PT. PFIZER INDONESIA
Local Product Document

Generic Name: Medroxyprogesterone Acetate
Trade Name: PROVERA®
CDS Effective Date: May 13, 2025
Supersedes: December 08, 2023

WARNINGS
CARDIOVASCULAR AND OTHER RISKS

Estrogens with progestins should not be used for the prevention of cardiovascular disease or dementia.

The Women's Health Initiative (WHI) estrogen plus progestin sub study reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) relative to placebo.

The Women's Health Initiative Memory Study (WHIMS), a sub study of the WHI study, reported increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with daily CE 0.625 mg combined with MPA 2.5 mg, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women.

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and MPA and other combinations and dosage forms of estrogens and progestins. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

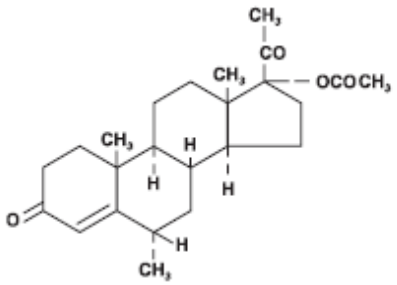
DESCRIPTION

PROVERA tablets contain medroxyprogesterone acetate, which is a derivative progesterone.

List of excipients:
Lactose monohydrate, corn starch, sucrose, talc, calcium stearate, liquid paraffin

It is a white, round, convex, one side scored tablets marked "UPJOHN 50" on the other one ,odorless crystalline powder, stable in air, melting between 200°C and 210°C. It is freely soluble in chloroform, soluble in acetone and in dioxane, sparingly soluble in alcohol and in methanol, slightly soluble in ether, and insoluble in water.

The chemical name for medroxyprogesterone acetate is pregn-4-ene-3, 20-dione, 17-(acetyloxy)-6-methyl-, (6α)-. The structural formula is:



Each PROVERA tablet for oral administration contains 10 mg medroxyprogesterone acetate.

ACTIONS

Medroxyprogesterone acetate, administered orally or parenterally in the recommended doses to women with adequate endogenous estrogen, transforms proliferative into secretory endometrium. The drug is progestational agent devoid of estrogenic activity.

Minimal androgenic and anabolic effects may occur. While parenterally administered medroxyprogesterone acetate inhibits gonadotropin production, which in turn prevents follicular maturation and ovulation, available data indicate that this does not occur when the usually recommended oral dosage is given as single daily doses.

Administration with food increases the bioavailability of MPA. A 10 mg dose of oral MPA, taken immediately before or after a meal, increased average MPA C_{max} (51% and 77%, respectively) and average AUC (18 and 33%, respectively). The half-life of MPA was not changed with food.

INDICATION AND USAGE

Secondary amenorrhea, dysfunctional uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as fibroids or uterine cancer, endometriosis.

CONTRAINDICATIONS

1. Patients with carcinoma of breast of reproductive organs (known or suspected to be estrogen-dependent).
2. Liver diseases of dysfunction.
3. Missed abortion.
4. Suspected pregnancy, should not be used in diagnostic test.
5. Thrombophlebitis, thromboembolic disorders of cerebral apoplexy, or patients with a past history of these conditions.
6. Undiagnosed vaginal bleeding.
7. Known sensitivity to PROVERA tablets.

Additional Contraindication(s) for Specific Use

Contraception/Gynecology*:* Known or suspected malignancy of the breast.

WARNINGS

Before using PROVERA Tablets, the status of the patient should be carefully evaluated.

This evaluation should exclude the presence of genital or breast neoplasia before considering the use of PROVERA.

PROVERA Tablets may cause weight gain and fluid retention. Caution should be exercised in treating any patient with a pre-existing medical condition that might be adversely affected by weight gain or fluid retention.

Some patients receiving PROVERA Tablets may exhibit a decreased glucose tolerance.

The mechanism for this is not known. This fact should be borne in mind when treating all patients and especially known diabetics.

