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PATIENT GUIDE

Estrogen management and fertility *for men on hormone therapy*

Testosterone turns partly into estradiol, and testosterone therapy lowers the signals that make sperm. These medicines act on both, and all but one of them are prescribed off label in men.

MEDICINES	CLASSES	FORMS	STATUS	SOURCES
7 in 4 classes	Four drug classes	Tablet, injection	Mostly off label	33 · PMID linked

§ 01

Overview

Testosterone does not work alone. An enzyme called aromatase turns some of it into estradiol, the main estrogen, and estradiol has work of its own to do in a man's body: it governs the skeleton[1] and it holds body fat in check.[2] Estradiol also signals back to the brain, so as it rises the pituitary sends out less luteinizing hormone. Testosterone given as a medicine raises estradiol and quiets those pituitary signals, so estrogen and fertility belong in the same conversation as testosterone.[21] Testosterone itself is covered in our testosterone guide (OCW WP 055).

The medicines here work on that loop without replacing the hormone. Aromatase inhibitors block the step that makes estradiol, selective estrogen receptor modulators block estradiol's signal back to the brain, human chorionic gonadotropin acts on the testis in place of luteinizing hormone, and gonadorelin is the hypothalamic hormone that starts the chain. Every number below comes from an FDA label, a published study or a named guideline.

1	**Of these medicines, the number with an approved use in men.** The American Urological Association states that of these agents, only human chorionic gonadotropin has been approved by the FDA for use in males, for hypogonadotropic hypogonadism.[21]
10 pg/mL	**The estradiol level that protected bone.** In 400 healthy men whose hormone production was switched off and replaced, estradiol above 10 pg/mL and testosterone above 200 ng/dL were generally enough to prevent bone loss.[1]
88%	**Reached a normal testosterone on clomiphene.** Of 400 men treated with clomiphene citrate for low testosterone, among the 120 who took it beyond three years 88 percent reached a normal level.[3]
10%	**Breast enlargement with tamoxifen.** Among 114 men on bicalutamide for prostate cancer, gynecomastia developed in 10 percent of those also given tamoxifen, 51 percent given anastrozole and 73 percent given neither.[4]

§ 02

What these medicines are

Four groups appear in this conversation. Aromatase inhibitors, anastrozole and exemestane, are tablets that stop the aromatase enzyme from making estradiol.[22] [23] Selective estrogen receptor modulators, which include clomiphene citrate, its isomer enclomiphene and tamoxifen, are tablets that sit on the estrogen receptor and block estradiol's signal in some tissues while imitating it in others.[21] Human chorionic gonadotropin is a hormone obtained from the urine of pregnant women, given by injection, whose action the label describes as virtually identical to that of pituitary luteinizing hormone.[24] Gonadorelin is gonadotropin releasing hormone itself, a chain of ten amino acids made by the hypothalamus.

Clomiphene citrate is a mixture of two isomers, enclomiphene and zuclomiphene, which behave differently in the body. Enclomiphene is the one that blocks the estrogen receptor and raises the pituitary hormones, so it was taken into trials on its own.[5]

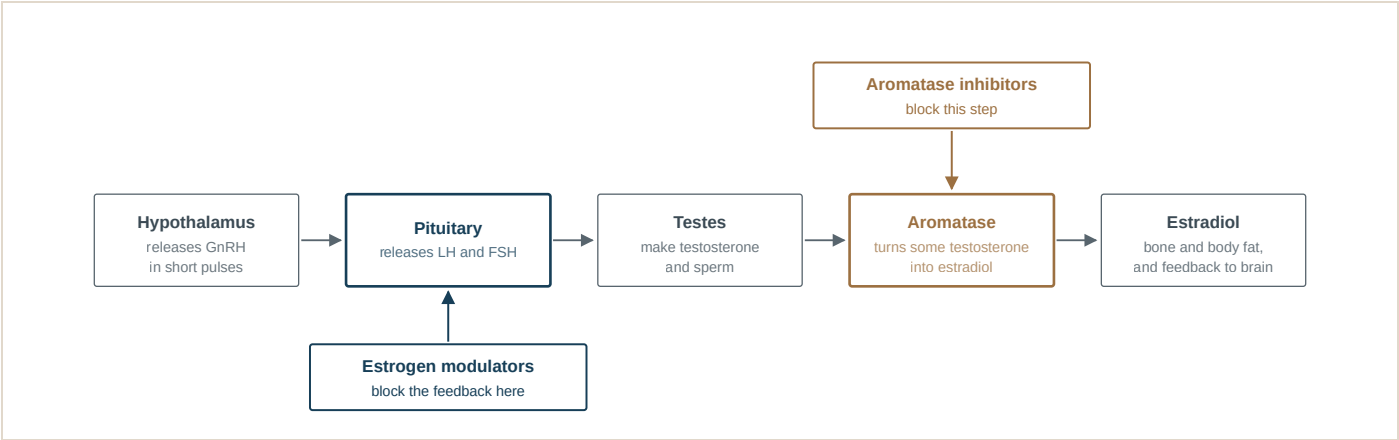
THE MEDICINES AT A GLANCE Approved uses are from the current FDA label of each product, or from Drugs@FDA where no product is approved.

