INJECTABLES	
Medication names	GnRH agonists (leuprolide, triptorelin)
Frequency	Injected monthly, every 3 months, or every 6 months depending on the medication and formulation. In most cases, this injection is done by a medical provider.
Additional comments	• Decreases one's own production of sex hormones, and is used for the purpose of blocking gonadal (testicular or ovarian) function. In youth, this can also reversibly block pubertal development prior to starting on gender-affirming hormone therapy. • GnRH agonists can and should be an option for some adults as part of a hormone therapy regimen, but it may be cost prohibitive.

Progesterone Therapy

The benefit of progestins for gender affirmation is not well studied. Some patients and medical providers report progesterone may help improve breast development, promote improvement in mood and libido, and have other positive benefits. However, progesterone has also been known to cause weight gain, fatigue, irritability and negative mood changes.[29-31] Progesterone is part of a cisgender female's hormonal makeup, and may be desired on this basis as part of a patient's gender affirming hormone therapy. It is important to weigh the benefits vs potential risks of starting progesterone or staying on progesterone long-term.

Additionally, progesterone has been shown to play a role in suppressing testosterone production, which supports its use as another, or alternative, anti-androgen when needed.[32] Estrogen alone or estrogen and spironolactone are not effective in adequately suppressing testosterone.

There is no evidence to suggest that using progesterone in the context of GAHT is harmful, however there is little safety data available for its role in this care. General concerns with prescribing progesterone with estrogen arose out of the Women's Health Initiative (WHI) studies, which showed a modest increased incidence of cardiovascular events and breast cancer when taking these hormones.[33] However, these results should not necessarily be extrapolated to assume the same risk when used for gender affirming care. The WHI studies were done with older cisgender females, some more than 10 years post-menopausal, who were taking conjugated equine estrogen and medroxyprogesterone – both of these medications now known to be associated with elevated rates of venous thromboembolic events over bioidentical hormone replacement options.[34,35] Additionally, in the setting of gender affirming care, patients tend to be younger overall and it is recommended to use micronized progesterone and 17-b estradiol. Therefore, for use in gender affirming care, it seems that the benefits may outweigh any perceived risks.

Micronized progesterone (Prometrium) is the bio-identical formulation and appears to be the safest option in terms of cardiovascular health risks.[34,35] In older individuals and those with higher than average cardiovascular risk, it is recommended to counsel patients on potential risks and lack of safety data.

ORAL AND INJECTABLES	
Medication name	micronized progesterone
Frequency	By mouth once daily, or cyclical dosing (10 days every month)
Additional comments	• Some patients may prefer cyclic dosing as its effects may mimic a menstrual cycle, which can be affirming for some. However, others may find the hormonal fluctuations with cyclic dosing troubling and may prefer to take this medication daily. • Progesterone's role in breast development has yet to be proven. Reported increases in breast size seem most likely due to general weight gain and fat deposition in the breasts, and not the direct effect of progesterone on the breast tissue itself. So far, there is no evidence to show any specific benefit (or lack of benefit) regarding progesterone's effect on breast development.[29]
Medication name	medroxyprogesterone acetate, MPA
Frequency	By mouth once daily or injected every 3 months (*Depo Provera*)
Additional comments	• Medroxyprogesterone has been shown to have a slightly higher risk of side effects than micronized progesterone — MPA is associated with bone loss in cisgender women, as well as mood changes (irritability, depression). There is also suggestion that MPA may pose in increased risk of blood clotting events as compared to the bioidentical micronized progesterone, but this needs to be studied further.[36,37] The 3-month injectable dosing may be beneficial given its ease, but the risks may outweigh the benefits in many individuals.

DOSING OPTIONS

Please note that these dosing recommendations reflect a more binary approach to care and treatment goals. Consider alternative, flexible dosing based on patient goals through safe and informed decision making with the patient.