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PATIENT GUIDE

Hormone therapy *for women in perimenopause and menopause*

Estradiol and progesterone remain the most effective treatment for hot flashes and night sweats. The forms available, including pellets, differ in how they are approved and how they are dosed.

MAIN HORMONE	FOR	FORMS	FDA STATUS	SOURCES
Estradiol	Menopause care	Skin, mouth, pellet	Varies by form	30 · PMID linked

§ 01

Overview

The years around menopause bring real changes in how many women sleep, feel and function. Hot flashes and night sweats are the best known, and for many women they last far longer than expected. Hormone therapy with estrogen, plus a progestogen when a woman has a uterus, remains the most effective treatment for these symptoms and for the vaginal and urinary changes of menopause, and it also prevents bone loss and fracture.[1]

Below we describe each form of treatment, including pellets, what the large trials found, which preparations are FDA approved or compounded, and what changed on FDA labels in 2025 and 2026. Every source is listed at the end.

75%	**Fewer hot flashes.** In a Cochrane review of 24 placebo controlled trials in 3,329 women, hormone therapy reduced weekly hot flash frequency by 75 percent compared with placebo.[2]
7.4	**Years, the median length of frequent hot flashes.** In the SWAN study of women followed through the transition, frequent hot flashes lasted a median of 7.4 years in total, and 4.5 years after the final period.[3]
Under 60	**Or within 10 years of menopause.** For healthy women in this group, The Menopause Society judges the balance of benefit and risk favorable for treating bothersome hot flashes and preventing bone loss.[1]
6%	**Versus 64 percent.** In a three year trial in women with a uterus, endometrial hyperplasia occurred in 6 percent of those taking estrogen with progesterone and 64 percent of those taking estrogen alone.[19]

§ 02

What hormone therapy is

Perimenopause and menopause. Perimenopause is the transition, often several years long, when the ovaries work less regularly and hormone levels swing. Menopause is the final menstrual period, and the average age at menopause is about 52.[1] Hot flashes can begin during perimenopause, and women whose hot flashes start early in the transition tend to have

them longest, a median of more than 11.8 years. [3]

The hormones. Estradiol is the main estrogen made by the ovaries before menopause. Progesterone is the hormone the ovary makes after ovulation, and micronized progesterone, the form in Prometrium, is structurally identical to it. Synthetic relatives of progesterone, such as medroxyprogesterone acetate, are called progestins, and the whole group is called progestogens. [1] Women also make testosterone, and treatment with it aims to keep blood levels within the normal range for premenopausal women. [4]

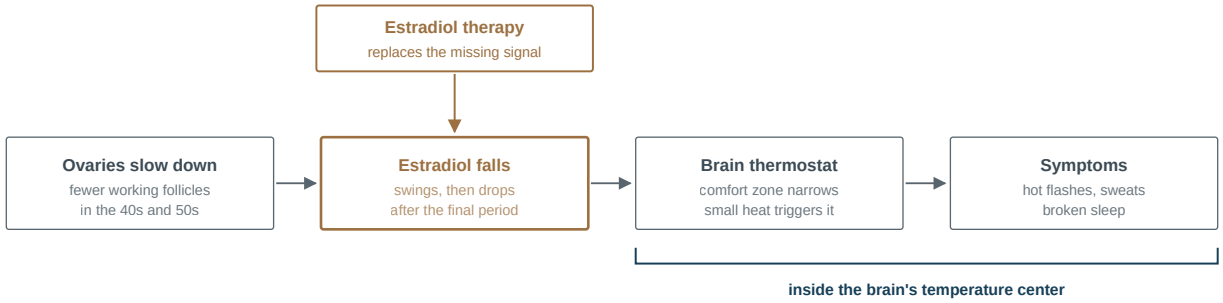
"Bioidentical". The word means a hormone with the same structure as the body's own. Estradiol and micronized progesterone are bioidentical and FDA approved; compounded bioidentical hormones are mixed by a pharmacy, sometimes in combinations or forms such as pellets that have not been tested in trials. [1]

HORMONE THERAPY AT A GLANCE	
Hormones used	Estradiol; progesterone or another progestogen when the uterus is present; testosterone in selected women [1] [4]
Also called	Menopausal hormone therapy, hormone replacement therapy (HRT) [20]
Structure	Estradiol and micronized progesterone are identical to the hormones made by the ovary [1] [19]
Origin	Synthesized; Prometrium's progesterone is made from a plant starting material [19]
Class	Steroid hormones
How it is given	Patch or gel on the skin, tablet or capsule, vaginal ring, cream, tablet or insert, and compounded pellets placed under the skin [1]