MEDICINE	CLASS	HOW IT IS GIVEN	WHAT THE FDA HAS APPROVED IT FOR
Anastrozole	Aromatase inhibitor	Tablet by mouth	Breast cancer in postmenopausal women[22]
Exemestane	Aromatase inhibitor, binds the enzyme permanently	Tablet by mouth	Breast cancer in postmenopausal women, after tamoxifen[23]
Clomiphene citrate	Estrogen receptor modulator, two isomers	Tablet by mouth	Ovulatory dysfunction in women desiring pregnancy[25]
Enclomiphene citrate	Estrogen receptor modulator, one isomer of clomiphene	By mouth, as a compounded preparation	Nothing. No enclomiphene product is approved in the United States[26]
Tamoxifen citrate	Estrogen receptor modulator	Tablet by mouth	Breast cancer in women and men, and lowering breast cancer risk in women[27]
Chorionic gonadotropin	Hormone with the action of luteinizing hormone	Injection into the muscle	Selected cases of hypogonadotropic hypogonadism in males, prepubertal cryptorchidism, and ovulation induction in women[24]
Gonadorelin	Gonadotropin releasing hormone	Injection; no human product is marketed	Nothing at present. The two human products were discontinued[26]

§ 03

How they work

The hypothalamus releases gonadotropin releasing hormone in pulses, the pituitary answers with luteinizing hormone and follicle stimulating hormone, and the testes make testosterone and sperm. Aromatase then converts a share of that testosterone into estradiol, in fat tissue and elsewhere, and estradiol acts on bone and fat and also restrains the hypothalamus and pituitary.[21] [6] In men carrying a lot of fat there is more of the enzyme at work, and the extra conversion of androgens to estrogens contributes to a form of low testosterone that comes from the brain rather than the testis.[6]



Each medicine interrupts the loop at a different point. An aromatase inhibitor blocks the conversion of testosterone to estradiol, and a modulator blocks estradiol's signal at the hypothalamus and pituitary; either way the pituitary releases more luteinizing hormone and the testes make more testosterone.[21] Chorionic gonadotropin acts on the testis in place of luteinizing hormone,[24] and gonadorelin acts at the pituitary as the hypothalamic hormone does.[10]

An aromatase inhibitor blocks the conversion step, so estradiol falls, the brake on the pituitary eases and the testes make more testosterone.[7] A modulator such as clomiphene or enclomiphene leaves aromatase alone and blocks the estrogen receptor in the hypothalamus and pituitary, which lifts the same brake, and estradiol rises alongside testosterone rather than falling.[21][8] Chorionic gonadotropin skips the brain and stimulates the Leydig cells of the testis directly, which is why it keeps working once testosterone therapy has silenced the pituitary.[24][9] Gonadorelin sits at the top of the chain, and the pituitary answers short bursts of it, so the human studies deliver it through a pump that imitates that rhythm.[10]

KEY POINT

Estradiol does real work in a man. In 400 healthy men whose hormone production was suppressed and then replaced at graded doses, with aromatase blocked in half of them, loss of estrogen accounted for most of the gain in body fat and both hormones contributed to the decline in sexual function.[2] Spine density measured by computed tomography fell substantially whenever aromatization was suppressed, whatever the testosterone dose.[1] Lowering estradiol a long way carries a cost, and treatment aims at a sensible level.[21]

§ 04

What the research shows

The AUA guideline states: "Clinicians may use aromatase inhibitors, human chorionic gonadotropin, selective estrogen receptor modulators, or a combination thereof in men with testosterone deficiency desiring to maintain fertility," a conditional recommendation at evidence level Grade C.[11] It adds that the benefits of testosterone therapy "cannot be extrapolated to the benefits provided by these alternative therapies."[21] The Endocrine Society guideline names no aromatase inhibitor among the treatments it describes, and of the modulators it says only that clomiphene citrate "has been used empirically in men with hypogonadotropic hypogonadism; however, neither its efficacy nor its safety has been demonstrated in randomized trials."[12] Randomized trials have since been published.

