Information Re Progesterone: Leeds GIS

The aim of this document is to respond to queries around the use of progesterone in Transwomen.

We are frequently asked about the use of progesterone in transfeminine healthcare from service users and health professionals. We are seeing increasing use of micronized progesterone (body identical progesterone known as Utrogestan) in transfeminine/trans female patients from some private providers. This is off licence use. **There are no NHS gender services in the UK that are currently routinely prescribing progesterone.**

The **WPATH** (World Professional Association for Transgender Health) standards of care version 8 states:

"Data to date do not include quality evidence supporting a benefit of progestin therapy for transgender women. However, the literature does suggest a potential harm of some progestins, at least in the setting of multi-year exposure."

What is Progesterone?

Progesterone belongs to a group of steroid hormones called 'Progestogens' or 'Progestins' that are produced by the ovaries during the menstrual cycle. Progestogens are secreted by the ovary at higher levels in the first 10 weeks of pregnancy followed by the placenta in later pregnancy.

Almost all breast growth in cis female adolescents occurs before they start to produce progesterone although there is a **theoretical** argument for Progesterone augmenting breast growth. There is a small amount of anecdotal evidence to back this up.

What is the Benefit of Progesterone in Trans Healthcare?

We don't know what the benefits are and how many people who use progesterone see these benefits. There are anecdotal reports that for some people it ***may***:

- Improve breast growth and support feminisation after an individual has had 18 months of Estrogen therapy
- Improve general sense of well-being
- Improve sleep
- Improve libido

It is not known if any of these reported benefits are transient or permanent.

What we know about progesterone in trans affirming care:

- There is a tiny amount of research, a small number of anecdotal reports and a few opinion pieces
- Much of the good evidence and data is extrapolated from cis people
- We need to make pragmatic decisions using this little evidence to weigh up the risks and benefits

What do we know about progesterone from post-menopausal cis women?

Progestogens are used in post-menopausal cis women to protect the endometrium from the estrogen used for hormone replacement therapy (HRT). In postmenopausal cis women, estrogen and progestogen combined HRT is associated with **increased risk of breast cancer** and **increased cardiovascular risk** (heart attacks, strokes and blood clots). Meanwhile, estrogen-only HRT is ***not*** associated with an increased risk of breast cancer in cis-women, without a uterus. The cardiovascular risk of estrogen-only HRT is also less that of combined HRT, for this group.

However; these studies were undertaken with different forms of synthetic progestogens. We know **micronised progesterone** is safer than synthetic progestogens. Using a micronised progesterone would be lower risk but would not remove all risk. This is also a different population of post-menopausal cis women.

There is no evidence that progesterone improves libido for post-menopausal cis women.

Side-effects with Progesterone

The progestogen component of HRT for some cis menopausal women causes significant side effects and in some progesterone intolerance. Some progestogens cause masculinising side-effects such as acne and increased body and facial hair. They can cause fluid retention and weight gain. They can be associated with mood changes and lipid changes. These side effects are more common with progestogens and less common with micronised progesterone, but they can still occur and for some individuals be intolerable.

Benefits versus Risks

Some people use progesterone and say it helps with their general sense of well-being. It is hard to quantify this but there may be other medications or management options for 'well-being' or mood that are **lower risk**.

The data around breast growth with Progesterone is poor. We think there is an increased risk of breast cancer with Progesterone but transwomen are at a lower risk of breast cancer than cis women.

There are anecdotal reports of progesterone improving bone health, but again Trans women are at a lower risk of Osteoporosis than cis women. There are also safer management options for bone health than Progesterone.

At the moment there is no evidence of benefit of these agents in terms of feminisation but there are risks. These risks are lower with micronised progesterone. More research is needed and we will continue to watch this space.