§ 03

How hormone therapy works

A hot flash begins in the brain. The hypothalamus keeps core body temperature inside a comfort zone, sweating when it rises past an upper limit and shivering when it drops below a lower one. In a laboratory study of 12 postmenopausal women with hot flashes and 8 without, the women with symptoms had a much narrower zone, so a very small rise in core temperature was enough to set off a flash. [5] Animal research and studies of brain tissue from postmenopausal women suggest that a group of estradiol sensitive neurons in the hypothalamus, known as KNDy neurons, relays the effect of falling estradiol to the brain areas that release heat. [6]



Hot flashes start in the brain's temperature control center when estradiol falls. Women with hot flashes have a much narrower zone between the body temperatures that set off sweating and shivering, so a small rise in core temperature can trigger a flash.[5] Animal work and studies of brain tissue point to estradiol sensitive neurons in the hypothalamus as the link.[6] Estradiol therapy restores the signal; a progestogen is added when a woman has a uterus.[1]

Estradiol therapy restores the signal those neurons have lost,[6] and in trials it relieves hot flashes more reliably than any other treatment studied.[2] [1] Estradiol also acts directly on the tissues of the vagina, vulva and bladder, and on bone, where it slows the loss that speeds up after menopause.[1]

Estrogen also makes the lining of the uterus grow. Taken alone over time by a woman who has a uterus, it raises the risk of endometrial hyperplasia, an overgrowth of the lining that can lead to cancer. A progestogen counters that growth, and preventing it is the reason a progestogen is added to estrogen in menopause care.[1] [7]

KEY POINT

Estradiol treats the symptoms; progesterone protects the uterus. A woman who has had a hysterectomy generally needs estradiol alone, while a woman with a uterus who uses estradiol through the skin or by mouth needs an adequate dose of a progestogen as well.[1] [21] Low dose vaginal estrogen used for vaginal symptoms is the exception, since a progestogen is not advised with it.[1]

§ 04

What the research shows

The largest trials, the Women's Health Initiative (WHI), followed more than 27,000 women for up to 18 years, and later analyses changed how experts read them by looking closely at age and timing.[8] [9] [10]

What the evidence supports

Symptom relief is large and consistent. Across 24 randomized trials, hormone therapy cut hot flash frequency by 75 percent relative to placebo and also reduced their severity.[2] Patches, gels, tablets and rings at their approved doses relieve hot flashes about equally well.[1] In the 12 month trial behind Bijuva, a daily capsule of estradiol with progesterone reduced the frequency and severity of moderate to severe hot flashes more than placebo at weeks 4 and 12, and endometrial hyperplasia was found in 1 of 281 women (0.36 percent) on the 1 mg/100 mg capsule.[22]

Bone is protected. Hormone therapy prevents bone loss and, in the WHI, reduced fractures in women who did not have osteoporosis. The benefit lasts only while treatment continues.[1]

Age and timing shape the risks. The WHI tested oral conjugated equine estrogens with or without medroxyprogesterone acetate in women aged 50 to 79, whose average age at entry was 63.[8] [9] Measured by a global index of serious events, women in their 50s taking estrogen alone had 19 fewer events per 10,000 women each year than on placebo, while women in their 70s had 51 more. With estrogen plus the progestin, the excess ranged from 12 per 10,000 a year in women in their 50s to 38 in women in their 70s.[8] After 18 years of follow up, deaths from any cause were 27.1 percent with hormone therapy and 27.6 percent with placebo.[9] In the ELITE trial of 643 healthy women, oral estradiol slowed thickening of the neck arteries when it was started within 6 years of menopause, with no such effect when it was started 10 or more years after.[11]

How the WHI is read today. The WHI investigators conclude that the trials do not support hormone therapy to prevent heart disease, dementia or other chronic disease, but do support starting it before 60 for bothersome symptoms.[10] The Menopause Society agrees that the balance is favorable under 60 or within 10 years of menopause, and less favorable later, when coronary disease, stroke, clots and dementia are more likely.[1]

What is not yet known

Most outcome data come from the oral products tested in the WHI. Trials of the patch, the gel or micronized progesterone on heart attack, stroke, breast cancer and clots have not been done, so the lower clot risk with patches comes from observational studies.[1] [12] Trial evidence beyond five to seven years of use is thin, and compounded hormones and pellets lack good quality data on safety and effectiveness.[1] [13] For testosterone, the evidence supports one use, low sexual desire causing distress in postmenopausal women, and long term safety has not been established.[4] [14]

MAJOR HUMAN STUDIES Randomized trials unless noted.

