TAPROS® 3M DEPOT Powder for Injection

LEUPRORELIN ACETATE

1 NAME OF THE MEDICINAL PRODUCT

TAPROS® 3M DEPOT 11.25 mg Powder for Injection

2 COMPOSITION

Each vial contains 11.25 mg Leuprorelin Acetate
For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White powder and clear, colorless solvent for suspension for injection.
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.
- Treatment of central precocious puberty.

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.

- Central Precocious Puberty
  The treatment of children with leuprorelin acetate should be under the overall supervision of the paediatric endocrinologist.
  The dosing scheme needs to be adapted individually.
  The recommended starting dose is dependent on the body weight.

  Children with a body weight ≥ 20 kg
  2 ml (11.25 mg leuprorelin acetate) suspension of 1 vial injection powder in 2 ml vehicle solution (1 ampoule) are administered every 3 months as a single subcutaneous injection.

  Children with a body weight < 20 kg
  Tapros 3M Depot is not recommended for use in children with a bodyweight under 20 kg.
  In these rare cases Tapros 1.88mg 1M depot is available for use in these patients.

4.3 Contraindications

All patient populations

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

All females (adult and pubescent pediatric 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.

All females (adult and pubescent pediatric females)
Before starting treatment with leuprorelin acetate, pregnancy must be excluded (see Contraindications, 4.3).

Adult females
During treatment with leuprorelin acetate, patients should be instructed to prevent conception e.g. with the use of non-hormonal methods

Endometriosis, Breast cancer indications
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 risks and benefits including the potential for Torsade de pointes prior to initiating leuprorelin acetate.

Pediatric patients (Central precocious puberty)

- LH-RH test should be performed at regular intervals. When suppression of the action of LH and FSH in blood is not achieved, the administration of this drug should be discontinued.
- The treatment of children with progressive brain tumours should follow a careful individual appraisal of the risks and benefits.
- Bone mineral density (BMD) may decrease during GnRH analogue therapy in children with central precocious puberty. However, after cessation of treatment subsequent bone mass accrual is preserved and peak bone mass in late adolescence does not seem to be affected by treatment.

Pseudotumor cerebri / idiopathic intracranial hypertension

Pseudotumor cerebri (PTC)/idiopathic intracranial hypertension has been reported in pediatric patients receiving leuprorelin acetate. Patients should be monitored for signs and symptoms of PTC, including papilledema, headache, blurred vision, diplopia, loss of vision, pain behind the eye or pain with eye movement, tinnitus, dizziness, and nausea. If PTC is confirmed permanently discontinue use of leuprorelin acetate and treat the patient in accordance with the established treatment guidelines.

CAREFUL ADMINISTRATION

TAPROS should be administered with care in the following patients :

Endometriosis and Breast cancer

Patients with submucous myoma (fibroid), bleeding symptom may be aggravated.

Central precocious puberty

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 clinical condition. However, such an aggravation usually disappears in the course of continued administration

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.

Precautions concerning use

- Route of administration
  Tapros should be used only by the subcutaneous or intramuscular route. [Intravenous injection of Tapros may induce thrombosis].

- Method of administration
  For subcutaneous injection, the following cautions should be exercised.
  - The site for subcutaneous injection should be the brachial, abdominal or gluteal region.
  - The injection site should be changed each time. The repeated injection should not be given at the same site.
  - The check should be made to see that the needle is not piercing a blood vessel.
  - The patients should be instructed not to massage the injection site.
- Preparation :
  - The injectable solution should be prepared at the time of use and be used immediately after reconstituting.
  - 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

Other Precautions

For all indications

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.

Endometriosis , central precocious puberty and breast cancer

It has been reported that the administration of TAPROS brought about venous thrombosis or pulmonary embolism.

Prostate cancer

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).**

Prostatic cancer
- 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		

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

Endometriosis, Breast cancer and Central Precocious Puberty

- 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 ,	Decreased libido, coldness, visual disturbance or emotional lability		

	≧ 5%	0.1% - < 5%	< 0.1%	Frequency unknown
	insomnia, dizziness or diaphoresis			
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		Pseudotumor cerebri / idiopathic intracranial hypertension
6) Hypersensitivity		Rash or pruritus		
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		

	≧ 5%	0.1% - < 5%	< 0.1%	Frequency unknown
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 excipient

Polylactic acid, Mannitol.

Solutions
CMC, Mannitol, Polysorbate 80, water for injection

6.2 Incompatibilities

This drug must be injected alone.

6.3 Special precaution for Storage

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

6.4 Package

Box, 1 vial @ 11.25 mg and 1 diluent ampoule @ 2 mL

Reg. No. DKI0770700244B1

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

HARUS DENGAN RESEP DOKTER.

