impairment

	≥5%	0.1% - < 5%	< 0.1%	Frequency unknown
		or limbs, weight increase, paresthesia, deafness, tinnitus, fever, increased total cholesterol, triglyceride or uric acid, hyperkalemia, or increased blood sugar level.		

Endometriosis and Breast cancer

- Since a depressed state may occur (<0.1%-<5%), the patient's condition should be closed observed.

	≥ 5%	0.1% - < 5%	< 0.1%	Frequency unknown
1) Symptoms resulting from decreased estrogen	Hot flushes, feeling of warmth, feeling of hot flushes, shoulder stiffness, headache, insomnia, dizziness or diaphoresis	Decreased libido, coldness, visual disturbance or emotional lability		
2) Female reproductive		Metrorrhagia, Vaginal dryness, coital pain, Vulvovaginitis, increased fluor, ovarian hyperstimulation syndrome, or pain, swelling or atrophy of the breast		
3) Musculoskeletal	Pains, such as arthralgia and bone pain	Stiffness of fingers or other joints, lumbar pain, muscle ache, muscular spasm, decreased bone mass, increased serum phosphorus or hypercalcemia		Osteoporosis (including vertebral body fractures)
4) Dermatologic		Acne, dry skin, alopecia, hypertrichosis or nail abnormality		
5) Psycho-neurologic		Sleepiness, irritated feeling, hypomnesia, decreased attentiveness or paresthesia		
6) Hypersensitivity		Rash or pruritus		

	≥ 5%	0.1% - < 5%	< 0.1%	Frequency unknown
7) Hepatic close observation should be made		Increased AST(GOT), ALT(GPT), ALP, LDH, γ-GTP or bilirubin	Jaundice	
8) Gastrointestinal		Nausea, vomiting, anorexia, abdominal pain, feeling of enlarged abdomen, diarrhea, constipation, stomatitis or thirst		
9) Cardiovascular		Palpitation or increased blood pressure		
10) Hematologic		Red blood cell count increased, anemia, white blood cell decreased, platelet count decreased or prolonged partial thromboplastin time		
11) Urinary		Pollakiuria, dysuria or increased BUN		
12) Administration site		Pain, induration and redness		Reactions at the injection site, such as abscess, swelling, ulcer, pruritus, granuloma, mass, warmth and necrosis
13) Others		Fatigue, malaise, weakness, numbness of lips or limbs, carpal tunnel syndrome, tinnitus, deafness, chest discomfort, edema, weight increase, pain of lower extremities, respiratory distress, fever, increased total cholesterol, LDL cholesterol or triglyceride, or hyperkalemia	Weight decrease, taste abnor-mality or abnormal thyroid function	Seizures

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of TAPROS® is important. It allows continued monitoring of the benefit/risk balance of TAPROS®. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system (e-meso.pom.go.id) and/or to Takeda Indonesia (email: AE.Indonesia@takeda.com).

4.9 Overdose

In case of overdose, the patients should be monitored closely and management should be symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

ATC Code: L02AE02

Pharmacotherapeutics group: Antineoplastic and Immunomodulating Agents

Leuprorelin is a synthetic nonapeptide analogue of natural Gn-RH. The studies performed in human as well as in animals have demonstrated that, after an initial stimulation, the prolonged administration of leuprorelin induces a decrease of gonadotropin secretion, consequently suppressing the testicular function in men, and inducing an atrophy of the uterine and ectopic endometrial tissue in women. This effect is reversible upon discontinuation of drug therapy.

Through some studies in animals, another mechanism of action has been evoked: a direct effect by the decrease of sensitivity of the gonadotropin receptors.

In human, after administration of the first dose, an increase in circulating levels of LH and FSH is induced, leading to an initial increase in levels of the gonadal steroids (testosterone and dihydrotestosterone in men and estradiol in women). The pursuit of the treatment leads to a decreased in LH and FSH levels, inducing within 3 to 4 weeks, to androgen or estrogen levels equivalent to those obtained after castration or menopause, as long as drug administration continues.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polylactic acid, D-Mannitol.

Suspensions

D-Mannitol, Carmellose Sodium, Polysorbate 80, water for injection

6.2 Incompatibilities

This drug must be injected alone.

6.3 Special precaution for Storage

Store below 30^{o}C, avoiding heat.