STUDY	N	WHO AND HOW	MAIN FINDING
Cochrane review 2004[2]	3,329	24 placebo controlled trials of oral estrogen with or without a progestogen	Hot flash frequency 75 percent lower than placebo
WHI trials 2013[8]	27,347	Women aged 50 to 79; oral estrogens with or without a progestin for 5.6 to 7.2 years	Not supported for chronic disease prevention; risks lowest in women in their 50s
ELITE 2016[11]	643	Oral estradiol 1 mg daily, early vs late after menopause, about 5 years	Slower artery thickening only when started within 6 years
Bijuva trial[22]	1,835	Estradiol with progesterone in one capsule, 12 months, women with a uterus	Fewer, milder hot flashes; hyperplasia 0.36 percent on 1 mg/100 mg
Blood clot study 2019, observational[12]	80,396	UK women with a clot, compared with 391,494 matched controls	Oral therapy linked to higher clot risk; skin preparations were not
Testosterone meta analysis 2019[14]	8,480	36 trials of testosterone in women	Better sexual desire and satisfaction in postmenopausal women
Pellet records review 2021, observational[15]	539	Women on compounded pellets vs FDA approved therapy	More side effects and higher peak hormone levels with pellets

SUMMARY

For a healthy woman with bothersome symptoms who starts within 10 years of menopause or before 60, FDA approved estradiol, with a progestogen if she has a uterus, gives large symptom relief and protects bone, and its serious risks are rare. Hormone therapy is not used to prevent heart disease or dementia. The forms with the least trial evidence are the compounded ones, including pellets.

§ 05

How hormone therapy is given

The Menopause Society recommends using the most appropriate, often lowest, effective dose for each woman's goals, with the form, dose and route chosen individually and reviewed over time.[1] The doses below come from FDA labels or from the society's statement. At OC Wellness, women's hormone care is offered as an ongoing monthly program, and your physician chooses the products and doses with you.

Estradiol through the skin

Patches deliver a steady amount of estradiol each day. For hot flashes, the Vivelle Dot label starts at 0.0375 mg per day, with strengths from 0.025 to 0.1 mg per day; the patch is changed twice a week on the lower abdomen or buttocks, never on the breasts, rotating sites.[21] For prevention of bone loss the starting strength is 0.025 mg per day.[21] Gels and sprays are other skin forms.[1] Skin forms bypass the first pass through the liver, and in observational studies they have not been linked to a higher risk of blood clots.[1][12]

Estradiol by mouth

Estradiol tablets are taken once a day. The label for generic estradiol tablets gives a usual starting range of 1 to 2 mg daily, adjusted to control symptoms, with the lowest effective maintenance dose found by titration.[23] Lower doses, such as 0.5 mg or less, may take 6 to 8 weeks to give full relief.[1] Among oral forms, estradiol carried less clot risk than conjugated equine estrogens.[12]

Progesterone for women with a uterus

Prometrium (micronized progesterone) capsules are approved to prevent endometrial hyperplasia in postmenopausal women with a uterus who take conjugated estrogen tablets. The labeled dose is 200 mg once a day at bedtime for 12 days of each 28 day cycle.[19] The Menopause Society gives the same dose, 200 mg a day for 12 to 14 days a month, as adequate protection when micronized progesterone is used with estrogen therapy more broadly.[1] It is taken at bedtime because it can cause drowsiness or dizziness, and the capsules contain peanut oil.[19]

Bijuva combines estradiol and progesterone in one capsule, 1 mg/100 mg or 0.5 mg/100 mg, taken each evening with food, for hot flashes in women with a uterus.[22]

Vaginal estrogen

For vaginal dryness, painful sex and some urinary symptoms, low dose estrogen placed in the vagina treats the tissue directly. Estring is a ring that releases about 7.5 micrograms of estradiol a day and stays in place for three months before it is replaced.[24] Creams, small vaginal tablets and a softgel insert are other forms.[1] A progestogen is not advised with low dose vaginal estrogen, and it does not appear to increase the risk of endometrial cancer, though trials with biopsy results last only a year.[1]