Based on CCDS ver. 22.0

Takeda

Manufactured by Takeda Pharmaceutical Company, Limited, Osaka, 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
Serbuk injeksi 11.25 mg dalam vial dan Pelarut dalam Ampul 2 ml

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 Anda 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 metastatis, endometriosis, dan kanker payudara pada wanita.

Pada Anak :

TAPROS 3M DEPOT digunakan untuk pengobatan pubertas dini yang disebabkan oleh pelepasan hormon tertentu dari kelenjar pituitari (pubertas prekoks sentral).

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

Penggunaan pada anak :

Dokter akan membuat diagnosis yang tepat untuk CPP.

Jangan menggunakan TAPROS 3M DEPOT:

- Jika Anda alergi (hipersensitif) terhadap hormon Gn-RH sintetik, hormon Gn-RH analog, leuprorelin acetate atau kandungan lain yang terdapat pada 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:

Pada Pria, Wanita dan Anak

- Saat memulai pengobatan dengan TAPROS 3M DEPOT, mungkin diawali dengan gejala-gejala yang ada memburuk akibat level hormon testosterone atau estrogen dalam tubuh meningkat. Oleh karena itu, pemberian sekali setiap 12 minggu perlu diamati.
- Dilaporkan adanya kejang pada pasien yang diberikan TAPROS 3M DEPOT. Hal ini terjadi pada pasien dengan atau tanpa riwayat epilepsi, kejang, atau memiliki faktor lain yang menyebabkan kejang. Informasikan ke dokter Anda :
    - Bila Anda penyandang epilepsi atau memiliki resiko kejang.
    - Bila Anda mengalami kejang setelah diberikan pengobatan TAPROS 3M DEPOT.
- 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.

Pada Pria dan Wanita

- Jika Anda menderita masalah jantung, Anda harus memberitahu dokter Anda.
- Jika Anda diabetes, TAPROS 3M DEPOT bisa memperburuk diabetes Anda. Oleh karena itu, pasien diabetes memerlukan pengecekan kadar glukosa darah lebih sering.
- 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. Informasikanlah ke dokter Anda :
    - Jika Anda depresi atau memiliki riwayat depresi, sehingga dokter dapat monitor gejala depresi selama pengobatan dengan TAPROS 3M DEPOT.
    - Jika muncul perasaaan depresi setelah diberikan pengobatan TAPROS 3M DEPOT.

Pada 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 wanita dengan endometriosis, beritahukan dokter Anda jika Anda menderita osteoporosis.
- Jika Anda wanita dengan endometriosis, beritahukan dokter Anda segera jika Anda mempunyai tanda-tanda adanya tumor.
- Jika Anda seorang wanita usia subur, Anda harus menggunakan kontrasepsi non hormonal saat 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.
- Jika Anda diberikan TAPROS 3M DEPOT untuk pengobatan kanker payudara :
    - Dokter mungkin memeriksa kepadatan tulang dan fungsi rahim sebelum Anda mulai pengobatan dan memonitor Anda selama pengobatan.
    - Sebelum pengobatan, dokter akan memeriksa apakah Anda hamil atau tidak.
- Jika Anda depresi atau mengalami riwayat depresi , informasikan ke dokter Anda sehingga mereka dapat menambahkan monitor gejala depresi selama pengobatan dengan TAPROS 3M DEPOT.

Pada 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.
- Informasikan ke dokter Anda jika Anda mengalami hal-hal berikut :
  kondisi jantung atau pembuluh darah yang tidak normal, atau Anda sedang menggunakan obat-obatan untuk kondisi ini. Resiko masalah irama jantung akan meningkat ketika mengkonsumsi TAPROS 3M DEPOT.

Pada Anak :

- Jika anak memiliki tumor otak progresif, dokter Anda akan memutuskan apakah pengobatan dengan TAPROS 3M DEPOT tepat.
- Dokter mungkin akan memeriksa darah saat pengobatan dengan TAPROS 3M DEPOT untuk memeriksa tingkat hormon.
- Kepadatan tulang dapat menurun selama perawatan central precocious puberty dengan TAPROS 3M DEPOT. Namun, setelah pengobatan dihentikan, pertumbuhan massa tulang berikutnya dapat dipertahankan dan puncak massa tulang pada saat remaja akhir tampaknya tidak terpengaruh oleh pengobatan
- Pada penggunaan TAPROS 3M DEPOT, mungkin ada papiledema, sakit kepala, penglihatan kabur, penglihatan ganda, kehilangan penglihatan, nyeri di belakang mata atau gerakan mata, tinitus, pusing dan mual. Gejala-gejala ini bisa menjadi tanda dari hipertensi interkranial idiopatik (peningkatan tekanan intrakranial tanpa penyebab yang jelas). Jika Anda memiliki gejala-gejala ini, silakan hubungi dokter Anda.