A negative pregnancy test should be demonstrated before starting therapy with PROVERA.

Detectable amounts of PROVERA have been identified in the milk of mothers receiving the drug. The effect of this on nursing infant has not been determined.

Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia or migraine if examination reveals papilledema or retinal vascular lesions, medication shoud be withdrawn.

The age of the patient constitutes no absolute limiting factors although treatment with PROVERA may mask the onset of the climacteric.

The use of PROVERA during the first four months of pregnancy is not recommended.

The physician should be alert to the earliest manifestation of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism, and retinal thrombosis).

Should any of these occur or be suspected, the drug should be discontinued immediately.

MPA has not been causally associated with the induction of thrombotic or thromboembolic disorders, however MPA is not recommended in any patient with a history of venous thromboembolism (VTE). Discontinuation of MPA is recommended in patients who develop VTE while undergoing therapy with MPA.

Additional Warnings and Precautions for Specific Use or Formulation

Breast Cancer

The use of combined estrogen/progestin by post-menopausal women has been reported to increase the risk of breast cancer. Results from a randomized placebo-controlled trial,

the WHI trial, and epidemiological studies have reported an increased risk of breast cancer in women taking estrogen/progestin combinations for HT for several years. In the WHI conjugated equine estrogens (CEE) plus MPA trial and observational studies, the excess risk increased with duration of use (see section **DOSAGE AND ADMINISTRATION**). The use of estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation.

In several epidemiologic studies no overall increased risk for breast cancer was found among users of injectable depot progestogens in comparison to non-users. However, an increased relative risk (e.g., 2.0 in one study) was found for women who currently used injectable depot progestogens or had used them only a few years before. It is not possible to infer from these data whether this increased rate of breast cancer diagnosis among current users is due to increased surveillance among current users, the biological effects of injectable progestogens, or a combination of reason.

Cardiovascular Disorders

Estrogens with or without progestins should not be used for the prevention of cardiovascular disease. Several randomized, prospective trials on the long-term effects (see section **DOSAGE AND ADMINISTRATION**) of a combined estrogen/progestin regimen in postmenopausal women have reported an increased risk of cardiovascular events such as myocardial infarction, coronary heart disease, stroke, and venous thromboembolism.

- Coronary Artery Disease

There is no evidence from randomized controlled trials of cardiovascular benefit with continuous combined conjugated estrogen and medroxyprogesterone acetate (MPA). Two large clinical trials [WHI CEE/MPA and Heart and Estrogen/progestin Replacement Study (HERS)] showed a possible increased risk of cardiovascular morbidity in the first year of use and no overall benefit.

In the CEE/MPA substudy of WHI, an increased risk of coronary heart disease (CHD) events (defined as nonfatal myocardial infarction and CHD death) was observed in women receiving CEE/MPA compared to women receiving placebo (37 vs. 30 per 10,000 person years).

- Stroke

In the same substudy of WHI, an increased risk of stroke was observed in women receiving CEE/MPA compared to women receiving placebo (29 vs. 21 per 10,000 person-years). The increase in risk was observed in year one and persisted over the observation period (see section **DOSAGE AND ADMINISTRATION**).

- Venous Thromboembolism/Pulmonary Embolism

HT is associated with a higher relative risk of developing venous thromboembolism (VTE), i.e., deep vein thrombosis or pulmonary embolism. In the CEE/MPA substudy of WHI, a 2-fold greater rate of VTE, including deep venous thrombosis and pulmonary embolism was observed in women receiving CEE/MPA compared to women receiving

placebo. The increase in VTE risk was observed in year one and persisted over the observation period.

Dementia
Pooling data from the Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, for CEE-alone and CEE/MPA reported an increased risk of developing probable dementia and mild cognitive impairment (MCI) in postmenopausal women 65 years of age or older. Use of HT to prevent dementia or MCI in women is not recommended.

