

**DRUG NAME: MEDROXYPROGESTERONE****SYNONYM(S):** Methylacetoxypregesterone, Metipregnone**COMMON TRADE NAME(S):** DEPO-PROVERA®, PROVERA®**CLASSIFICATION:** Endocrine Hormone*Special pediatric considerations are noted when applicable, otherwise adult provisions apply.***MECHANISM OF ACTION:** [1,2,3]

Medroxyprogesterone is a progestin. The mode of anticancer action of the progestins includes an indirect action on the hypothalamic-pituitary axis consisting of inhibition of gonadotrophin releasing hormone release as well as a direct action resulting in the inhibition of cellular proliferation. The growth inhibitory effects of progestins are not cell cycle phase-specific, but may be maximal in the G<sub>1</sub> phase of dividing cells.

**PHARMACOKINETICS:** [4,5,6,7,8,9]

Oral Absorption	rapid, subject to first-pass metabolism in the liver	
Distribution	not elucidated, detectable in breast milk	
	cross blood brain barrier?	no information found
	Vd	no information found
	PPB	no information found
Metabolism	promptly metabolized in liver, first pass effect	
	active metabolite(s)	no
	inactive metabolite(s)	yes
Excretion	urine (20-40%) and feces (5-13%)	
	urine	20-42%
	t <sub>1/2</sub>	apparent t <sub>1/2</sub> 30 hours
	Cl	no information found

**USES:** [4]

- \* Breast cancer
- \* Endometrial cancer

Less frequent uses include:  
 \* Renal cell cancer

No pediatric indications.

- \* Health Protection Branch approved indication.

**SPECIAL PRECAUTIONS:** [4]

Medroxyprogesterone is **contraindicated** in patients with a history of significant thromboembolic disease.

Contraindicated in **pregnancy**. Detectable levels of progestin have appeared in breast milk of nursing mothers receiving the drug. The effect on the nursing infant is not significant and, if **breast feeding** is desired, it may be used safely.

**SIDE EFFECTS:** [4]

ORGAN SITE	SIDE EFFECT	ONSET			
cardiovascular	fluid retention, edema		E		
	<u>thrombophlebitis, pulmonary embolism, retinal embolism</u>		E	D	
central nervous system	headache, dizziness, fatigue, insomnia, nervousness, depression (rare)		E		
dermatologic	acne (rare)		E		
	alopecia (rare)		E		
	pigmentation			D	
	hirsutism (rare)			D	
endocrine	breast tenderness (rare)		E		
	galactorrhea (rare)		E		
	breakthrough bleeding		E		
	amenorrhea		E	D	
	Cushing's syndrome (moon face, elevated blood pressure)			D	
<b>extravasation hazard</b>	none				
gastrointestinal	nausea (rare)	I			
	appetite changes, weight gain		E		
hepatic	elevated liver function tests		E		
hypersensitivity	Type I (anaphylactoid), (rare)	I			
injection site	pain at injection site	I			
	sterile abscess		E		
renal/metabolic	decreased glucose tolerance		E		
	hypercalcemia (breast cancer, during first 2 weeks)		E		

Dose-limiting side effects are underlined.

I = immediate (onset in hours to days); E = early (days to weeks);  
D = delayed (weeks to months); L = late (months to years)

Medroxyprogesterone can cause **mild fluid retention and body weight gain** which is usually not clinically significant. The effect on body weight gain has been used therapeutically.

Medroxyprogesterone should be discontinued at the first sign of **thromboembolic disorders** or sudden onset of ocular problems (eg, loss of vision, protrusion of the eyeball, double vision).

May cause **acute hypercalcemia** in breast cancer patients with bone metastases during the first 2 weeks of therapy.

### **INTERACTIONS:** [6,10,11]

AGENT	EFFECT	MECHANISM	MANAGEMENT
aminoglutethimide	decreased plasma medroxyprogesterone levels	aminoglutethimide increases hepatic metabolism of medroxyprogesterone	caution; clinical significance not known
rifampin	decreased plasma medroxyprogesterone levels	rifampin increases hepatic metabolism of medroxyprogesterone	caution; possibly increase the dose of medroxyprogesterone but % increase required is not known
thyroid function test	elevated T <sub>4</sub> (thyroxine)	medroxyprogesterone causes an increase in the amount of thyroxine-binding globulin	thyroid function is probably not affected; abnormal results usually return to pre-treatment levels 2-4 months after therapy is discontinued