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.
- Pengobatan dengan Androgen dapat memperpanjang interval QT atau menginduksi Torsades de pointes.

Kehamilan dan Menyusui

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

Berkendara dan menggunakan mesin

Jangan berkendara atau mengoperasikan mesin jika Anda mengalami 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. 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 kanker prostat atau kanker payudara, Anda akan diberikan suntikan TAPROS 3M DEPOT setiap 3 bulan sekali.

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

Pada Anak :

Pengobatan pada anak harus dibawah pengawasan dokter anak ahli endokrinologi.

Dosis perlu disesuaikan secara individu.

Dosis awal yang direkomendasikan tergantung dari berat badan :

a. Anak dengan berat badan 20 kg atau lebih

2 ml **TAPROS 3M DEPOT** (11,25 mg leuprorelin acetate) diberikan setiap 3 bulan sekali, disuntikkan di bawah kulit, yaitu di lengan, paha atau perut.

b. Anak dengan berat badan kurang dari 20 kg

TAPROS 3M DEPOT tidak direkomendasikan untuk anak dengan berat badan kurang dari 20 kg. Kasus ini jarang, namun dapat diberikan **TAPROS 1.88 mg 1 M DEPOT.**

4. EFEK SAMPING YANG MUNGKIN TERJADI

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

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: Penyakit radang paru disertai dengan demam, batuk, nafas pendek atau hasil rontgen yang tidak normal.
- Reaksi alergi berat
- Gangguan pada hati
- Peningkatan kadar gula darah
- Gangguan pada hipofisa (bagian dari otak) : Pusing, gangguan penglihatan
- Gangguan aliran darah pada jantung, otak, paru dan pembuluh darah
- Gangguan metabolik: penumpukan lemak di dalam hati (steatosis hati)
- Gangguan kulit dan jaringan lunak: Sindroma Stevens Johnson, Nekrolisis Epidermal Toksik, *Erythema multiforme,* Dermatitis bulosa, Dermatitis eksfoliatif, *Acute generalized exanthematous pustulosis, Toxic skin eruption*.
- Gangguan psikiatri: memiliki pikiran, perasaan, atau dorongan untuk mengakhiri hidup.

Kanker Prostat

Anda mungkin mengalami efek samping sebagai berikut :

- Depresi
- Nyeri tulang, gangguan saluran kemih atau tulang belakang
- Gagal jantung mungkin terjadi

Efek samping yang terjadi pada lebih dari 5 dari 100 orang

- Peningkatan enzim hati yang membantu pembentukan energi tubuh
- Rasa hangat di wajah, leher, dan dada
- Tubuh terasa hangat

Efek samping yang terjadi antara 1 dari 1000 orang hingga 5 dari 100 orang

- Gangguan hati: peningkatan enzim hati Jaundice, atau peningkatan AST(GOT), ALT(GPT), γ-GTP or ALP
- Gangguan hormonal : sakit kepala, sulit untuk memulai tidur, rasa hangat pada wajah, pusing, berkeringat, penurunan hasrat seksual, gangguan ereksi, pembesaran payudara, pengecilan testis, rasa tidak nyaman pada daerah antara anus dengan kantung zakar.
- Otot rangka : nyeri sendi, nyeri tulang, nyeri pada bahu, pinggang, sulit berjalan, kaku pada jari atau sendi lain.
- Kulit : peradangan pada kulit atau pertumbuhan rambut di kepala
- Kelainan berkemih : sering kencing tapi jumlahnya sedikit, kencing berdarah atau peningkatan kadar sisa metabolisme protein dalam darah
- Kardiovaskular : abnormalitas hasil rekaman listrik jantung
- Hematologi : kurang darah, penurunan jumlah trombosit darah
- Pencernaan : mual, muntah, tidak nafsu makan, sembelit
- Alergi : ruam, gatal
- Nyeri di lokasi penyuntikan, pembengkakan, kemerahan
- Lain-lain : bengkak, rasa tertekan di dada, kaku, lemah, baal, peningkatan berat badan, kesemutan, gangguan pendengaran, telinga berdenging, demam, peningkatan kolesterol total, trigliserida, asam urat, peningkatan kalium darah, atau peningkatan gula darah.