Ovarian Cancer
Current use of estrogen only or estrogen plus progestin products in post-menopausal women for five or more years, has been associated with an increased risk of ovarian cancer in some epidemiological studies. Past users of estrogen only or estrogen plus progestin products were at no increased risk for ovarian cancer. Other studies did not show a significant association. The WHI CEE/MPA trial reported that estrogen plus progestin increased the risk of ovarian cancer, but this risk was not statistically significant. In one study, women who use HRT are at increased risk of fatal ovarian cancer.

History and Physical Exam Recommendation
A complete medical and family history should be taken before the initiation of any hormone therapy. Pretreatment and periodic physical examinations should include special reference to blood pressure, breasts, abdomen, and pelvic organs, including cervical cytology.

Oncology
- MPA may produce cushingoid symptoms.
- Some patients receiving MPA may exhibit suppressed adrenal function. MPA may decrease ACTH and hydrocortisone blood levels.
- The physician/laboratory should be informed that in addition to the endocrine biomarkers listed in Special Warnings and Special Precautions for Use (see section **WARNINGS**), the use of MPA in oncology indications may also cause partial adrenal insufficiency (decrease in pituitary-adrenal axis response) during metyrapone testing. Thus the ability of adrenal cortex to respond to ACTH should be demonstrated before metyrapone is administered.

Oral Formulations and High Dose Parenteral Formulations (e.g., oncology use in pre-menopausal women)
Decrease in Bone Mineral Density
There are no studies on the bone mineral density (BMD) effects of orally administered MPA or the high doses of parenteral MPA (e.g., for oncology use). An evaluation of BMD may be appropriate in some patients who use MPA long-term.

PRECAUTIONS
Patients with a history of treatment for mental depression should be carefully monitored while receiving PROVERA therapy. Some patients may complain of premenstrual like depression while on PROVERA therapy.

Pathologists should be informed of the patients ingestion of PROVERA if endometrial or endocervical tissue is submitted for examination.

The following laboratory tests may be affected by the use of PROVERA: Gonadotropin levels, plasma progesterone levels, urinary pregnanediol levels, plasma testosterone levels (in the male), plasma estrogen levels (in the female), plasma cortisol levels, glucose tolerance test, metyrapone test and sex-hormone-binding-globulin.

Aminoglutethimide administered concomitantly with PROVERA may significantly depress the bioavailability of PROVERA.

The pretreatment physical examination should include special reference to breast and pelvic organs, as well as papanicolaou smear.

Because progestogens may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation.

In cases of breakthrough bleeding, as in all cases of irregular bleeding per vaginum, non-functional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated.

A decrease in glucose tolerance has been observed in a small percentage of patients on estrogen-progestin combination drugs. The mechanism of this decrease is obscure.

For this reason, diabetic patients should be carefully observed while receiving progestin therapy.

Interactions with Other Medicaments and Other Forms of Interaction
Aminoglutethimide administered concomitantly with high doses of MPA may significantly depress the serum concentrations of medroxyprogesterone acetate. Users of high-dose MPA should be warned of the possibility of decreased efficacy with the use of aminoglutethimide.

MPA is metabolized *in-vitro* primarily by hydroxylation via CYP3A4. Specific drug-drug interaction studies evaluating the clinical effects with CYP3A4 inducers or inhibitors on MPA have not been conducted, inducers and/or inhibitors of CYP3A4 may affect the metabolism of MPA.

Fertility, Pregnancy and Lactation
Pregnancy
MPA is contraindicated in women who are pregnant.

Some reports suggest under certain circumstances, an association between intrauterine exposure to progestational drugs in the first trimester of pregnancy and genital abnormalities in fetuses.

If the patient becomes pregnant while using this drug, the patient should be apprised of the potential hazard to the fetus.

Lactation
MPA and its metabolites are excreted in breast milk. There is no evidence to suggest that this presents any hazard to the nursing child.