### **SUPPLY AND STORAGE:** [4]

**Tablets:** 2.5 mg, 5 mg, 10 mg, 100 mg; gluten-free; store at room temperature.

### **SOLUTION PREPARATION AND COMPATIBILITY:** [4,12]

**For basic information on solution preparation and compatibility, see Chemotherapy Chart in Appendix.**

### **PARENTERAL ADMINISTRATION:** [4,6,8]

Subcutaneous	no information available on this route
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Medroxyprogesterone

Intramuscular	deep IM, rotate gluteal sites
Direct intravenous	no information available on this route
Intermittent infusion	no information available on this route
Continuous infusion	no information available on this route
Intraperitoneal	no information available on this route
Intrapleural	no information available on this route
Intrathecal	no information available on this route
Intra-arterial	no information available on this route
Intravesical	no information available on this route

**DOSAGE GUIDELINES:** [4,6,8]

Refer to protocol by which patient is being treated.

***Adults:*** daily 2.5 mg (replacement therapy)  
*Oral:* daily: usual 200-400 mg (range 200-2400 mg) in divided doses  
 three times weekly (tiw): 500 mg  
*Intramuscular:* daily: 500 mg/day x 28 days then 500 mg twice weekly (biw)  
 q1-4w: 400-1000 mg  
*Adequate trial:* 8-12 weeks

*Dosage in myelosuppression:* no adjustment required  
*Dosage in renal failure:* no adjustment required  
*Dosage in hepatic failure:* adjustment required, no details found

## MEDROXYPROGESTERONE FACT SHEET FOR THE HEALTH CARE PROFESSIONAL

<b>OTHER NAMES</b>	methylacetoxypregesterone, metipregnone, PROVERA®, DEPO-PROVERA®
<b>USES</b> * HPB approved	endometrial cancer*, breast cancer*, renal cell carcinoma*
<b>DOSAGE FORMS</b>	oral tablet: 2.5 mg, 5 mg, 10 mg, 100 mg (PROVERA®) injection: 50 mg/mL (250 mg vial), 100 mg/mL (400 mg vial), 150 mg/mL (500 & 1000 mg vials) (DEPO-PROVERA®)
<b>USUAL DOSE RANGE</b>	Adults: 2.5 mg po daily (replacement therapy) oral: 200-400 mg/day po in divided doses 500 mg po three times weekly intramuscular: 500 mg IM daily x 28 days, then 500 mg IM twice weekly 400-1000 mg IM q1-4w
<b>DOSE REDUCTIONS</b>	liver (hepatic) failure
<b>ROUTES</b>	oral (divided doses) intramuscular (deep IM, rotate gluteal sites)
<b>EXTRAVASATION HAZARD</b>	none
<b>ONSET</b>	<b>SIDE EFFECT</b>
<b>IMMEDIATE</b> (hours to days)	* may be life-threatening side effects in <b><i>bold, italic</i></b> type are common  * anaphylaxis (rare) nausea (rare) pain at injection site
<b>EARLY</b> (days to weeks)	<b><i>fluid retention</i></b> (edema, weight gain) * blood clots (thrombophlebitis, pulmonary embolism) sterile absces at injection site breast tenderness discharge from the nipple (rare, galactorrhea) breakthrough bleeding loss of menses (amenorrhea) central nervous system problems (depression, headache, dizziness, fatigue, insomnia, nervousness) appetite changes (weight gain) loss of diabetic control liver problems (elevated liver function tests) increased serum calcium levels (hypercalcemia) skin problems (rare, acne) hair loss (rare, reversible alopecia)

Medroxyprogesterone

<b>ONSET</b>	<b>SIDE EFFECT</b>
	* may be life-threatening side effects in <b>bold, italic</b> type are common
<b>DELAYED/LATE</b> (weeks to years)	* blood clots (pulmonary embolism) loss of menses (amenorrhea) skin problems (pigmentation) unwanted hair growth (rare, hirsutism) Cushing's syndrome (moon face, elevated blood pressure)
<b>CONTRAINDICATIONS</b>	known hypersensitivity to medroxyprogesterone or vehicle pregnancy and breast feeding history of thromboembolic disorders, thrombophlebitis or cerebral apoplexy (stroke) undiagnosed vaginal bleeding undiagnosed urinary tract bleeding severe liver (hepatic) failure
<b>SIGNIFICANT INTERACTIONS</b>	aminoglutethimide, rifampin, thyroid function test
<b>LABORATORY MONITORING</b>	periodically: liver function, blood glucose, Papanicolaou (Pap) test
<b>TEACHING AIDS</b>	· <i>For the Patient: Medroxyprogesterone</i>

**NOTES:** · Medroxyprogesterone may cause some degree of fluid retention which may be of concern for patients with epilepsy, migraine, asthma, cardiac or renal dysfunction.

