

ESTROGEN THERAPY FOR GENDER AFFIRMATION

The use of hormone therapy for gender affirmation (sometimes referred to as “transition”) is based on many years of experience in treating transgender and gender-diverse persons. Research on hormone therapy is continually providing us with more information on the safety and effectiveness of hormone therapy, but all of the long-term impacts of hormone therapy may not be fully understood yet.

This information is meant to help you consider the expected benefits and possible side effects of hormone therapy so that you can decide, with your healthcare provider, if hormone therapy is right for you.

Estrogen (estradiol) is used to feminize the body. Your healthcare provider will help you determine the form of estrogen (for instance, shots, pills, or patches) and the dose that is best for you based on your personal needs and wishes, as well as any health conditions you might have. Each individual person responds to estrogen differently, and this can be difficult to predict. This is why your specific therapy may be different from other people’s. Taking higher levels of estrogen may not lead to faster changes but could endanger your health. It is important to take estrogen only as prescribed and to discuss your treatment with your healthcare provider before making any changes.

Anti-androgens (testosterone blockers) are used to decrease the amount and/or block the effect of testosterone to reduce the masculine features of the body. Not all people need or desire these medications. Your healthcare provider can discuss whether an anti-androgen is necessary for you, and what your options are.

Progestogens (like progesterone) are another form of hormonal medication sometimes used in combination with estrogen. At this time, there have been no well-designed studies of the role of progestogens in feminizing hormone therapy. Some patients may find benefit, while others may experience negative effects. Your clinician can discuss whether a progestogen may be helpful for you, and when to consider this.

We look forward to partnering with you to achieve your desired goals.

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The Expected Effects of Estrogen Therapy

The feminizing changes in your body may take several months to become noticeable and usually take 3 to 5 years to be complete. Some changes are permanent, and others may be reversible if you stop estrogen. Remember that the degree to which you experience each change is difficult to predict. Please see **Table 1** for a summary and expected timeline of changes.

Changes that will not go away, even if you decide to stop estrogen treatment include:

- Breast growth and development. Breast size and shape vary in all people.
- The testicles will get smaller and softer.
- The testicles will produce less sperm, and this will likely affect your fertility – the ability to have biological children. How long this takes to happen, how much it happens, and whether and when it becomes permanent varies greatly from person to person. If it is important to you to have this option later in life, you should consider preserving sperm before starting hormones. You can also meet with a fertility specialist to better understand your options, now and later in life. Your healthcare provider can give you more information about these options.

Changes that will likely reverse if estrogen treatment is stopped include:

- Loss of muscle mass and decreased strength, particularly in the upper body.
- Weight gain, which is unpredictable. On average people gain just a few pounds. If you gain weight, this fat will tend to go to the buttocks, hips, and thighs, rather than the abdomen and mid-section.
- Skin will become softer and less oily. Acne may decrease.
- Facial and body hair will get softer and lighter and grow more slowly. For many people, this effect may be inadequate, and other treatments such as electrolysis or laser hair removal may be necessary to remove unwanted hair.
- “Male pattern” baldness of the scalp may slow down or stop, but hair will generally not regrow.
- Reduced sex drive.
- Decreased strength of erections or inability to get an erection.
- The ejaculate will become thinner or watery and there may be less of it. Even if it seems like nothing comes out with orgasm, it is still possible that sperm are produced, and pregnancy prevention should be considered depending on how you have sex.
- Changes in mood or thinking may occur. You may find that you have increased emotional reactions to things. Many people find that their mental health improves after starting hormone therapy. The effects of hormones on the brain are not fully understood, and you should let your healthcare provider know if you feel your mental health is worsening.

The following are NOT affected by hormone treatment. If they create discomfort for you, please let your healthcare provider know so that effective treatments can be discussed:

- The pitch of your voice
- Bone structure, including the face and Adam’s apple. It is possible that some people in their late adolescence may see some mild changes.