No refrigeration necessary.

6.4 Package

Box, 1 Dual Chamber Prefilled Syringe @ 11.25 mg & 1 ml solvent

Reg. No. DKI0770700244B2

6.5 Instruction for Use/ Handling

INSTRUCTIONS FOR USE
TAPROS® 3M DEPOT 11.25 MG DPS

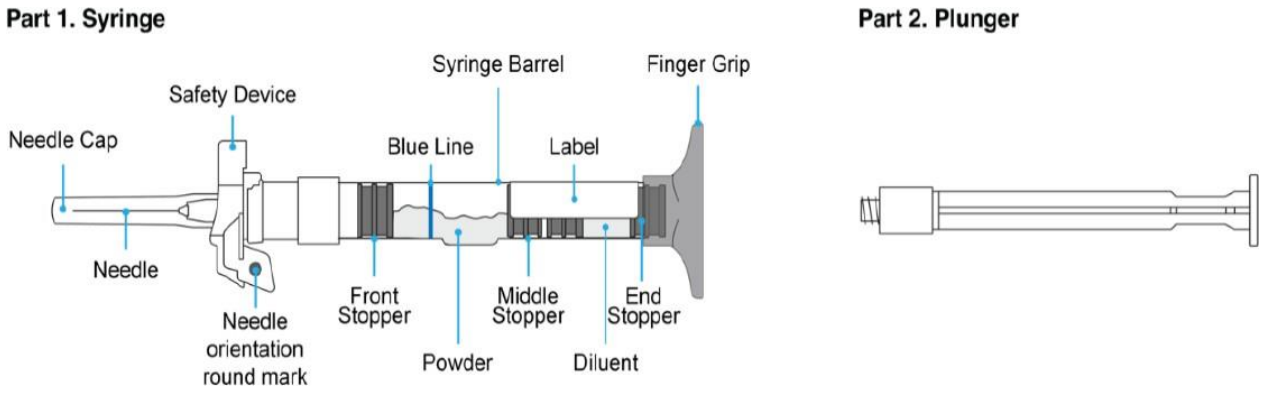
TAPROS® is supplied as dual-chamber prefilled syringe for subcutaneous or intramuscular injection. This Instructions for Use contains information on how to reconstitute and inject TAPROS® for prostatic cancer, breast cancer, endometriosis and uterine myoma (fibroid).

Important Information:

- **Do not** use if medication is expired.

- **Do not** use if syringe or packaging appears damaged.
- **Do not** use the syringe if the powder appears clumped or caked.
- **Do not** use the syringe if the powder or diluent appears discolored.
- Storage condition: Store below 30°C, avoiding heat. No refrigeration necessary.
- Keep the dual-chamber syringe in the outer carton in order to protect from light.
- Hold the syringe upright (with the needle side up) throughout entire preparation to prevent leakage. If leaking occurs, the dose should not be administered.
- Use immediately after mixing as the suspension settles out very quickly following reconstitution.
- This medication may be injected intramuscularly or subcutaneously for endometriosis and uterine myoma (fibroid) and subcutaneously for prostatic cancer and breast cancer.

Parts Overview



The device may have the plunger already attached to the syringe.

Preparation

1. Wash hands before opening the syringe package. **(Figure1)**

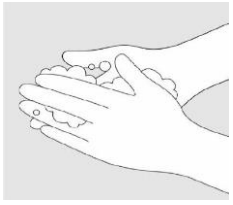


Figure 1: Wash hands

Reconstitution

2. Open package and remove the syringe (Parts Overview Part 1). **(Figure 2)**

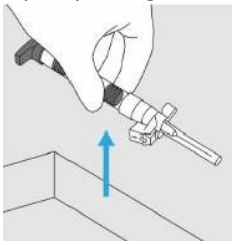


Figure 2: Remove Syringe

3. Check the expiration date printed on the syringe, and the powder and diluent in the syringe barrel. The powder should be white and dry, and the diluent should be clear.
4. Inspect the syringe for any damage. **(Figure 3)**

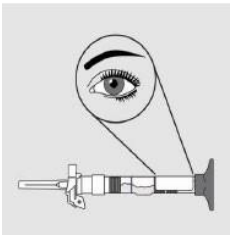


Figure 3: Inspect Syringe

a. **Do not** use the syringe if the expiration date has passed.
b. **Do not** use the syringe if the powder appears clumped or caked.
c. **Do not** use the syringe if the powder or diluent appear discolored.
d. **Do not** use the syringe if any part of it is damaged.