Hormone pellets under the skin

Pellets are small cylinders of crystalline hormone placed under the skin, where they slowly release the hormone over a long period.[25] The estradiol and testosterone pellets used for women are compounded, and no estradiol pellet is FDA approved.[1][26] No FDA label sets a pellet dose for women, so we cannot give one here.[26][16]

The dose of a pellet is fixed when it is placed and cannot be adjusted afterward short of removing it. The FDA label for the one approved pellet, a testosterone pellet for men, states that pellets are much less flexible for dose adjustment than other forms and that, if a complication means the hormone must be stopped, the pellets would have to be removed.[25] Compounded pellets also produce marked and prolonged rises in estradiol and testosterone, often far above the normal

range, and they are difficult to remove if a problem arises. [16] In a review of 539 women's records, peak estradiol averaged 237.70 pg/mL with pellets against 93.45 pg/mL with FDA approved therapy, and peak testosterone 194.04 ng/dL against 15.59 ng/dL. [15]

Testosterone

No testosterone product is FDA approved to treat menopause symptoms or low sexual desire in women, so any use in women is off label. [4] [25] For postmenopausal women with distressing low desire, the international consensus statement supports a trial of testosterone through the skin at doses that keep blood levels in the normal premenopausal range, using an approved male product at a female dose. It does not recommend compounded testosterone, and it advises against pellets and injections that produce levels above that range. [4] It advises measuring total testosterone before starting and again 3 to 6 weeks later, and stopping if there is no benefit by 6 months. [4]

COMPARING THE OPTIONS

	PATCH OR GEL	TABLET OR CAPSULE	VAGINAL	PELLET
How often	Patch twice weekly [21]	Daily [23] [22]	Ring every 3 months [24]	Lasts months [25] [16]
Dose can be changed	YES	YES	YES	NO, UNLESS REMOVED [25]
FDA approved	YES [21] [1]	YES [23] [19]	YES [24]	NO, COMPOUNDED [1]
Progestogen if uterus present	Needed [21]	Needed, or combined capsule [22]	Not advised at low dose [1]	Needed for estradiol [1]

§ 06

What to expect

The first weeks. In the patch trials, the two higher strengths eased hot flashes more than placebo by week 4, and the 0.0375 mg strength did the same by week 4 in its own 12 week trial. [21] Lower doses can take 6 to 8 weeks to reach full effect. [1] Breast tenderness, headache and some vaginal bleeding are among the more common side effects. [22] [1] Progesterone at bedtime can make you sleepy, and in studies it shortened the time taken to fall asleep. [19] [1]

Bleeding. Some progestogen regimens bring a monthly bleed, and many women choose regimens that avoid it. Bleeding that starts unexpectedly more than 6 months into treatment needs to be checked. [1]

The longer term. Vaginal symptoms tend to worsen without treatment, while hot flashes usually ease with time. [1] There is no fixed age at which hormone therapy must stop, and The Menopause Society does not advise routinely stopping it at 60 or 65; the decision rests on your symptoms, your risks and your preferences. [1] When hormone therapy is stopped, hot flashes come back in about half of women, and the protection of bone fades within months. [1]

§ 07

Safety

The more common side effects of hormone therapy include breast tenderness, bloating, nausea, headaches, fluid retention, unscheduled bleeding and mood changes, the last mostly related to the progestogen. [1] The serious risks are rare, which The Menopause Society defines as fewer than 10 extra cases per 10,000 women a year, and in women under 60 they include blood clots and gallbladder disease, a small rise in breast cancer with estrogen plus progestogen, and endometrial cancer if estrogen is not adequately opposed. [1]

SIDE EFFECTS WITH ESTRADIOL AND PROGESTERONE IN ONE CAPSULE Percent of women in the 12 month trial, from the Bijuva FDA label.[22]

SIDE EFFECT	ESTRADIOL 1 MG WITH PROGESTERONE 100 MG (N=415)	PLACEBO (N=151)
Breast tenderness	10.4%	0.7%
Headache	3.4%	0.7%
Vaginal bleeding	3.4%	0%
Vaginal discharge	3.4%	0.7%
Pelvic pain	3.1%	0%
Nausea	2.2%	0.7%

