

## Guidance for progesterone prescribing for gender affirming care

**Progesterone is not a standard component of gender affirming feminising hormone therapy. There is not currently an evidence base to support its use for people on feminising hormones. There are no well-designed studies to support a role for progesterone in feminising hormone regimens and the risk of harm of prescribing progesterone for these populations is not known.**

### Background

Anecdotally, some transgender women report improved breast and/or areolar development, mood, sleep, or libido with the use of progesterone although these findings have not been supported by the very limited studies available.

Progestogens are an essential component of menopausal hormone treatment in post-menopausal cis women with a uterus, and there are good quality studies regarding their safety and efficacy in this population. Concerns exist from the Women's Health Initiative (WHI) regarding a potential increased risk of cardiovascular disease and breast cancer when medroxyprogesterone acetate is used in combination with oral oestrogen in an older post-menopausal population. Progestins may increase the risk of venous thromboembolism when combined with oral oestrogen. Progesterone and dydrogesterone appear to be safer option when compared with medroxyprogesterone, in terms of cardiovascular, breast and clotting risk, but these data are based on observational studies, or studies with surrogate endpoints. Although generally well tolerated, progesterone can cause weight gain, fatigue, irritability and low mood. 6-8% of cis women do not tolerate micronised progesterone for these reasons.

It is unlikely that similar study data will be available for transwomen, however there are numerous differences between the setting of gender affirming care and the management of menopausal women: populations tend to be younger (and therefore have lower baseline cardiovascular, breast cancer and clotting risks), equine oestrogens are not used, and the benefits of gender affirming interventions on mental health and quality of life need to be weighed against the potential for increased risk due to use of exogenous hormones. To date there is no evidence to suggest that using progesterone in the setting of transgender care is harmful. Please note that cyproterone acetate which is a commonly prescribed anti-androgen also has progestogenic effects.

### Guidance

While not part of routine care, the Auckland Sexual Health Transgender Service provides the following guidance for clinicians who wish to prescribe progesterone for clients who request it, after a careful discussion about the potential risks and benefits as detailed above. This guidance is based on expert opinion, and is not evidence based.

The following guidance is for the use of utrogestan (micronised progesterone) only. Utrogestan is funded in Aotearoa New Zealand, however use for transwomen is off label.

### Medication and dosing regimens

Utrogestan 100-200 mg orally once daily at night. Some clients may prefer to use this cyclically, eg 10 days per month, in order to approximate the luteal phase of a cis woman's menstrual cycle, which can be affirming for some. Others may find the hormonal fluctuations with cyclic dosing troubling, and may prefer to take this medication daily.

We do not recommend other dosing regimens or other methods of administration.

### Cautions and contraindications (from the New Zealand Formulary)

Contraindications: history of liver tumours; genital or breast cancer (unless specifically used in the management of these conditions); severe arterial disease; severe pruritus, severe hepatic dysfunction; thromboembolic disorders; acute porphyrias, hypersensitivity to peanut or soya.

Cautions: conditions that worsen with fluid retention (e.g. epilepsy, hypertension, migraine, asthma, cardiac dysfunction); those at risk of thromboembolism; history of depression; diabetes.

### **When to commence utrogestan**

The optimal time to commence utrogestan is unknown, however suggested practice is to commence utrogestan after at least 6 months of continuous systemic oestrogen, and with oestradiol levels >200 or maximum recommended oestrogen dose (progynova 4-6 mg daily or estradot 100-200 mcg patches twice weekly).

### **Duration of treatment**

Utrogestan can be trialled for a period of 6-12 months, then reviewed for evidence of benefit or harm. Continue to review safety and efficacy 6-12 monthly thereafter.

### **Monitoring**

It is not necessary or recommended to monitor progesterone levels, and there are no guidelines for interpretation of progesterone levels in this context. It is not necessary to titrate to a particular level.

It is recommended that individuals receiving progesterone have an annual breast examination, with screening mammograms commencing as per standard guidelines.