Effects on Ability to Drive and Use Machines
The effect of MPA on the ability to drive and use machinery has not been systematically evaluated.

UNDESIRABLE EFFECTS
The following medical events, listed in order of seriousness rather than frequency of occurrence, have been occasionally to rarely associated with the use of progestogens:
1. Anaphylaxis and anaphylactoid-like reactions.
2. Thromboembolic disorders including thrombophlebitis and pulmonary embolism.
3. Central nervous system-nervousness, insomnia, somnolence, fatigue, depression, dizziness, and headache.
4. Skin and mucous membranes-urticaria, pruritus, rash, acne, hirsutism and alopecia.
5. Gastrointestinal-nausea.
6. Breast tenderness and galactorrhea.
7. Miscellaneous-pyrexia, changes in weight and moon faces.
8. Breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, change in weight (increase or decrease), change in cervical erosion and cervical secretions, cholestatic jaundice.

GYNECOLOGY:
The table below provides a listing of adverse drug reactions with frequency based on all-causality data from Phase 3 clinical studies that evaluated efficacy and safety of MPA in gynecology. Those most frequently (>5%) reported adverse drug reactions were dysfunctional uterine bleeding (19%), headache (12%) and nausea (10%).

System Organ Class	Very Common ≥ 1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Not known (cannot be estimated from available data)
Immune system disorders		Drug hypersensitivity		Anaphylactic reaction, Anaphylactoid reaction, Angioedema
Endocrine disorders				Prolonged anovulation
Psychiatric disorders		Depression, Insomnia, Nervousness		
Nervous system disorders	Headache	Dizziness		Somnolence

System Organ Class	Very Common ≥ 1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Not known (cannot be estimated from available data)
Vascular disorders				Embolism and thrombosis
Gastrointestinal disorders	Nausea			
Hepatobiliary disorders				Jaundice, Jaundice cholestatic
Skin and subcutaneous tissue disorders		Alopecia, Acne, Urticaria Pruritus	Hirsutism	Lipodystrophy acquired*, Rash
Reproductive system and breast disorders	Dysfunctional uterine bleeding (irregular, increase, decrease, spotting)	Cervical discharge, Breast pain, Breast tenderness	Galactorrhoea	Amenorrhoea, Uterine cervical erosion
General disorders and administration site conditions		Pyrexia, Fatigue	Oedema, Fluid retention	
Investigations		Weight increased		Glucose tolerance decreased, Weight decreased
*ADR identified post-marketing				

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:
Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

PT Pfizer Indonesia
Email: IDN.AEReporting@pfizer.com

Website: www.pfizersafetyreporting.com

OVERDOSE
Overdosage of estrogen plus progestin therapy may cause nausea and vomiting, breast tenderness, dizziness, abdominal pain, drowsiness/fatigue and withdrawal bleeding may occur in women. Treatment of overdose consists of discontinuation of CE/MPA together with institution of appropriate symptomatic care.

DOSAGE AND ADMINISTRATION
Secondary amenorrhea: 2.5 to 10 mg daily for 5 to 10 days.

Dysfunctional Uterine Bleeding Due to Hormonal Imbalance in the Absence of Organic Pathology: 2.5 to 10 mg daily for 5 to 10 days, starting on the 16th or 21st day of the cycle. Treatment is given for 2 consecutive cycles and then discontinued to see if the dysfunction has regressed. Withdrawal bleeding usually occurs within 3-7 days after discontinuing therapy. Note: For inducing an optimum secretory transformation of an endometrium that has been adequately primed with estrogen therapy, 5-10 mg daily for 10 days starting on the 16th for dysfunctional uterine bleeding.

Endometriosis: 10 mg PROVERA TID for 90 days beginning on cycle day 1. Breakthrough bleeding, which is self-limited, may occur in 30-40% of patients treated. No additional hormonal therapy is recommended for the management of this breakthrough bleeding.