Less common but important

- **Endometrial cancer** (**boxed warning** on systemic estrogen alone). Unopposed estrogen raises the risk in a woman with a uterus; in a Cochrane review of 72 studies, unopposed estrogen raised the odds of endometrial hyperplasia beyond one year of use by about nine times (odds ratio 8.97). Adding a progestogen lowers this risk.[21] [7]
- **Blood clots and stroke.** Oral therapy was linked to a higher risk of clots in veins, while patches and gels were not; stroke risk rose in the WHI, mostly in older women.[12] [21] [1]
- **Breast cancer.** In a meta analysis of prospective studies that included 108,647 women who developed breast cancer, five years of therapy starting at 50 was estimated to cause about one extra case for every 50 users of estrogen with a daily progestogen and one for every 200 users of estrogen alone; vaginal estrogen was not linked to excess risk.[17] In the WHI, estrogen alone was linked to fewer breast cancers than placebo.[8]
- **Gallbladder disease.** Estrogen raises the risk of gallbladder disease needing surgery 2 to 4 times.[21]
- **Memory.** In WHI studies of women 65 and older, probable dementia was more frequent with hormone therapy; whether this applies to younger women is unknown.[21] [19]
- **Pellets.** In the records review, side effects were reported in 57.6 percent of women on pellets and 14.8 percent on FDA approved therapy, abnormal uterine bleeding in 55.3 percent and 15.2 percent of women with a uterus, and hysterectomy in 20.3 percent and 6.3 percent. Four women on pellets had estradiol levels above 1,000 pg/mL.[15] The approved testosterone pellet label also reports infection and pellets working their way out at the insertion site.[25]

TELL YOUR PHYSICIAN BEFORE STARTING IF ANY OF THESE APPLY

- You have had breast cancer, endometrial cancer or another estrogen sensitive cancer.[1] [21]
- You have vaginal bleeding that has not been explained.[21]
- You have had a blood clot, stroke, heart attack or coronary disease, have an inherited clotting disorder, or have surgery or a long period of immobility coming up.[1] [21]
- You have liver or gallbladder disease, very high triglycerides, migraine, epilepsy, asthma, diabetes, lupus or endometriosis, or you take thyroid hormone.[21]
- You are allergic to peanuts, which matters for Prometrium.[19]
- You may be pregnant, or you are still having periods and need contraception.[1]
- You take any prescription medicine, over the counter product or supplement. Please bring the full list.

Long term safety data are limited in two places. Trials have not followed women on the patch, gel or micronized progesterone for heart, breast and clot outcomes, and compounded hormones and pellets lack safety trials.[1] [13] We therefore review how you are doing at set points.

§ 08

Is this right for you

Your consultation is where we work out which form of hormone therapy, if any, fits you. If hormones are not right for you, nonhormone medicines with good evidence include certain antidepressants, gabapentin, fezolinetant and oxybutynin, along with cognitive behavioral therapy and clinical hypnosis.[18]

Before we begin

- [ ] A review of your medical history, family history, current medications and supplements
- [ ] Blood pressure, weight, and a record of your periods and symptoms
- [ ] Baseline bloodwork, so that anything we see later can be compared against where you began
- [ ] A written note of your goals, for symptoms, sleep and how you want to feel, so we can judge progress together

Hot flashes that first appear years after menopause can have other causes, such as thyroid disease, sleep apnea or a medicine, which we look for first.[1] Salivary and urine hormone tests are unreliable for setting doses, so estrogen treatment is guided by your symptoms, and blood hormone levels are rarely needed.[1] Testosterone is the exception, since blood levels are checked to keep them in the normal female range.[4]

Reviewing your progress

We will reassess against your documented starting point at defined intervals, adjusting the dose or form if needed. The decision to continue is revisited with you over time, and you are welcome to stop at any time; we will plan together how to do it.

> QUESTIONS TO ASK YOUR PHYSICIAN
>
> Which form would you choose for someone with my history, and why? Do I need progesterone, and how will my bleeding change? How do patches compare with pellets for me? How long might I stay on treatment, and how would we stop?

§ 09

Regulatory status

FDA approved estradiol and progesterone. Estradiol patches such as Vivelle Dot are FDA approved for moderate to severe hot flashes, for moderate to severe vulvar and vaginal atrophy due to menopause, for low estrogen from ovarian failure or removal, and to prevent postmenopausal osteoporosis.[21] Estring is approved for vulvar and vaginal atrophy, and Bijuva for hot flashes in women with a uterus.[24] [22] Prometrium is approved to prevent endometrial hyperplasia in postmenopausal women taking conjugated estrogen tablets and to treat absent periods; its use with estradiol follows The Menopause Society's dosing and is off label, which a physician may lawfully prescribe.[19] [1]