5. Gently tap the syringe to remove any lumps and release any powder stuck on the syringe walls. **(Figure 4)**

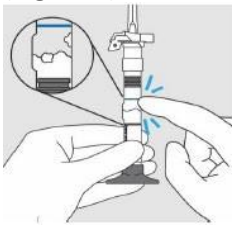


Figure 4: Check Powder

6. **Without removing the needle cap, twist the needle to the right (clockwise) to ensure it secured tightly. (Figure 5)**
   a. **Do not** remove needle cap until you are ready to inject.

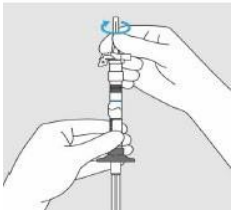


Figure 5: Twist needle to tighten

7. Holding the syringe upright, release the diluents by slowly pushing the plunger until the middle stopper reaches the blue line in the middle of the syringe. You should see the diluent flowing into the interior chamber above the blue line. **(Figure 6)**
   a. **Do not** remove the needle cap before releasing the diluent.
   b. **Do not** push the plunger too quickly or push past the blue line as these actions may cause leaking.
   c. **Do not** withdraw plunger again.

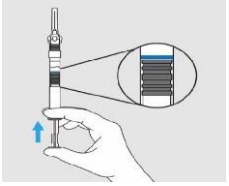


Figure 6: Release diluent

8. Gently tap the syringe against the palm of your hand to mix the powder and diluent until it forms a uniform suspension. When properly mixed, the suspension should appear milky with no visible lumps. **(Figure 7)**
   a. If particles stick to the stopper during mixing, dislodge them by gently tapping the syringe

with your finger.

b. Avoid hard tapping or shaking to prevent the generation of bubbles.

c. Use immediately after mixing as the suspension settles out very quickly following reconstitution.

Figure 7: Tap syringe against palm to mix

9. Remove the needle cap by pulling it straight upwards. **(Figure 8)**

a. **Do not** twist the needle cap.

Figure 8: Pull upwards without twisting to remove needle cap

10. Prime the syringe by pushing the plunger upward until all air has been expelled from the syringe. **(Figure 9)**

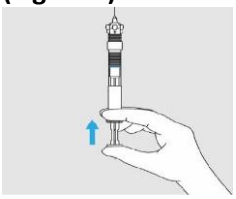


Figure 9: Push plunger to prime syringe

11. The syringe is now ready for injection. Use immediately as the suspension settles out very quickly following reconstitution.

Intramuscular and Subcutaneous Administration

1. Choose the injection site. Intramuscular injection sites include shoulder (deltoid), upper buttock (ventrogluteal), and thigh. **(Figure 10)** Subcutaneous injection sites include stomach area (abdomen), thighs, upper arms, and buttock. **(Figure 11)**

2. Clean the skin at the injection site with an alcohol swab and allow to air-dry.
   a. **Do not** inject at a location where the skin is red, swollen, scarred, or damaged.
   b. **Do not** use the same injection site for more than one injection consecutively.

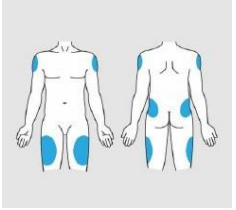


Figure 10: Intramuscular injection site

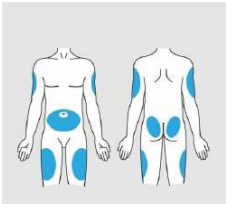


Figure 11: Subcutaneous injection site

3. For intramuscular injection:
   a. Gently pull the skin at the injection site taut and insert needle at a 90º or 180º angle to the skin. Before inserting the needle, check the orientation of the safety device. The arrow on the safety device should be pointed towards the patient, with the round mark directed upward. **(Figure 12)**

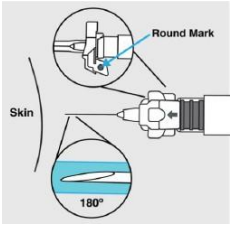


Figure 12: Pull skin taut and insert needle

   b. Once the needle has been inserted, aspirate the needle by pulling the plunger backward for 5–10 seconds. Care should be taken to avoid inadvertent injection into a blood vessel. If blood is visible in the needle barrel, stop the injection and withdraw the needle immediately. **(Figure 13)**

