A DRUG NAME: CYPROTERONE

SYNONYM(S): CPA

COMMON TRADE NAME(S): Androcur®, Androcur Depot® (Berlex)

B MECHANISM OF ACTION AND PHARMACOKINETICS

Cyproterone is a steroidal antiandrogen with weak progestational activity, it blocks androgen binding to the androgen receptor as well as progestational activity which results in the partial suppression of pituitary gonadotropin, and a decrease in serum testosterone. Treatment with cyproterone alone results in incomplete suppression of serum testosterone levels.

Oral Absorption	Oral absorption complete (at 50mg dose)	
Distribution	Tissue distribution is one of the major causes of the rapid fall of plasma levels	
	Cross blood brain barrier?	No information found
	Vd	No information found
	PPB	No information found
Metabolism	The principal metabolite is 15 β-hydroxy-cyproterone acetate	
	Active metabolite(s)	No information found
	Inactive metabolite(s)	Yes
Excretion	Drug is excreted unchanged in urine (unconjugated) and feces (glucuronized)	
	Feces	60%
	Urine	33%
	t ½	38 ± 5 hours (oral route) 96 hours (depot IM route)
	Cl	No information found

C INDICATIONS AND STATUS

* Palliative treatment of prostate cancer
* Health Canada approved indication

D

ADVERSE EFFECTS

ORGAN SITE	SIDE EFFECT	ONSET	
Cardiovascular	Shortness of breath on exertion	E	
	Thromboembolism (increased when used in combination with estrogens)	E	
	Edema and fluid retention	E	
Central nervous system	Optic neuritis / abnormal vision		
	Depression		D
Dermatologic	Rash		
	Dry skin (due to ↓ sebum production)		D
Endocrine	Impotence and decreased libido (common)	E	
	Gynecomastia and breast tenderness	E	
	Inhibition of spermatogenesis		D
	Hot flashes		D
	Decreased cortisol levels (high doses 100mg/m^2)	E	
Extravasation hazard	N/A		
Gastrointestinal	Nausea and vomiting	I	
	Diarrhea	E	
	Constipation	E	
Hematologic	Hypochromic anemia (rare)	E	
Hepatic	Acute hepatitis, liver failure	E	D
Renal/metabolic	Hypercalcemia	E	
	Changes in lipid profiles		
	Impaired carbohydrate metabolism and diabetes	E	
Other	Fatigue, lethargy, weakness (common in 1st few weeks, less pronounced after 3rd month)	E	
	Dyspnea, pulmonary fibrosis		

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)

D ADVERSE EFFECTS (Continued)

Side effects are rarely of sufficient severity to require dosage reduction or discontinuation of treatment. The most common side effects are ***hormona***l with changes in libido, breast tenderness and gynecomastia and impotence, which are reversible. Hepatotoxicity, including liver failure has been reported especially after several months use.

Decreased response to ACTH and lowered cortisol levels have been reported. Adrenocortical function tests should be monitored by serum cortisol assay.

Impairment of carbohydrate metabolism may occur. Diabetic patients should be monitored closely.
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A ***negative nitrogen balance*** occurs at the start of therapy, but corrects within 3 months of continued therapy.

When cyproterone is used alone it has a minor effect on blood clotting factors; the risk is increased when used in combination with estrogens. Cyproterone should be discontinued at the first sign of ***thrombophlebitis*** or ***thromboembolism***, and the patient should be carefully re-evaluated if manifestations of thrombotic disorders occur.

E DOSING

Refer to protocol by which patient is being treated. Some protocols combine cyproterone with diethyl stilbestrol or other agents.

Adults:

Oral:	100 mg bid or tid Post-orchiectomy: 50-100mg bid
Intramuscular:	q1w: 300 mg (Depot injection) Post-orchiectomy: q2w 300mg
Dosage in myelosuppression:	no adjustment required
Dosage in renal failure:	no adjustment required for mild to moderate renal failure; Contraindicated in severe renal dysfunction
Dosage in hepatic failure:	no adjustment required for mild to moderate hepatic failure; contraindicated in severe hepatic dysfunction. Discontinue immediately if drug related hepatic toxicity occurs

F ADMINISTRATION GUIDELINES

Oral self-administration; drug available by retail prescription.

G SPECIAL PRECAUTIONS

Cyproterone is **contraindicated** in patients with hypersensitivity to the drug, active liver disease and hepatic dysfunction, and renal insufficiency.

Hepatic dysfunction resulting in fatal hepatic failure has been reported; patients should be carefully assessed.

The ***mutagenic and carcinogenic*** potential of prolonged use of cyproterone is not known.

Production of abnormal sperm during therapy has been observed.

H INTERACTIONS

AGENT	EFFECT	MECHANISM	MANAGEMENT
alcohol	theoretical possibility of reduced tumour control	reduced anti-androgenic effect	manufacturer recommends against use of alcohol
ethinyl estradiol	thrombosis	increased coagulation capability	monitor

I RECOMMENDED CLINICAL MONITORING

Recommended Clinical Monitoring	**Suggested Clinical Monitoring**
• Baseline & periodic liver function tests	• Intermittent cortisol levels • Plasma lipids and blood sugars in patients at risk