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Possible Risks of Estrogen Treatment

Having any of the following health conditions could make estrogen unsafe for you. Please let your healthcare provider know if you have any of these health conditions:

- Active blood clot or a history of blood clots, including deep venous thrombosis (DVT) or pulmonary embolism (PE)
- Estrogen-sensitive cancer (like breast cancer)
- Cancer or other disorder of the pituitary gland (like prolactinoma)
- Severe, complicated migraines (for instance, with neurological symptoms)

Risks of estrogen therapy may include:

- **Loss of fertility**, as discussed above.
- Increased risk of developing **blood clots**. Blood clots in the legs or arms (DVT) can cause pain and swelling. Blood clots to the lungs (PE) can interfere with breathing and getting oxygen to the body. Blood clots in the arteries of the heart can cause heart attacks. Blood clots in the arteries of the brain can cause stroke. Blood clots to the lungs, heart, or brain could result in disability or death.
- Possible increased risk of **heart attack or stroke**. This risk is higher if you smoke cigarettes, are over 45 years old, or if you have high blood pressure, high cholesterol, diabetes, or a family history of cardiovascular disease.
- Possible changes to your **blood pressure and cholesterol**. How much these changes actually lead to heart disease or other complications is not well known.
- Increased risk of **breast cancer**, because the estrogen stimulates breast growth. This risk is less than the risk of breast cancer for cisgender women.
- **Nausea and vomiting**, especially when starting estrogen therapy.
- **Gallbladder disease and gallstones**.
- Often people have improved **mood** on estrogen therapy. However, in some patients it may worsen depression or cause mood swings; let your healthcare provider know if you have worsening mood or other mental health symptoms.

Smoking may greatly increase the risks of taking estrogen, especially the risk of blood clots and cardiovascular disease. If you smoke, you should try to cut back or quit. If you have other risks for blood clots or cardiovascular disease, your healthcare provider may ask you to quit smoking before you start on hormone therapy. Your healthcare provider can discuss ways to help you quit.

Because we are still learning about the long-term health of people on estrogen for gender affirmation, you should work with your healthcare professional to reduce any potential risks and discuss the appropriate health screenings for you.

How to Take Estrogen

There are different ways estrogen can be prescribed. There are pros and cons for each of these methods. For gender affirmation, estradiol is the preferred and safest form of estrogen.

Different ways to take estradiol include:

- Estradiol injections: These are usually given subcutaneously (under the skin) once a week by you at home.

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- Estradiol tablets: These are taken by mouth either daily or twice a day. Putting the tablet under the tongue to dissolve may be safer than swallowing them.
- Estradiol patches: These are applied to the skin and changed once or twice a week. Some people have skin reactions to the patch.

We will work with you to determine which type of estradiol treatment is best for you.

Alternatives to Estrogen Therapy

There are ways other than hormones to feminize your body. These may be used along with or instead of hormones. Please let us know if you would like more information at this time about any of the following treatments. You may always ask for this information in the future.

- Voice therapy to change voice pitch and/or style.
- Voice surgery to change voice pitch: Generally not recommended until you have worked with a voice therapist first.
- Electrolysis or laser hair removal.
- Surgery to feminize the chest: Generally not recommended until at least 1-2 years on hormones to see what breast development you get with hormones.
- Surgery to change facial bone structure: Generally not recommended until at least 1-2 years on hormones to see what change in facial appearance you get with hormones.
- Surgery to reduce the Adam’s apple.
- Surgery to change the appearance and function of the genitals: Generally not recommended until at least 1-2 years on hormones, to ensure you are comfortable continuing the hormones lifelong, and to see the effects of the hormones on the genitals.
- Surgery to remove the testicles: Generally not recommended until at least 1 year on hormones, to ensure you are comfortable continuing the hormones lifelong.
- Other body shaping procedures, like liposuction or plastic surgery.

We want to help you achieve your gender-related goals in the safest way possible. In order to do this, we need to be well-informed about your health. Please inform your healthcare provider if there are any changes to your health at any time during treatment. We will do everything we can to continue your treatment if it can be done safely, which is almost always the case.

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Table 1. Feminizing Effects of Estrogen Treatment

Effect	Onset[†]	Maximum[†]
Breast growth*	3-6 months	2-3 years
Decreased testicular size*	3-6 months	2-3 years
Decreased sperm production*	Unknown	> 3 years
Redistribution of fat to hips and thighs	3-6 months	2-3 years
Decrease in muscle mass and strength	3-6 months	1-2 years
Decreased libido (sex drive)	1-3 months	3-6 months
Decreased spontaneous erections	1-3 months	3-6 months
Decreased facial and body hair growth	6-12 months	> 3 years
Scalp hair	no regrowth	
Voice changes	none	

Adapted from 2017 Endocrine Society Guidelines Hembree et al.

* Permanent changes

† People on low-dose hormone therapy may expect slower or less pronounced changes