



# Anti-androgens:

**Cyproterone  
Spironolactone**

Androgens, including testosterone, are a group of sex hormones which help start puberty and play a role in reproductive health and body development. All genders make androgens but those assigned male at birth make more androgens which contribute to voice deepening, hair growth (on the face, scalp, chest, armpits and genitals) and sperm development. In all genders, androgens are important for health and development, playing a role in bone density, muscle development, red blood cell production, libido and sexual function. Testosterone is the most common androgen and the main target in estradiol-based gender affirming hormonal care.

Anti-androgens, also known as androgen antagonists, testosterone blockers or T-blockers are medications that block the effects of androgens in the body. They can work at the tissue or cell level to block the androgen receptors thereby preventing the normal actions of androgens. They can also work in the brain to suppress the production of androgens. They are used in cis gendered men and women for various reasons, e.g. prostate cancer, early puberty, acne, hirsutism, and are also a common component of estradiol-based hormonal therapy.

Anti-androgens can be used in combination with oestrogen, particularly in those wishing for maximal feminisation, where oestrogen alone is insufficient to suppress the testosterone. Only a small number of people will have their testosterone fully suppressed with estradiol and most will require at least a small amount of anti-androgen if they wish to have their testosterone significantly suppressed.

Anti-androgens can also be used as stand alone treatment in lower doses for those wishing to have reduced testosterone without the feminising effects of oestrogen. However, as androgens are important in general health, long term significant suppression without oestrogen supplementation is not recommended and may cause osteoporosis.

There are two main anti-androgens in common use in Australia, cyproterone and spironolactone, and both are available on the PBS. They are both relatively inexpensive. A third anti-androgen, bicalutamide, is only clinically indicated for use in prostate cancer treatment and is only on the PBS for this indication. As cyproterone and spironolactone are standard practice in Australia, these are recommended as first line options at Rainbow Care Clinic. Orchiectomy (removal of the testes) is an alternative option for reduction of androgens instead of lifelong anti-androgen medication.



# Anti-androgens:

## Cyproterone Spironolactone

### Cyproterone

Cyproterone (*psy-pro-tear-own*) is a very strong anti-androgen which blocks the action of testosterone at the androgen receptors as well as blocking the hormone in the brain that stimulates testosterone production. It also has progestogenic effects which also reduces the production of testosterone. Because it is quite potent, it can be used in lower doses. Cyproterone efficacy can be monitored by checking testosterone levels.

Long term use of cyproterone carries a small risk of developing a meningioma, a benign tumour of the lining of the brain, which is non-cancerous but in rare instances can cause pressure in the brain and require surgery. Fortunately, these tumours are rare and associated with higher doses. Cyproterone at lower doses has been shown to be just as effective as lower doses so the lowest effective dose of cyproterone is used.

Other risks of cyproterone include depression (care advised for those with a history of severe chronic depression), liver damage (can cause liver failure in very rare cases) and clots. Regular blood tests to check your liver function are required and if you notice yellowing of the skin or eyes, dark urine or pale stools, seek medical attention. Lastly, because cyproterone is such a strong anti-androgen it often results in complete suppression of erections and low sexual drive, which may or may not be preferred. Cyproterone is not approved in the USA but is approved for use in Europe, UK and Australia.

### Spironolactone

Spironolactone (*spear-ron-oh-lack-tone*) is the most commonly used anti-androgen in the USA in feminising hormonal therapy. It works in several ways to suppress androgens including partially blocking the androgen receptors, blocking enzymes that are needed to make testosterone as well as some weak progestogenic and oestrogenic activity. Because it works at the receptor level, efficacy is monitored by clinical reduction in testosterone effects rather than testosterone levels.

Spironolactone has a risk of high potassium which is rare and usually only in people with kidney impairment or on drugs that affect the kidneys. It does have a diuretic effect which can cause increased urination (usually short term), increased thirst or low blood pressure, especially when changing postures causing symptoms of dizziness. Because it lowers the blood pressure it can be useful in those with underlying high blood pressure. Spironolactone should be used with care in those with liver or kidney impairment and regular blood tests are required to check for these.

Spironolactone is associated with an increased risk of upper gastrointestinal bleeds, particularly for doses over 100 mg or those aged 55-74. Other side effects including stomach upset, rashes, allergy and blood abnormalities.

# Anti-androgens:

## Cyproterone Spironolactone

	Cyproterone	Spironolactone
<b>Formulation</b>	Oral tablet	Oral tablet
<b>Starting dose</b>	12.5mg daily or second daily	50mg daily
<b>Usual dose</b>	12.5mg daily or second daily - 25mg daily	100mg twice a day
<b>Side effects</b>		
<i>Common &gt; 1%</i>	Nausea, vomiting Tiredness, difficulty concentrating Fluid retention Reduced sperm Increased liver counts	Electrolyte abnormalities Weakness Headache Nausea, vomiting Breast pain
<i>Infrequent (0.1-1%)</i>	Breathlessness Liver damage Depression	Stomach cramps Diarrhoea Drowsiness, confusion Impotence Kidney impairment Upper GI bleeding
<i>Rare (&lt;0.1%)</i>	Liver failure Allergic reactions Clots Meningioma	Abnormalities in blood cell counts Liver damage Rashes
<b>Monitoring</b>	Regular checks of liver function (3-6 monthly)	Regular checks of liver and kidney function and electrolytes (3-6 monthly)
<b>Contraindications</b> (should not take this medication or care should be exercised if you have these conditions)	Liver disease Liver tumours History of meningioma History of clots Chronic severe depression Uncontrolled diabetes Sickle cell anaemia	Severe cardiac disease Heart failure Uncontrolled diabetes Prostate cancer (effects PSA) Renal failure Liver disease High potassium (> 5nmol/L) Treatment with drugs that increase potassium, e.g. trimethoprim, anti-inflammatories, ACE-inhibitors