The boxed warning. On 10 November 2025 the FDA announced that it would remove references to cardiovascular disease, breast cancer and probable dementia from the boxed warning on menopausal hormone therapy labels, keep the boxed warning for endometrial cancer on systemic estrogen alone products, and recommend starting systemic therapy within 10

years of menopause or before age 60.[20] Updated labels have since been approved for products including Prometrium, Bijuva and Estring, which now carry no boxed warning, and estradiol alone products such as Vivelle Dot carry only the endometrial cancer warning. [19] [22] [24] [21] Many other labels on DailyMed, including generic estradiol tablets, still show the earlier broader warning until they are updated. [23]

Compounded hormones and pellets. Compounded hormones, including creams, troches and pellets, are not FDA approved. A licensed pharmacy prepares them on a prescription for an individual patient under section 503A of federal law.[13] The only hormone pellet the FDA has approved is a testosterone pellet for men, so estradiol and testosterone pellets for women are compounded. [26] [25] The National Academies advised in 2020 limiting compounded hormones to a documented allergy to an approved product or need for a form not otherwise available, and reviewing pellets for the FDA's list of drugs difficult to compound. [13]

Testosterone. No testosterone product is FDA approved to treat menopause symptoms or low sexual desire in women, so its use in women is off label.[4] [25] Testosterone is a Schedule III controlled substance under the federal Controlled Substances Act. [25]

For athletes. The 2026 World Anti Doping Agency Prohibited List bans testosterone and prasterone (DHEA, also used as a vaginal insert in menopause) at all times under section S1. Estradiol and progesterone are not named on the list, though aromatase inhibitors and anti estrogen medicines are prohibited under section S4.[27] [1]

If you would like details about the preparation used in your treatment, please ask.

§ 10

Common questions

Is hormone therapy FDA approved?

Estradiol in patch, gel, tablet and vaginal forms, micronized progesterone and the combined estradiol and progesterone capsule are FDA approved.[21] [1] [24] [22] [19] Compounded hormones, including pellets, are not FDA approved, and no testosterone product is approved for menopause symptoms or low desire in women. [13] [26] [4]

Are "bioidentical" hormones safer?

Estradiol and micronized progesterone are bioidentical and FDA approved. Compounded bioidentical hormones lack good evidence of safety and effectiveness, and The Menopause Society lists concerns including overdosing, underdosing and impurities.[1]

How soon will I feel better?

In the patch trials, hot flashes eased more than with placebo by week 4.[21] Lower doses can take 6 to 8 weeks to reach full effect. [1]

Can the dose of a pellet be changed once it is in?

Not without removing it. A pellet releases its hormone slowly over a long period.[25] The FDA label for the approved testosterone pellet states that pellets are much less flexible for dose adjustment than other forms and would have to be removed if the hormone needed to be stopped. [25] Compounded pellets can raise estradiol and testosterone well above the normal range for months. [16] [15]

Who should not use hormone therapy?

Estrogen through the skin or by mouth is generally not used after an estrogen sensitive cancer such as breast cancer, with unexplained vaginal bleeding or liver disease, or after a heart attack, stroke or blood clot; starting after 60 needs careful thought.[1]

Will it affect drug testing in sport?

Testosterone and DHEA are prohibited at all times on the 2026 World Anti Doping Agency list; estradiol and progesterone are not named on it.[27] Athletes should check with their testing authority.

What happens if I stop?

Hot flashes return in about half of women and bone protection fades within months; experts generally advise lowering the dose gradually, and we will plan it with you.[1]

Where is a compounded medicine made, and who oversees it?

Federal law sets out two kinds of compounding. Under section 503A, the state board of pharmacy carries the day to day oversight of the pharmacy that prepares your medicine, and the FDA inspects for cause and on surveillance.[28] Under section 503B, an outsourcing facility registers with the FDA, works to federal manufacturing quality standards, reports adverse events to the agency and is inspected on a risk based schedule, and it may supply a clinic directly rather than for one named patient. [29] We use both kinds, and which one prepares your medicine depends on the preparation.

Is a compounded medicine the same as an FDA approved one?

No, and the difference matters. An approved estradiol or progesterone product is the first choice whenever one fits your situation.[28] What a prescription from a licensed pharmacy or a registered outsourcing facility does give you is a named prescriber, a facility answerable to a state board or to the FDA, ingredients that meet federal requirements, and a route for reporting a problem. A cream or vial bought online and labelled for research use only has none of that, and the FDA treats those products as unapproved new drugs when they are meant for people, so please do not use one. [30]

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PATIENT SIGNATURE	DATE	REVIEWING PHYSICIAN

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