

A note on terminology. *Progestogens* are a class of hormones that act on the progesterone receptor in the body. *Progesterone* is the hormone made in the body. Micronised progesterone is made from yams and is very similar to the progesterone your body makes and is the preferred prescribed progestogen. *Progestins* are synthetic progestogens.

Progestogens were routinely used in the past for gender affirming care when the combined oral contraceptive pill (containing an oestrogen and a progestogen) was stand of care. The pill is no longer used in gender affirming care as the type of oestrogen used (ethinyl estradiol) has a much high risk of clots than the safer forms of oestrogen now commonly used in gender affirming care.

Progesterone is not involved in breast development in cis gender females and the levels of progesterone only increase in late puberty when breast development is complete. Current available evidence does not support the use of progestins to enhance breast development for transgender women. However, there is insufficient high-quality evidence to form an absolute conclusion regarding their usefulness. Furthermore, the two most commonly used anti-androgens, spironolactone and in particular cyproterone, have progestogenic effects so adding progesterone may not have any additional benefit.

Individual patient reported benefits of progestogen, which are not yet supported by data in transgender women, include:

- Improved breast development and maturation, in particular, enlargement of the areola
- Improved feminisation and further suppression of androgens
- Improved sleep
- Improved libido
- Improved bone mineral density
- Improved cardiovascular risk profile

There are known side effects of progestogens from large studies in cis-gender post menopausal women. These studies involved an older age group and a higher risk type of progestogen, medroxyprogesterone acetate (MDA), but these side effects have also been observed in those taking progestogens as part of a feminising hormonal regime. These risks include:

- Mood changes including depression and suicidal thoughts
- Weight gain
- Bloating
- Acne
- Breast pain
- Potential for increased risk of clots in the legs (deep vein thrombosis) or lungs (pulmonary embolism), which can be life threatening
- Potential increased risk of breast cancer (the overall risk of breast cancer with feminising hormonal therapy remains lower than for cis gender females but much higher than for cis gender males)
- Potential increased risk of cardiovascular disease

There are two types of progestogens available for prescribing in Australia. The first type is MDA (mentioned above and also known commercially as Provera) which has higher risk of side effects,

Progesterone

blood clots and potentially breast cancer. However, most of the data comes from studies in older cis-gendered females who were also taking a higher risk oestrogen thus the risk for younger healthier individuals may not be as high. Reassuringly, there was no increase in mortality in the studies involving post-menopausal women due to the MDA. Nonetheless, the preferred option in feminising hormonal therapy is micronised progesterone (which is commercially available as Prometrium, or can be compounded) as it has a lower risk of side effects and blood clots. It is more expensive than the MDA.

Different people have different opinions and experiences regarding the benefits of progestogens as part of a feminising hormonal regime. The benefits of progesterone, if there are any, are believed to have more impact if the progestogen is taken within the first 2 years of treatment but after there has been some breast development with oestrogen and androgen blockade. Thus somewhere around the 12 month mark is a reasonable time to consider progesterone if you wish to trial it. Based on discussions with other gender affirming clinicians, a small proportion of patients feel they have many benefits from it, another small proportion have quite a negative experience with progesterone and a large group in the middle have moderate effects. It is safe to stop the progesterone at any time.

Progesterone may cause sedation so it should be taken at night time. There is no need to cycle the progesterone, it can be simply taken every day.