Efek samping yang terjadi pada kurang dari 1 dari 1000 orang :
- Otot rangka : nyeri otot, osteoporosis
- Saluran cerna : diare
- Lain-lain : Lemah

Efek samping yang frekuensinya tidak diketahui :
- Reaksi pada tempat penyuntikan, seperti pengumpulan nanah, pembengkakan, tukak, gatal-gatal, benjolan akibat peradangan, terasa hangat, kerusakan jaringan.
- Kejang

Endometriosis, Pubertas Prekoks Sentraldan Kanker Payudara

Anda mungkin mengalami efek samping sebagai berikut :

Efek samping yang terjadi pada lebih dari 5 dari 100 orang
- Penurunan hormon estrogen : rasa hangat pada wajah, leher, dada dan bagian tubuh lain, sakit kepala, sulit tidur, pusing, berkeringat,
- Otot rangka : Nyeri sendi, nyeri tulang

Efek samping yang terjadi antara 1 dari 1000 orang hingga 5 dari 100 orang
- Penurunan hormon estrogen : penurunan libido, dingin, gangguan penglihatan, emosi labil, depresi.
- Reproduksi wanita : lama menstruasi bertambah, vagina terasa kering, nyeri saat berhubungan badan, peradangan pada vagina, keputihan, gejala rangsangan berlebihan pada ovarium, nyeri, pembengkakan atau pengecilan payudara.
- Otot rangka : kaku pada jari atau sendi, nyeri pinggang, nyeri otot, kaku otot, penipisan tulang, peningkatan kadar kalsium atau fosfat dalam darah,
- Kulit : timbul jerawat, kulit kering, kebotakan, pertumbuhan rambut halus atau kelainan pada kuku
- Psycho-neurologic : psikis – neurologis; mengantuk, mudah sensitif, penurunan perhatian, kesemutan
- Hipersensitivitas : ruam, gatal
- Gangguan hati: peningkatan enzim hati atau bilirubin
- Gangguan saluran cerna : mual, muntah, tidak nafsu makan, nyeri perut, perut kembung, diare,

sembelit, sariawan atau haus.
- Kardiovaskular : berdebar-debar, tekanan darah meningkat
- Darah : sel darah merah meningkat, kurang darah, sel darah putih menurun, jumlah trombosit darah menurun, perpanjangan waktu pembekuan darah
- Kelainan berkemih : sering kencing tapi jumlahnya sedikit, nyeri saat berkemih, peningkatan sisa metabolisme protein dalam darah.
- Nyeri di lokasi penyuntikan, pembengkakan, kemerahan
- Lain-lain : lelah, lesu, lemah, rasa baal pada bibir atau tungkai, sindrom gangguan saraf pergelangan tangan, telinga berdenging, gangguan pendengaran, dada terasa sesak, pembengkakan, peningkatan berat badan, nyeri tungkai bawah, sesak nafas, demam, peningkatan kolesterol total, kolesterol LDL, trigliserid atau peningkatan kadar kalium darah.

Efek samping yang terjadi kurang dari 1 dari 1000 orang
- Gangguan hati : kulit berwarna kekuningan
- Lain-lain : berat badan menurun, gangguan pengecapan, fungsi tiroid abnormal

Efek samping dengan frekuensi tidak diketahui :
- Reaksi pada tempat penyuntikan, seperti pengumpulan nanah, pembengkakan, tukak, gatal-gatal, benjolan akibat peradangan, terasa hangat, kerusakan jaringan.
- Kejang

Efek samping yang frekuensinya tidak diketahui :
- Reaksi pada tempat penyuntikan, seperti pengumpulan nanah, pembengkakan, tukak, gatal-gatal, benjolan akibat peradangan, terasa hangat, kerusakan jaringan.
- Kejang

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.

Simpan obat ini pada suhu di bawah 30°C, hindari dari panas. Gunakan segera, setelah produk dicampurkan. Tidak perlu disimpan di lemari es.

Obat tidak boleh dibuang melalui saluran limbah atau limbah rumah tangga. Dokter atau perawat yang akan membuang obat ini. Langkah ini akan membantu melindungi lingkungan.

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 untuk penggunaan dalam injeksi.

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

Setiap kemasan terdiri dari satu vial yang mengandung serbuk 11.25 mg leuprorelin acetate dan 2 ml pelarut steril di dalam ampul

No. Reg. : DKI0770700244B1

HARUS DENGAN RESEP DOKTER

Pemilik Izin Edar:

PT. Takeda Indonesia, Bekasi, Indonesia

Pabrik Pembuat:

Takeda Pharmaceutical Company Limited

17-85, Jusohonmachi 2-chome, Yodogawa-ku, Osaka 532-8686

Japan

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.

Berdasarkan Leuprorelin Acetate CCDS ver. 22.0

Diproduksi oleh Takeda Pharmaceutical Company Limited, Osaka, Japan
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