Gynecology
Use of combined estrogen/progestin therapy in postmenopausal women should be limited to the lowest effective dose and shortest duration consistent with treatment goals and risks for individual women, and should be re-evaluated periodically as clinically appropriate (for example, 3-month to 6-month intervals) to determine if treatment is still necessary. (see section **WARNINGS.**)

Hepatic Insufficiency
No clinical studies have evaluated the effect of hepatic disease on the pharmacokinetics of MPA. However, MPA is almost exclusively eliminated by hepatic metabolism and steroid hormones may be poorly metabolized in patients with severe liver insufficiency, (see section **CONTRAINDICATIONS**).

Renal Insufficiency
No clinical studies have evaluated the effect of renal disease on the pharmacokinetics of MPA. However, since MPA is almost exclusively eliminated by hepatic metabolism, no dosage adjustment should be necessary in women with renal insufficiency.

HOW SUPPLIED
PROVERA Tablets are available in the following strengths and package sizes:
10 mg, Boxes of 3 blisters @ 10 tablets; Reg.No. DKI0054200210C1

Store at maximum temperature 30°C

HARUS DENGAN RESEP DOKTER

Manufactured by:
Pfizer Italia S.r.l., Ascoli, Italy

Imported by:
PT. Pfizer Indonesia
Jakarta, Indonesia

Leaflet kemasan: Informasi untuk pengguna

Provera®
Tablet 10 mg
Medroksiprogesteron Asetat

Baca semua bagian leaflet ini dengan cermat sebelum mulai menggunakan obat ini karena berisi informasi penting bagi Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan berikan kepada orang lain. Obat ini dapat membahayakan mereka, sekalipun tanda-tanda penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 13.

Isi leaflet ini:

1. Nama obat
Provera®

2. Bentuk sediaan
Tablet

3. Deskripsi obat

Provera® mengandung zat aktif medroksiprogesteron asetat, yang merupakan salah satu golongan obat yang disebut “progestogen”. Progestogen mirip dengan hormon alami perempuan yaitu progesteron.

Tablet berwarna putih, bulat, cembung, di satu sisi diberi tanda “UPJOHN 50"

daftar eksipien:
laktosa monohidrat, pati jagung, sukrosa, talk, kalsium stearat, parafin cair

4. Apa kandungan obat ini?

Setiap Tablet Provera® untuk administrasi oral mengandung 10 mg medroksiprogesteron asetat.

5. Kekuatan obat

10 mg.

6. Apa kegunaan obat ini?

Provera® memiliki beberapa kegunaan. Anda dapat meminum Provera® untuk mengobati atau menangani:

- Menstruasi yang terlalu banyak
- Nyeri saat menstruasi
- Menstruasi yang tidak teratur atau menstruasi yang lebih sering daripada frekuensi normal
- Tidak mengalami menstruasi
- Endometriosis (ditemukannya jaringan rahim di luar rahim Anda)

7. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini? Apa yang harus dilakukan jika ada dosis yang terlewat?

Selalu gunakan obat ini dengan tepat sesuai anjuran dokter atau apoteker Anda. Tanyakan kepada dokter atau apoteker jika Anda merasa tidak yakin.

Jumlah tablet yang diberikan bergantung pada kondisi yang tengah diobati.

Informasi berikut ini akan membantu Anda untuk mengetahui dosis yang biasanya diberikan untuk gangguan tertentu.

Meminum Provera® jika Anda menderita amenore (tidak mengalami menstruasi)
Anda biasanya harus meminum dengan dosis 2,5 mg hingga 10 mg selama 5–10 hari.