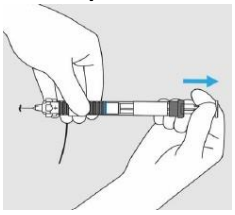


Figure 13: Pull plunger backward to aspirate

   c. Push the plunger all the way down slowly until entire contents of the syringe have been injected. Pull needle straight out at the same angle it was inserted, then use clean gauze to apply gentle pressure. **(Figure 14)**
      i. **Do not** rub the injection site.
      ii. **Do not** recap the needle after injection.

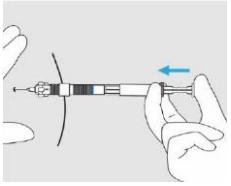


Figure 14: Push plunger to inject

   d. When injection is complete, withdraw the needle from the patient. Immediately activate the safety device by pressing upward from just below the arrow until a “CLICK” is heard or felt and the needle is fully covered. **(Figure 15)**

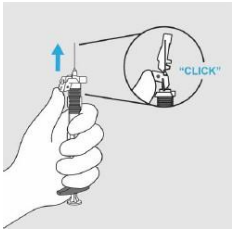


Figure 15: Activate safety device

4. For Subcutaneous Injection:
   a. Pinch a 2.5cm section of skin between your fingers and insert needle at a 30º – 90º angle. Before inserting the needle, check the orientation of the safety device. The arrow on the safety device should be pointed towards the patient, with the round mark directed upward. **(Figure 16)**

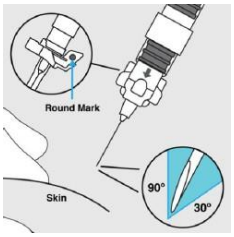


Figure 16: Pinch skin and insert needle

   b. Push the plunger all the way down slowly until the entire contents of the syringe have been injected. Pull needle straight out at the same angle it was inserted, then use clean gauze to apply gentle pressure. **(Figure 17)**
      i. **Do not** rub the injection site.
      ii. **Do not** recap the needle after injection.

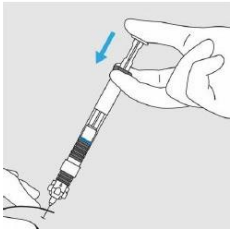


Figure 17: Push plunger to inject

   c. When the injection is complete, withdraw the needle from the patient. Immediately activate the safety device by pressing upward from just below the arrow until a "CLICK" is heard or felt and the needle is fully covered. **(Figure 18)**

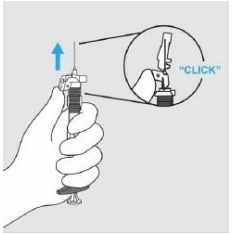


Figure 18: Activate safety device

Storing TAPROS DPS
Store below 30°C, avoiding heat. No refrigeration necessary.

Disposing of TAPROS DPS
Dispose of the used device in the appropriate sharp's container in accordance with your local standard procedure.

DOCTOR'S PRESCRIPTION IS REQUIRED FOR THE USE OF THIS PREPARATION.

HARUS DENGAN RESEP DOKTER.

Based on CCDS ver. 22.0

Manufactured by Takeda Pharmaceutical Company Limited, Hikari, Japan
Secondary packed by Aupa Biopharm Co., Ltd., Hsinchu, Taiwan

Marketing Authorization Holder: PT Takeda Indonesia, Bekasi, Indonesia

INFORMASI OBAT UNTUK PASIEN
TAPROS® 3M DEPOT

Leuprorelin acetate

Injeksi suspensi lepas lambat 11.25 mg Serbuk injeksi dan Pelarut dalam Dual-Chamber Prefilled Syringe

Baca keseluruhan isi brosur ini dengan seksama sebelum Anda mulai menggunakan obat ini karena mengandung informasi penting untuk Anda.

- Simpan brosur ini. Anda mungkin perlu untuk membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, Anda bisa bertanya pada dokter atau apoteker Anda.
- Obat ini diresepkan untuk Anda. Jangan memberikannya pada orang lain. Obat ini bisa membahayakan mereka, walaupun tanda-tanda penyakit mereka sama dengan Anda.
- Jika ada mengalami efek samping, bicarakanlah pada dokter atau apoteker Anda, termasuk efek samping yang tidak tercantum pada brosur ini. Lihat Bagian 4.

