

Oestrogen

Oestrogen (*es-tro-jen*) is a category of sex hormones and oestradiol (or estradiol)(*es-tro-die-ole*) is the oestrogen used in feminising hormonal therapy. It is naturally produced in human bodies and is responsible for the development of female secondary characteristics, amongst other things. Oestradiol is different from ethinylestradiol, the oestrogen most commonly used in the birth control pill. Ethinylestradiol is a synthetic oestrogen derived from oestradiol that has properties that make it better for use in preventing pregnancy and period regulation 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 cycle regulation in the setting of feminising gender affirmation, ethinylestradiol is too risky and thus the safer oestrogen, oestradiol, is used. Often the terms oestrogen and oestradiol are used interchangeably.

Oestradiol can be taken orally, via gels or patches on the skin, by injection and by implants that are inserted underneath the skin. There is proven 'best' approach to starting oestradiol. At Rainbow Care Clinic, oestradiol is started at a low or medium dose then increased over time until you are seeing changes in your body. Blood tests check that your oestrogen level is in the safe range suggested by the AusPATH Standards of Care (250-1000 pmol/L). Once your oestradiol levels are within this range, the actual number is less important than the changes that are happening in your body. These physical changes are the main guide for dosing. This is because each body responds differently to different levels of oestrogen and the tests for oestrogen have significant variability. Another reason Rainbow Care Clinic starts at a low to medium dose and steadily increases it rather than starting high, is there is weak evidence to suggest this approach may result in better breast development while there is no evidence that high oestradiol levels in patients with adequate testosterone suppression results in more breast development.

High levels of oestradiol 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. High levels of blood oestrogen may also cause tachyphylaxis which is 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 the oestrogen.

Types of oestradiol

Oestradiol can be delivered to your body in several ways. Oral or transdermal (across the skin) preparations are used to start feminising hormonal therapy. Transdermal formulations (gels and patches) are the safest as they appear to have no increased risk of blood clots. Oral estradiol does have a small risk of blood clots but this is usually low for most people. People with risk factors for blood clots, e.g. smokers, previous history of blood clots or family history of blood clots, are generally recommended to use transdermal oestradiol. Oestradiol implants can be used once you have started oestrogen 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. Oestradiol injections are used infrequently as they are typically expensive, have 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 oestradiol into the skin. Patches are changed twice weekly on the same day, e.g. Mondays then 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 cuts. Do not apply moisturiser, powder or creams before applying the patch as this may prevent it from sticking. Don't apply the patch to the same area of skin twice in a row. You can shower as normal in patches 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 over to gels or oral oestradiol. Some people can have a reaction to the glue in the patches which causes mild skin irritation. It is ok 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 change you to gels or oral oestradiol.

Gel

Gels are rubbed into the skin and allowed to dry. Open the sachet and squeeze onto the application site, 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 coming 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 applications site before doing so to reduce the risk of transfer. The gel is applied once daily, to alternating sides. 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 are finding the gel takes too long to dry. Try to use the same area of the body to have a consistent 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 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 to swallow them whole. Some people prefer to put it under their tongue (sublingual) or in their cheeks (buccal) to dissolve. This is recommended by several 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 more risky due to rapid high peaks and troughs causing 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 oestradiol, no matter how you take it, if you are on a dose of more than 2mg it is suggested that you take it as a divided dose, that is, twice or more times a day.



Oestrogen Information

Implants

Oestradiol implants are custom ordered pellets of 50mg or 100mg. They must be sterilised before insertion, thus are 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 (< 10 mm). Implants are usually replaced every 6-12 months. Implants are not suitable for starting oestrogen or those wishing to have low dose oestrogen and they are not reversible. They are suitable for those not able to achieve or maintain therapeutic doses on other preparations and/or those wishing to have less frequent dosing of oestradiol.

(see below for table of types of oestradiol available in Australia)

Types of oestrogen available in Australia

Oestrogen	Dosing information*	Cost*	Information
Transdermal (across the skin)			
Estradiol patches - Estradot - Estraderm MX - Climara (discontinued)	Avail. in 25 to 100mcg patches Typical dose range: 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 due to small size - Occasionally shortages
Estradiol gel - Sandrena	1g (1mg/g) sachets Typical dose range: 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 - Prodynova	Avail. in 1 & 2mg tabs Typical dose range: 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	Avail. in 2mg tabs Avail. in 1 & 2mg tabs Typical dose range: 2 - 8mg	PBS listed ~\$10 for 56 tablets Private script ~\$30 per 56 tablets	
Implants			
Estradiol implants - compounded	Avail. in 50 & 100mg pellets Typical dose range: 50 - 200mg every 4-12 months	Private script Cost is variable depending on pharmacy and fees apply for assessment & insertion appts	<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