## FOR THE PATIENT: Medroxyprogesterone Tablets

Other names: PROVERA®

- **Medroxyprogesterone** (meh-DROX-ee-proe-JESS-ter-own) is a drug that is used to treat some kinds of cancer. It is a progestin type of female hormone. Medroxyprogesterone is a tablet that you take by mouth.
- It is important to **take** medroxyprogesterone exactly as directed by your doctor. Make sure you understand the directions. Medroxyprogesterone may be taken **with food or on an empty stomach** with a glass of water or juice.
- For once a day dosing: If you **miss a dose** of medroxyprogesterone, take it as soon as you can if it is within 12 hours of the missed dose. If it is over 12 hours since your missed dose, skip the missed dose and go back to your usual dosing times.
- **Store** medroxyprogesterone tablets out of the reach of children, at room temperature, away from heat, light and moisture.
- Other drugs such as aminoglutethimide or rifampin may **interact** with medroxyprogesterone. Tell your doctor if you are taking these or any other drugs as your dose may need to be changed. Check with your doctor or pharmacist before you start taking any new drugs.
- The **drinking of alcohol** (in small amounts) will not affect the safety or usefulness of medroxyprogesterone.
- For women: Medroxyprogesterone may cause **menopause** in women which may be permanent. If you plan to have children, discuss this with your doctor before being treated with medroxyprogesterone.
- For women: Medroxyprogesterone may harm the baby if used during pregnancy. Ask your doctor if your dose of medroxyprogesterone will act as **birth control** or if you need to use another form of birth control. Tell your doctor right away if you become pregnant.
- **Tell** doctors or dentists that you are being treated with medroxyprogesterone before you receive any treatment from them.

SIDE EFFECTS	MANAGEMENT
<b>Swelling</b> of hands, feet or lower legs occur if your body retains extra fluid.	·Elevate your feet when sitting. ·Avoid tight clothing.
<b>Blood clots</b> can sometimes occur. This is more likely to happen if you have had blood clots before. Signs to watch for include tenderness or hardness over a vein; calf tenderness; sudden onset of cough, chest pain or shortness of breath.	To help prevent blood clots: ·Keep active. ·Drink plenty of fluids. ·Avoid tight clothing. ·Do not sit with your legs crossed at the knees.
<b>Breast swelling</b> , soreness and/or leaking from the nipple may occur.	This will return to normal when you stop taking medroxyprogesterone.
You may <b>gain or lose weight</b> due to a change in	Your appetite will return to normal when you stop

SIDE EFFECTS	MANAGEMENT
appetite. Weight gain is more common.	taking medroxyprogesterone.
<b>Sugar control</b> may be affected in diabetics.	·Check your blood sugar regularly if you are diabetic.
Your <b>skin may darken</b> in some areas.	This will slowly return to normal once you stop treatment with medroxyprogesterone.
<b>Nausea</b> rarely occurs with medroxyprogesterone. Nausea should go away as treatment continues.	·Divide your daily dose into 2 or more smaller doses. ·Take your dose(s) after eating.
<b>Hair loss</b> rarely occurs with medroxyprogesterone. Your hair will grow back once you stop treatment. Colour and texture may change.	·Use a gentle baby shampoo and soft brush. ·Avoid hair spray, bleaches, dyes and perms.

**STOP TAKING MEDROXYPROGESTERONE AND SEE YOUR DOCTOR OR GET EMERGENCY HELP IMMEDIATELY IF YOU HAVE:**

- Signs of a **stroke** such as sudden onset of: severe headache, eyesight changes, slurred speech, loss of coordination, weakness or numbness in arm or leg.
- Signs of a **blood clot** such as tenderness or hardness over a vein, calf tenderness, sudden onset of cough, chest pain or shortness of breath.