Meminum Provera® untuk keluarnya darah yang sangat banyak atau tidak teratur dan gangguan menstruasi lainnya
Anda biasanya harus meminum dengan dosis 2,5 mg hingga 10 mg selama 5–10 hari, dimulai dari hari ke-16 hingga hari ke-21 setelah menstruasi terakhir Anda. Pengobatan harus diberikan selama 2 siklus berturut-turut. Dalam beberapa kasus, dokter Anda juga dapat meresepkan estrogen untuk diminum pada waktu yang sama dengan Provera® dengan dosis 5 hingga 10 mg selama 10 hari. Beberapa hari setelah Anda berhenti meminum tablet, Anda mungkin akan mengalami perdarahan menyerupai menstruasi (*breakthrough bleeding*).

Meminum Provera® untuk endometriosis (ditemukannya jaringan rahim di luar rahim Anda)
Anda biasanya akan meminum dengan dosis 10 mg 3 kali sehari (30 mg) selama 3 bulan (90 hari) dimulai sejak tanggal pertama menstruasi Anda. Jika Anda mengalami bercak darah atau perdarahan yang tidak teratur selama pengobatan ini, hal tersebut tergolong normal dan tidak ada yang perlu dikhawatirkan.
Jika Anda tidak mengalami menstruasi setelah menyelesaikan rangkaian pengobatan dengan Provera®, konsultasikan dengan dokter Anda untuk memastikan apakah Anda hamil.

Jika Anda lupa meminum Provera®
Jika dosis yang terlupa hanya terlambat beberapa jam, segera minum dosis yang terlupa tersebut. Jika hampir mencapai waktu untuk dosis yang Anda berikutnya, lewatkan dosis yang terlupa. **Jangan meminum dosis ganda untuk mengejar dosis yang tertinggal.**

Jika Anda berhenti meminum Provera®
Jangan berhenti meminum obat Anda atau mengubah dosis yang Anda minum saat ini tanpa berkonsultasi dengan dokter Anda terlebih dahulu. Anda perlu terus meminum obat ini.

Jika Anda memiliki pertanyaan lebih lanjut seputar penggunaan obat ini, tanyakan kepada dokter atau apoteker Anda.

8. Kapan seharusnya Anda tidak menggunakan obat ini?

Jangan menggunakan Provera®
- jika Anda alergi terhadap medroksiprogesteron asetat atau terhadap bahan lain yang terkandung dalam obat ini
- jika Anda sedang hamil atau ada kemungkinan hamil. Dokter Anda dapat meminta Anda melakukan tes kehamilan sebelum memulai pengobatan atau jika Anda tidak mengalami menstruasi selama pengobatan.
- jika Anda sedang atau pernah terkena kanker payudara atau kanker organ reproduksi
- jika Anda sedang atau pernah mengalami tromboflebitis (proses inflamasi yang menyebabkan terbentuknya bekuan darah dan menyumbat satu atau beberapa pembuluh vena, biasanya di tungkai Anda), kelainan tromboemboli apopleksi serebral (bekuan darah dalam otak (‘stroke’))
- jika Anda menderita gangguan hati
- jika Anda mengalami keguguran tanpa gejala
- jika Anda mengalami perdarahan vagina yang tidak terdiagnosis

9. Apa pertimbangan saat menggunakan obat ini?

Provera® mungkin tidak sesuai untuk semua perempuan. Harap baca daftar berikut ini dengan saksama untuk melihat apakah ada poin yang sesuai dengan Anda. Konsultasikan dengan dokter Anda jika Anda merasa tidak yakin.

Konsultasikan dengan dokter Anda sebelum menggunakan Provera® jika Anda mengalami kondisi berikut ini untuk membantu mereka memutuskan apakah Provera® sesuai untuk Anda:
- Epilepsi
- Sakit kepala migrain
- Asma

- Gangguan jantung
- Masalah ginjal
- Diabetes
- Depresi atau riwayat depresi
- Tekanan darah tinggi

Provera®, khususnya dengan dosis tinggi, dapat menyebabkan penambahan berat badan dan retensi cairan.

