

Oestrogen

Oestrogen (*es-tro-jen*) is a category of sex hormones and estradiol (*es-tra-die-ole*) is the oestrogen used in estradiol-based hormonal therapy. It is naturally produced in human bodies and is responsible for the development of female secondary sexual characteristics, amongst other things. Estradiol is different from ethinylestradiol, the oestrogen most commonly used in the birth control pill. Ethinylestradiol is a synthetic oestrogen derived from estradiol that has properties making it better for use in preventing pregnancy and regulating periods but these same properties also result in an increased risk of blood clots and other side effects. As there is no need for pregnancy prevention or period regulation in the setting of estradiol-based gender affirmation, ethinylestradiol is too risky and thus the safer oestrogen, estradiol, is used. Often the terms oestrogen and estradiol are used interchangeably.

Estradiol can be taken orally, via gels or patches on the skin, by injection and by implants that are inserted underneath the skin. There is *no* proven 'best' approach to starting or using estradiol. At Rainbow Care Clinic, estradiol is started at a low to medium dose and then increased until you are seeing changes in your body. This approach is based on several foundations: firstly, that oestrogen levels gradually increase during puberty for cis females; secondly, all current guidelines recommend utilising the lowest effective dose to reduce potential side effects and risks; and lastly, because there is no evidence that higher estradiol doses are associated with larger breasts. While estradiol levels can be checked in the blood, the physical changes happening in your body are the most important guide for dosing as the lab tests for estradiol are not reliable and give widely different results depending on the individual, the type of estradiol formulation, and the timing of testing and application of estradiol. Furthermore, individual responses to different levels of estradiol vary significantly. High estradiol levels in your blood does not automatically translate to more breast development. Your response to estradiol is mostly genetically determined, and it is common for breast development to be modest.

Persistent high levels of estradiol in the blood, i.e. > 1000 pmol/L are avoided due to the risk of causing side effects such as bloating, headaches, nausea and potentially higher blood clot risk. Very high levels of oestrogen in the blood may also cause tachyphylaxis, which is a condition where your body becomes less and less responsive to oestrogen despite there being lots of oestrogen in your body stream. The only fix for this condition is to stop all oestrogen until the body recovers its normal responsiveness to oestrogen.

Types of estradiol

Estradiol can be delivered to your body in several ways. Oral and transdermal (through the skin) preparations are used to start estradiol-based hormonal therapy. Transdermal formulations (gels and patches) are the safest as they appear to have no increased risk of blood clots. Oral estradiol does carry a small risk of blood clots but this is usually low for most people. People with risk factors for blood clots, e.g., smokers, a previous history of blood clots or a family history of blood clots, are generally recommended to use transdermal estradiol. Estradiol implants can be used once you have started oestrogen therapy and involve a minor procedure to have an oestrogen pellet inserted under the skin. Most people only require an implant every 6-12 months. There are fees for the implants themselves as well as the assessment and insertion appointments. Estradiol injections are used infrequently as they are typically expensive, cause wide fluctuations in levels with associated side effects and can be less satisfactory and 'user-friendly' than implants.

Patches

Oestrogen patches stick to your skin and release a constant, small amount of estradiol into the skin. Patches are changed twice weekly on the same day, e.g. Mondays and Thursdays. Apply patches to clean, dry, cool, hairless skin below the waist as soon as you open the protective pouch. Avoid any skin that is irritated or has broken skin. Do not apply moisturiser, powder or creams before applying the patch as this may prevent it from sticking. Avoid applying the patch to the same area of skin twice in a row. You can shower as normal with patches in place; just avoid scrubbing over the patch. You can also go swimming and do normal exercise. In Tasmania, most people do not have issues with patches staying on. However, if you do it is easy to change to gels or oral estradiol. Some people can have a reaction to the glue in the patches which causes mild skin irritation. It is okay to use an over-the-counter steroid cream for a few days to the skin after you have taken off the patch. Rainbow Care Clinic can provide you with a script for a steroid spray to use prior to your patches if you are having skin reactions or can switch you to gels or oral estradiol.

Gel

Gels are rubbed into the skin and allowed to dry. Open the sachet and squeeze the gel onto the application site, then allow to dry and avoid washing the area for one hour. Cover the application site with clothing once dry where possible and avoid letting others come into contact with the application site to reduce the risk of transfer. If you are having skin to skin contact with someone, shower or wash the application site before doing so to reduce the risk of transfer. The gel is applied once daily to alternating sides of the body. The product information suggests that the gel should be spread over the thigh or the abdomen with an application surface about the size of 1-2 of your hands. An alternative is to apply the gel to the forearm if you find the gel takes too long to dry. Try to use the same area of the body to have a consistently for uniform absorption.