Brosur ini terdiri dari:

1. APA ITU TAPROS 3M DEPOT DAN APA KEGUNAANNYA

TAPROS 3M DEPOT adalah hormon sintetik yang dapat digunakan untuk menurunkan kadar testosteron dan estrogen yang beredar dalam tubuh.

TAPROS 3M DEPOT dapat digunakan untuk mengobati kanker prostat pada pria dan endometriosis, mioma uteri (fibroid), dan kanker payudara pada wanita.

2. APA YANG PERLU ANDA KETAHUI SEBELUM MENGGUNAKAN TAPROS 3M DEPOT

Jangan menggunakan TAPROS 3M DEPOT:

- Jika Anda alergi (hipersensitif) terhadap leuprorelin acetate (TAPROS 3M DEPOT atau TAPROS) atau kandungan lain TAPROS 3M DEPOT (tercantum pada bagian 6).
- Jika Anda hamil, berencana untuk hamil atau sedang menyusui.
- Jika Anda mengalami pendarahan vaginal yang tidak normal yang belum Anda diskusikan dengan dokter Anda.

Peringatan dan Perhatian:

- Jika Anda diabetes, TAPROS 3M DEPOT bisa memperburuk diabetes Anda. Oleh karena itu, pasien diabetes memerlukan monitoring kadar glukosa darah lebih sering.
- Jika Anda memiliki diabetes atau menderita masalah jantung, Anda harus memberitahu dokter Anda. Jika Anda beresiko mengalami pengeroposan tulang (osteoporosis), Anda harus memberitahu dokter Anda sebelum menggunakan TAPROS 3M DEPOT. Faktor risiko termasuk:
    - Jika Anda atau salah satu keluarga dekat Anda mengalami penipisan tulang.
    - Jika Anda minum alkohol berlebihan, dan / atau perokok berat.
    - Jika Anda menggunakan obat untuk epilepsi atau mengkonsumsi steroid seperti hidrokortison atau prednisolon untuk waktu yang lama.
- Terdapat laporan depresi pada pasien TAPROS 3M DEPOT yang mungkin parah. Jika Anda menggunakan TAPROS 3M DEPOT dan muncul perasaan depresi, informasikanlah ke dokter Anda.
- Jika Anda mengalami reaksi alergi berat yang ditandai dengan ruam dan lepuhan di kulit, lapisan bola mata, rongga

mulut, dubur, dan kelamin (Sindrom Stevens-Johnson) atau reaksi hipersensitivitas pada kulit (Nekrolisis Epidermal Toksik), segera hentikan pengobatan dan konsultasikan dengan dokter Anda.

Untuk wanita:

- Jika Anda seorang wanita dengan fibroid submukosa (tumor jinak pada otot di bawah lapisan rahim), TAPROS 3M DEPOT bisa menyebabkan perdarahan hebat ketika *fibroid break-down*. Hubungi segera dokter Anda jika Anda mengalami perdarahan berat atau tidak biasa atau nyeri.
- Jika Anda seorang wanita dan mengalami menstruasi berkelanjutan setelah memulai pengobatan dengan TAPROS 3M DEPOT, Anda harus memberitahu dokter Anda.
- Jika Anda seorang wanita usia subur, Anda harus menggunakan kontrasepsi non hormonal selagi menggunakan TAPROS 3M DEPOT. Meskipun TAPROS 3M DEPOT menyebabkan menstruasi berhenti, obat ini bukanlah alat kontrasepsi. Jika Anda tidak yakin dengan ini, diskusikanlah dengan dokter Anda.

Untuk pria:

- Jika Anda mengalami obstruksi (sumbatan) urin atau kompresi (tekanan) sumsum tulang belakang, dokter Anda akan memonitor Anda dengan seksama pada beberapa minggu pertama pengobatan.
- Jika Anda pasien kanker prostat, dan sebelumnya pernah menerima injeksi hormone sintetik lain yang tidak berefek pada Anda dengan baik, atau Anda pernah menerima operasi pembuangan testis, Anda harus menginformasikannya ke dokter Anda.
- Informasikan ke dokter Anda jika Anda mengalami kondisi jantung atau pembuluh darah yang tidak normal, atau Anda sedang menggunakan obat-obatan untuk kondisi ini.