To Summarise:

Benefits	Risks	Potential Side-effects
• Possible improved breast growth • Possible improvement to 'well-being' • Possible improvement to sleep • Anecdotal reporting of improved bone health • Possible improved libido	• Possible increased risk of breast cancer • Possible increase to risk of cardiovascular disease • Side effects with Progesterone which can be significant	• Acne • Increased body and facial hair • Fluid retention • Weight gain • Mood changes • Lipid changes

On balance, the Leeds GIS does not support the routine prescribing of progesterone due to the lack of evidence sufficiently supporting the benefits of progesterone outweighing the risks.

My patient has started Progesterone: what do I do?

Though the Leeds GIS does not prescribe progesterone at this time, we have developed a framework to support GP's in their decision-making and potential management of progesterone if the situation arises.

Some people are accessing Progesterone from private providers or buying over the internet. We would never advise buying medication over the internet. There is no guarantee that the products obtained are the medication stated or that the dose is accurate, as the substances are not necessarily from regulated pharmaceutical suppliers. Please see our other guidance on **'Self-prescribing'** which is available through our health care professional hormone support hub: https://www.leedsandyorkpft.nhs.uk/our-services/gender-identity-service/

If an individual is taking Progesterone, it is important that they are aware of the risks detailed above. If they are not willing to stop taking Progesterone, we would consider a **harm minimisation approach**.

Suggested Management Approach

At the Leeds GIS we think Progesterone should only be considered 18 months after starting Estrogen therapy (we are seeing some private clinics that are starting this when initiating hormone therapy) and we would suggest that they take it as a trial. A trial would be Utrogestan 100mg on a night for 6 months. If the individual felt that the benefits were worth the risks then to continue this for 2 years and then withdraw. If after 2 years and a pause in Utrogestan, if the individual felt there was breast regression this could be continued until the individual is in their early 50s. In older patients we would consider this for 2 years or up to the age of 55, for example if starting at 62 the patient could have a 2 year trial.

This is unlicenced medication. Most of the hormones we use in trans affirming healthcare are off license use and unlikely to be licenced for this indication in the future. Prescribing off license medication GMC Guidance;

"Most of the medications used for the treatment of gender dysphoria are not licensed for this specific indication, although GPs will be familiar with their use in primary care for other purposes."

The Leeds GIS would not issue an NHS prescription for this medication. It may be that after reading this information together with a patient, the health care professional feels that they would support a private prescription.

We value our relationships with GPs and do not want to put them in an uncomfortable position, but we also recognise that many patients are accessing this privately or through unregulated sources from the internet. We also recognise that trans people suffer from health inequalities and their relationship with their GP is critical to their healthcare needs and bridging these inequalities.

Monitoring

We have no guidelines to direct or manage Progesterone use other than as a trial as detailed above. We would suggest no additional monitoring of progesterone other than the routine reviews which would be required for monitoring Estradiol. A review of the progesterone after six to twelve months would be to think about side effects and if the individual is seeing any of the benefits.

Where are we now?

Leeds GIS can only give general advice and guidance in these circumstances, which will not be specific to a particular patient, patient group or constitute a recommendation. We hope this has given you some advice and guidance in relation to factors to consider in assessment and potential strategies, but we cannot make a risk assessment for you, formulate a treatment plan for the patient or take any shared responsibility for interventions delivered in primary care in this way. These approaches lie outside specialist pathways and the treatment decisions lie entirely with the prescribing GP.

We admit that we as clinicians have seen a small number of patients who have had a trial of Progesterone and found it beneficial. We have also seen patients that have had side effects.

Considering the current evidence and WPATH guidance, Leeds GIS feel that the unknown benefits of Progestogens do not currently outweigh the risks.

We are listening to the trans community and talking in expert groups regularly around the use of Progesterone in our hormone team and on a national level. We want more robust evidence and guidelines in this area to support us make these decisions. In the future there may be a place for micronized progesterone but this is not part of our routine NHS care.

More research is needed and we will continue to watch this space and advocate for the trans community.

Leeds GIS