Risiko Tromboemboli Vena (VTE)
Semua perempuan memiliki peluang kecil mengalami bekuan darah dalam pembuluh vena di kaki, paru, atau bagian tubuh lainnya. Peluang untuk mengalami bekuan darah menjadi sangat sedikit lebih tinggi jika Anda meminum obat hormon seperti Provera®. Kemungkinan Anda untuk mengalami bekuan darah menjadi lebih tinggi, baik Anda meminum Provera® atau tidak, jika Anda:

- memiliki berat badan yang sangat berlebih
- pernah mengalami bekuan darah dalam pembuluh vena atau paru sebelumnya
- memiliki kerabat yang pernah mengalami bekuan darah
- tidak dapat bergerak untuk jangka waktu yang lama (misalnya setelah operasi)
- mengalami cedera serius atau menjalani pembedahan besar
- memiliki riwayat keguguran berulang kali

Beri tahu dokter Anda jika Anda baru saja menjalani operasi atau jika Anda akan menjalani operasi selama menggunakan Provera®.

10. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?

Beri tahu dokter atau apoteker Anda jika Anda sedang meminum, baru-baru ini meminum, atau mungkin akan meminum obat-obatan lainnya:

- Aminoglutetimid
- Pemicu atau penghambat CYP3A4

11. Apakah obat tersebut aman bagi ibu hamil dan menyusui?

Kehamilan
Jika Anda sedang hamil atau menduga diri Anda hamil, atau berencana untuk hamil, Anda harus menghubungi dokter sebelum meminum Provera®.

Provera® tidak boleh diminum saat Anda hamil karena obat-obatan hormonal dapat memengaruhi perkembangan bayi. Penting bagi Anda untuk menggunakan metode kontrasepsi lainnya (misalnya kondom) selama meminum Provera®, karena obat ini tidak bersifat kontraseptif.

Menyusui
Beri tahu dokter Anda jika Anda akan menyusui selama meminum Provera® karena obat ini dapat dialirkan ke dalam ASI.

Jika Anda sedang menyusui, konsultasikan dengan dokter Anda yang akan menyarankan apakah Anda sebaiknya menggunakan metode pemberian asupan makanan alternatif bagi bayi Anda.

12. Apakah pasien diizinkan mengemudi dan mengoperasikan mesin saat menggunakan obat ini?

Efek Provera® terhadap kemampuan mengemudi dan mengoperasikan mesin belum dievaluasi secara sistematis.

13. Apa saja potensi efek yang tidak diinginkan dari penggunaan obat ini

Seperti semua obat-obatan yang ada, obat ini bisa menimbulkan efek samping, meskipun tidak semua orang mengalaminya.

Alasan menghentikan pengobatan Provera® dengan segera

Meskipun jarang terjadi, Provera® dapat menyebabkan reaksi alergi berat yang dalam beberapa kasus dapat mengancam jiwa. Anda bisa mengalami sebagian atau semua gejala berikut ini: mengi, kesulitan bernapas, merasa lemah, pembengkakan wajah atau lidah, telapak tangan, dan telapak kaki, ruam kulit yang sangat gatal. Jika Anda merasakan reaksi yang negatif terhadap obat ini, dapatkan penanganan medis darurat **secepatnya**.

Jika Anda mengalami gejala mana pun berikut ini, Anda harus **berhenti meminum** tablet dan mengunjungi dokter Anda **secepatnya**.

Ini merupakan gejala **adanya bekuan darah di paru** yang semuanya dapat terjadi bersamaan:

- Rasa nyeri yang tajam, parah, dan muncul tiba-tiba dalam dada Anda
- Batuk darah
- Anda tiba-tiba merasa sesak napas
- Jantung Anda berdenyut lebih cepat

Ini dapat menjadi gejala **adanya bekuan darah dalam otak ('stroke'):**

- Anda mengalami sakit kepala yang luar biasa parah atau berkepanjangan
- Anda mengalami gangguan penglihatan
- Anda kesulitan berbicara
- Anda roboh atau pingsan
- Ada bagian dari tubuh Anda yang terasa lemah atau kebas