Obat-obatan lain dan TAPROS 3M DEPOT

Infomasikan dokter atau apoteker jika Anda menggunakan atau baru saja menggunakan obat lain, termasuk obat-obatan tanpa resep dokter..

Diperlukan kehati-hatian pada penggunaan TAPROS 3M DEPOT bersamaan dengan obat hormon sex lain.

Kehamilan dan Menyusui

TAPROS 3M DEPOT tidak boleh digunakan pada wanita muda yang sedang hamil atau menyusui (lihat juga bagian "Jangan menggunakan TAPROS 3M DEPOT")

Berkendara dan menggunakan mesin

Jangan berkendara atau mengoperasikan mesin jika Anda mengalami kantuk, pusing atau gangguan penglihatan selama pengobatan dengan TAPROS 3M DEPOT.

3. BAGAIMANA MENGGUNAKAN TAPROS 3M DEPOT

Dokter atau perawat akan memberikan suntikan TAPROS 3M DEPOT 3M DEPOT. injeksi biasanya akan diberikan di lengan, paha atau perut. Tempat suntikan dapat bervariasi secara berkala.

Anda biasanya akan diberikan suntikan setiap 3 bulan sekali. Jika Anda memiliki endometriosis, Anda akan diberikan suntikan TAPROS 3M DEPOT 3M DEPOT untuk jangka waktu 6 bulan saja dan pengobatan akan dimulai selama lima hari pertama siklus menstruasi.

Jika Anda terlewat dalam menerima injeksi

Sesegera setelah Anda sadar bahwa Anda terlewat menerima injeksi, hubungi dokter Anda yang dapat memberikan injeksi lanjutan kepada Anda.

Untuk wanita:

Jika injeksi TAPROS 3M DEPOT terlewat, pendarahan atau ovulasi dapat terjadi dengan kemungkinan konsepsi. Jika Anda mengira Anda hamil, Anda harus menghentikan menggunakan TAPROS 3M DEPOT dan hubungi dokter Anda segera.

4. EFEK SAMPING YANG MUNGKIN TERJADI

Seperti obat-obat lain, TAPROS 3M DEPOT dapat menyebabkan efek samping, meskipun tidak semua orang dapat mengalaminya.

Hubungi dokter Anda segera atau berangkat ke rumah sakit:

- Jika Anda mengalami ruam, gatal atau nafas pendek atau kesulitan bernafas. Ini bisa merupakan gejala reaksi alergi parah.

Informasikan ke dokter Anda:

- Jika Anda mengalami sakit kepala parah yang tidak kunjung membaik setelah Anda minum obat pereda nyeri.
- Jika Anda menderita memar yang tidak diketahui penyebabnya atau pendarahan atau merasa tidak enak badan selama Anda menggunakan TAPROS 3M DEPOT. Meskipun jarang, ini bisa merupakan gejala-gejala perubahan jumlah sel darah merah atau sel darah putih.
- Kadar gula darah dapat berubah selama pengobatan dengan TAPROS 3M DEPOT, yang mana dapat mempengaruhi control pasien diabetes dan memerlukan monitoring yang lebih sering.
- Jika Anda menjalani tes darah, dokter Anda akan melihat perubahan kadar lemak darah (kolesterol) untuk menguji bagaimana hati Anda bekerja. Perubahan ini biasanya tidak menimbulkan gejala.
- Jika Anda mengalami gangguan metabolik, seperti penumpukan lemak di dalam hati (steatosis hati).
- Jika Anda mengalami gangguan kulit dan jaringan lunak, seperti Sindroma Stevens Johnson, Nekrolisis Epidermal Toksik, *Erythema multiforme,* Dermatitis bulosa, Dermatitis eksfoliatif, *Acute generalized exanthematous pustulosis, Toxic skin eruption*.
- Jika Anda memiliki pikiran, perasaan, atau dorongan untuk mengakhiri hidup.