**STOP TAKING MEDROXYPROGESTERONE AND SEE YOUR DOCTOR AS SOON AS POSSIBLE (DURING OFFICE HOURS) IF YOU HAVE:**

- Signs of **liver problems** such as yellow eyes or skin.
- Changes in vaginal bleeding.
- Severe mental depression.
- Rapid weight gain greater than 5 pounds

**CHECK WITH YOUR DOCTOR IF ANY OF THE FOLLOWING CONTINUE OR BOTHER YOU:**

- For diabetics: uncontrolled blood sugars.
- Excessive breast swelling or soreness.
- Swelling of hands, feet or lower legs.

**REPORT ADDITIONAL PROBLEMS TO YOUR DOCTOR.**

See ***Chemotherapy and You: a Guide to Self-help During Treatment*** available free from the Canadian Cancer Society for more information on managing side effects.

Notes:

## FOR THE PATIENT: Medroxyprogesterone Injection

Other names: DEPO-PROVERA®

- **Medroxyprogesterone** (meh-DROX-ee-proe-JESS-ter-own) is a drug that is used to treat some kinds of cancer. It is a progestin type of female hormone. Medroxyprogesterone is a milky liquid that is injected into a muscle.
- Other drugs such as aminoglutethimide or rifampin may **interact** with medroxyprogesterone. Tell your doctor if you are taking these or any other drugs as your dose may need to be changed. Check with your doctor or pharmacist before you start taking any new drugs.
- The **drinking of alcohol** (in small amounts) will not affect the safety or usefulness of medroxyprogesterone.
- For women: Medroxyprogesterone may cause **menopause** in women which may be permanent. If you plan to have children, discuss this with your doctor before being treated with medroxyprogesterone.
- For women: Medroxyprogesterone may harm the baby if used during pregnancy. Ask your doctor if your dose of medroxyprogesterone will act as **birth control** or if you need to use another form of birth control. Tell your doctor right away if you become pregnant.
- **Tell** doctors or dentists that you are being treated with medroxyprogesterone before you receive any treatment from them.

SIDE EFFECTS	MANAGEMENT
<b>Pain or tenderness</b> may occur where the needle was placed.	·Apply warm compresses or soak in warm water for 15-20 minutes several times a day.
<b>Swelling</b> of hands, feet or lower legs occur if your body retains extra fluid.	·Elevate your feet when sitting. ·Avoid tight clothing.
<b>Blood clots</b> can sometimes occur. This is more likely to happen if you have had blood clots before. Signs to watch for include tenderness or hardness over a vein; calf tenderness; sudden onset of cough, chest pain or shortness of breath.	To help prevent blood clots: ·Keep active. ·Drink plenty of fluids. ·Avoid tight clothing. ·Do not sit with your legs crossed at the knees.
<b>Breast swelling</b> , soreness and/or leaking from the nipple may occur.	This will return to normal when you stop taking medroxyprogesterone.
You may <b>gain or lose weight</b> due to a change in appetite. Weight gain is more common.	Your appetite will return to normal when you stop taking medroxyprogesterone.

SIDE EFFECTS	MANAGEMENT
<b>Sugar control</b> may be affected in diabetics.	·Check your blood sugar regularly if you are diabetic.
Your <b>skin may darken</b> in some areas.	This will slowly return to normal once you stop treatment with medroxyprogesterone.
<b>Nausea</b> rarely occurs with medroxyprogesterone.	Nausea should go away as treatment continues.
<b>Hair loss</b> rarely occurs with medroxyprogesterone. Your hair will grow back once you stop treatment. Colour and texture may change.	·Use a gentle baby shampoo and soft brush. ·Avoid hair spray, bleaches, dyes and perms.

**SEE YOUR DOCTOR OR GET EMERGENCY HELP IMMEDIATELY IF YOU HAVE:**

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**SEE YOUR DOCTOR AS SOON AS POSSIBLE (DURING OFFICE HOURS) IF YOU HAVE:**

- Signs of **liver problems** such as yellow eyes or skin.
- Changes in vaginal bleeding.
- Severe mental depression.
- Rapid weight gain greater than 5 pounds.

**CHECK WITH YOUR DOCTOR IF ANY OF THE FOLLOWING CONTINUE OR BOTHER YOU:**

- For diabetics: uncontrolled blood sugars.
- Excessive breast swelling or soreness.
- Swelling of hands, feet or lower legs.
- Redness, swelling, pain or sores where the needle was placed.

**REPORT ADDITIONAL PROBLEMS TO YOUR DOCTOR.**

See ***Chemotherapy and You: a Guide to Self-help During Treatment*** available free from the Canadian Cancer Society for more information on managing side effects.

Notes:

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