Ini merupakan gejala **trombosis vena dalam (DVT):**

- Anda mengalami nyeri yang parah, nyeri tekan, atau pembengkakan pada betis, pergelangan kaki, atau telapak kaki
- Anda mengalami perubahan warna kulit kaki menjadi keunguan atau kulit memerah dan hangat saat disentuh

Beri tahu dokter Anda jika Anda mengalami efek samping lain yang dilaporkan sehubungan dengan penggunaan Provera® yang dapat mencakup efek samping berikut ini:

Sangat umum**:** dapat dialami lebih dari 1 di antara 10 orang

- sakit kepala
- merasa mual
- perdarahan vagina atau bercak darah yang tidak diduga atau tidak biasa

Umum**:** dapat dialami hingga 1 di antara 10 orang
- reaksi alergi berat terhadap obat (misalnya mengi, kesulitan bernapas)
- depresi
- sulit tidur
- kegelisahan
- pusing
- rambut rontok
- jerawat
- ruam jelatang atau kaligata
- kulit gatal
- keputihan
- nyeri payudara
- nyeri tekan payudara
- demam
- kelelahan
- peningkatan berat badan

Tidak umum**:** dapat dialami hingga 1 di antara 100 orang
- pertumbuhan rambut pada wajah
- keluarnya cairan keputihan dari payudara saat tidak hamil atau menyusui
- edema/retensi cairan

Tidak diketahui: frekuensi tidak dapat diperkirakan dari data yang tersedia
- reaksi alergi berat (reaksi anafilaksis)
- pembengkakan pada wajah/tenggorok yang dapat menyebabkan kesulitan bernapas
- tertundanya pelepasan sel telur disertai siklus menstruasi yang lebih panjang
- mengantuk
- pembengkakan di dalam pembuluh vena akibat bekuan darah
- nyeri tekan atau pembengkakan pada betis, pergelangan kaki, atau telapak kaki
- ruam
- menstruasi terhenti atau tertunda untuk waktu yang lama
- abnormalitas serviks
- penurunan toleransi gula
- penurunan berat badan
- penyakit kuning, penyakit kuning kolestatik
- lipodistrofi dapatan

Beri tahu dokter atau perawat Anda jika teramati adanya efek samping yang tercantum di atas.

Melaporkan efek samping
Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam

leaflet ini. Dengan melaporkan efek samping, Anda bisa membantu memberikan informasi lebih lanjut mengenai keamanan obat ini.

Untuk melaporkan efek samping, hubungi www.pfizersafetyreporting.com atau email di IDN.AEReporting@pfizer.com

14. Tanda-tanda dan gejala-gejala overdosis
Mual dan muntah, nyeri tekan payudara, pusing, nyeri perut, mengantuk/kelelahan, dan perdarahan *withdrawal* mungkin saja terjadi.

15. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?
Jika Anda tanpa sengaja meminum terlalu banyak tablet Provera®, segera hubungi dokter Anda atau datangi unit gawat darurat di rumah sakit terdekat.

Bawa selalu kemasan obat berlabel, baik yang masih ada tablet Provera® yang tersisa di dalamnya atau tidak.

Jangan meminum tablet lagi hingga dokter Anda memerintahkan Anda.

16. Bagaimana cara menyimpan obat ini?
Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan gunakan obat ini setelah melewati tanggal kedaluwarsa yang tertera pada wadahnya.

Simpan pada suhu di bawah 30 °C.

17. Nomor otorisasi pemasaran
Provera® 10 mg: Dus berisi 3 blister @ 10 Tablet, No. Reg.: DKI0054200210C1

18. Nama dan alamat pemohon dan/atau pemilik obat sesuai dengan ketentuan yang berlaku

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PT. Pfizer Indonesia
Jakarta, Indonesia

19. Tanggal revisi
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20. Peringatan khusus
HARUS DENGAN RESEP DOKTER