Jika ada efek samping di bawah ini yang semakin serius, atau jika Anda merasakan timbulnya efek samping yang tidak tertera di brosur, informasikan ke dokter atau apoteker Anda:

TAPROS 3M DEPOT dapat menyebabkan efek samping serius seperti:

Gangguan pada paru. Hubungi dokter Anda jika Anda mengalami:
Penyakit paru disertai dengan demam, batuk, nafas pendek atau hasil rontgen yang tidak normal.

Reaksi alergi (hipersensitivitas). Hubungi dokter Anda jika Anda mengalami:
Pembengkakan wajah, bibir, tenggorokan dan area lain pada kulit, ruam, gatal.

Gangguan pada hati. Hubungi dokter Anda jika Anda mengalami:
Kekuningan pada kulit atau pada area putih pada bola mata, urin berwarna gelap.

Diabetes. Hubungi dokter Anda jika Anda mengalami:
Kadar gula darah yang tinggi, merasa haus, kelelahan, berat badan menurun, ada kandungan gula pada urin.

Gangguan pada pituitari (bagian dari otak). Hubungi dokter Anda jika Anda memiliki:
Pusing, gangguan penglihatan.

Pelaporan Efek Samping

Jika anda mengalami efek samping, informasikanlah pada dokter atau apoteker anda. Anda dapat juga melaporkan keluhan efek samping atau kondisi tidak nyaman tersebut secara langsung ke Industri Farmasi melalui kontak berikut: AE.Indonesia@takeda.com. Ini termasuk efek samping yang mungkin tidak tercantum pada brosur ini. Dengan melaporkan efek samping, anda sudah membantu dalam memberikan informasi tambahan mengenai keamanan obat ini.

5. BAGAIMANA MENYIMPAN TAPROS 3M DEPOT

Hindari dari jangkauan anak-anak.

Jangan menggunakan obat ini setelah tanggal kadaluarsa yang tercantum pada kemasan. Tanggal kadaluarsa mengacu pada tanggal akhir bulan.

Jangan menyimpan obat ini pada suhu di atas 30°C. Gunakan segera, setelah produk dicampurkan.

Jangan disimpan di lemari es atau dibekukan.
Simpan di kemasan asalnya untuk melindungi dari cahaya langsung.

6. ISI DARI KEMASAN DAN INFORMASI LAIN

Kandungan TAPROS 3M DEPOT:

- Bahan aktif dari serbuk TAPROS 3M DEPOT adalah leuprorelin acetate (11.25 mg).
- Bahan tambahan TAPROS 3M DEPOT lainnya : Polylactic acid and mannitol.
- Pelarut steril mengandung carmellose sodium, mannitol, polysorbate 80, dan air untuk injeksi.

Bagaimana bentuk kemasan TAPROS 3M DEPOT dan isi di dalamnya:

TAPROS 3M DEPOT adalah serbuk lepas berkala untuk penggunaan dalam injeksi.

Pelarut sterilnya adala cairan jernih, yang akan dicampurkan dengan serbuk TAPROS 3M DEPOT sebelum disuntikkan.

Setiap kemasan terdiri dari satu dual chamber pre-filled syringe yang mengandung serbuk 11.25 mg leuprorelin acetate di chamber bagian depan dan 1 ml pelarut steril di chamber bagian belakang.

Setelah dicampurkan, larutan akan menjadi suspensi berwarna putih. Jika dibiarkan, suspensi tersebut akan menghasilkan endapan putih yang mudah tersuspensi kembali jika dikocok.

Pemilik Izin Edar:

PT Takeda Indonesia

Bekasi, Indonesia

Pabrik Pembuat:

Takeda Pharmaceutical Company Limited

Hikari, Jepang

No. Reg. DKI0770700244B2

HARUS DENGAN RESEP DOKTER

Brosur ini tidak mengandung informasi lengkap tentang obat Anda. Jika Anda mempunyai pertanyaan atau Anda tidak yakin, sebaiknya Anda konsultasikan dengan dokter atau apoteker Anda yang dapat memberikan informasi lebih kepada Anda. Informasi di brosur ini hanya berlaku untuk TAPROS 3M DEPOT.

Based on CCDS ver. 22.0

Diproduksi oleh Takeda Pharmaceutical Company Limited, Hikari, Japan
Dikemas sekunder oleh Aupa Biopharm Co., Ltd., Hsinchu, Taiwan
Pemegang Izin Edar: PT Takeda Indonesia, Bekasi, Indonesia