Oral tablets

Oral estradiol tablets available in Australia are estradiol valerate (Progynova) and estradiol hemihydrate (Zumenon, Estrofem). They differ slightly in their chemical composition but are functionally the same once they have been absorbed. Estradiol hemihydrate may be slightly better absorbed but the two medications are considered interchangeable with the Zumenon brand being



Oestrogen Information

added to the Pharmaceutical Benefits Scheme (PBS) in 2021 due to a shortage of Progynova. Typically Progynova is more widely available and comes in 1mg and 2mg tablets so is the default oral tablet prescribed at Rainbow Care Clinic.

Both Progynova and Zumenon product information advise you to swallow them whole. Some people prefer to put the tablet under their tongue (sublingual) or in their cheeks (buccal) to dissolve. This is suggested by some clinics for transgender care and menopausal care online. There is no data to support this route over swallowing the medication. Some think it may be safer as it avoids passing from the gut through the liver in a similar way to transdermal preparations. Others suggest it might be riskier due to rapid high peaks and troughs that may more side effects. Lastly, some people think that the hormone might just end up being swallowed. In summary, we don't know. If you wish to try taking your oestradiol this way, please let Rainbow Care Clinic know how you are using it. For oral dosing, you can take all the tablets at once or split them up during the day as there is no evidence that one way is better. Take your oestrogen in the way it suits you.

Implants

Oestradiol implants are custom ordered pellets of 50mg or 100mg. They must be sterilised before insertion, and are thus only available from a handful of pharmacies and require a script. Implants are an unlicensed product which means they have not been approved by the Therapeutic Goods Administration. Implants are inserted under the skin under local anaesthetic in a minor procedure that leaves a small scar (< 10 mm). Implants are usually required every 6-12 months. Implants are not suitable for starting oestrogen therapy or those wishing to have low dose oestrogen, and they are not reversible. They are suitable for those who are unable to achieve or maintain therapeutic doses on other preparations and/or those wishing to have less frequent dosing of oestradiol.

Types of oestrogen available in Australia

Oestrogen	Dosing information*	Cost*	Information
Transdermal (across the skin)			
Estradiol patches - Estradot - Estraderm MX	25-100mcg patches <i>Typical dose range:</i> 50 - 200mcg twice weekly	PBS listed* ~\$21 for a pack of 8 patches	<ul style="list-style-type: none"> - Self-administered twice a week - Preferred oestradiol @ RCC, esp. if > 45 - Doses >100mcg = 2 patches - No increased risk of blood clots - Risk of mild skin irritation/ not sticking - Default brand is Estradot (smallest) - Occasionally shortages
Estradiol gel - Sandrena	1g (1mg/g) sachets <i>Typical dose range:</i> 0.5 - 2g daily	PBS listed ~\$16 for 28 x 1mg sachets	<ul style="list-style-type: none"> - Self-administered to skin daily - No increased risk of blood clots - Small risk of transfer to others - Good for people who can't use patches but want the safest type of oestradiol
Oral			
Estradiol valerate - Progynova	1 & 2mg tabs <i>Typical dose range:</i> 2 - 8mg	PBS listed ~ \$9-11 per 56 tabs	<ul style="list-style-type: none"> - Self-administered daily to a few times a day - Easier self management of dosing - Avoids skin irritation, transfer risk - Small risk of blood clots
Estradiol hemihydrate - Zumenon - Estrofem	2mg tabs 1 & 2mg tabs <i>Typical dose range:</i> 2 - 8mg	PBS listed ~\$11 for 56 tablets Private script ~\$30 per 56 tablets	
Implants			
Estradiol implants - compounded	Avail. in 50 & 100mg pellets <i>Typical dose range:</i> 50 - 200mg every 6-12 months	Private script Cost is variable depending on pharmacy and fees apply for assessment & insertion apmnts	<ul style="list-style-type: none"> - Infrequent dosing (1-2x per year) - Suitable for those unable to achieve/ maintain therapeutic levels on other forms OR those wishing for less frequent dosing - Fees for implants & appointments - Compounded unlicensed medication - Cannot be reversed

* Prices are approximate and based on a 2024 Chemist Warehouse online search; prices are subject to change and individual pharmacy pricing

❖ The Pharmaceutical Benefits Schedule (PBS) lists all of the medicines available to be dispensed to patients at a Government-subsidised price; prices listed are regular prices, lower prices apply for PBS medications for those with Health Care Card or pension