What the evidence supports

Aromatase inhibitors raise testosterone and lower estradiol. In a one year randomized, placebo controlled trial of 69 men aged 60 and older, anastrozole 1 mg daily raised mean testosterone from 319 ng/dL to 524 ng/dL at three months while estradiol fell from 15 pg/mL to 12 pg/mL.[7] Trials in 88 men and in 43 men aged 65 to 82 found the same pattern, the second

bringing testosterone above 500 ng/dL over twelve months. [13] [14] In 23 severely obese men, adding anastrozole to six months of diet and exercise gave higher testosterone and lower estradiol than diet and exercise alone. [6] In twelve healthy young males, ten days of exemestane 25 mg daily lowered estradiol by 38 percent and raised testosterone by 60 percent. [15]

Estrogen receptor modulators raise testosterone as much as a gel does. A 2025 meta analysis of randomized trials in men with functional hypogonadism found that clomiphene or enclomiphene raised total testosterone by 273.76 ng/dL against placebo (95 percent confidence interval 191.87 to 355.66), with luteinizing hormone up by 4.66 IU/L, and no significant difference in testosterone against a testosterone gel.[16] In 26 infertile hypogonadal men randomized for twelve weeks, clomiphene 25 mg daily raised testosterone more than anastrozole 1 mg daily (571 against 408 ng/dL), estradiol rose on clomiphene and fell on anastrozole, and neither changed semen measurements. [8]

Enclomiphene raised testosterone while sperm counts held. Two parallel randomized, double blind, placebo controlled phase III studies compared two daily doses of enclomiphene citrate with a testosterone gel in overweight men aged 18 to 60 whose morning testosterone was 300 ng/dL or below with a normal or low luteinizing hormone. Over sixteen weeks the pituitary hormones rose on enclomiphene and fell on the gel, and sperm concentration stayed in the normal range on enclomiphene while spermatogenesis was markedly reduced on the gel.[5]

Chorionic gonadotropin keeps the testis working while testosterone is given. Testosterone enanthate 200 mg weekly cut the testosterone inside the testis by 94 percent within three weeks in 29 healthy men, and adding hCG restored it in proportion to the dose, with 250 IU every other day leaving it 7 percent below baseline and 500 IU leaving it 26 percent above.[9] In 26 hypogonadal men taking testosterone with hCG 500 IU every other day, no man became azoospermic, semen measurements did not change over more than a year, and nine contributed to a pregnancy. [17] In 282 men who wished to preserve fertility, clomiphene 50 mg, hCG 5000 IU twice weekly and the two together all raised testosterone to a similar degree. [18]

Tamoxifen does more for breast tissue than an aromatase inhibitor. Among 114 men taking bicalutamide for prostate cancer, randomized for 48 weeks to tamoxifen 20 mg daily, anastrozole 1 mg daily or placebo, gynecomastia developed in 10, 51 and 73 percent and breast pain in 6, 27 and 39 percent; the authors concluded that anastrozole did not significantly reduce either, while tamoxifen was effective.[4] In a crossover study of ten men with benign gynecomastia, seven had a smaller breast after a month of tamoxifen and none on placebo, the four men with breast pain got relief, and the reduction in size was partial. [19]

What is not yet known

None of this work has shown that lowering estradiol makes a man feel better. Body composition and strength did not move over a year of anastrozole,[13] symptoms and muscle strength did not differ from diet and exercise alone in the obese men, [6] only testosterone improved spine density in the head to head trial, [14] and the authors of the one year bone study concluded that aromatase inhibition "does not improve skeletal health in aging men with low or low normal testosterone levels." [7] The FDA label for anastrozole reports a randomized trial in 80 boys aged 11 to 18 with pubertal gynecomastia in which six months of 1 mg daily produced no significant difference in the proportion whose breast tissue shrank by half or more. [22] Breast symptoms are also less common than the conversation around them suggests: the AUA notes that symptomatic gynecomastia is an uncommon side effect of testosterone therapy and a rarely reported event in randomized trials, and no trial has tested treating a raised estradiol in a man on testosterone against leaving it alone. [21]

The enclomiphene studies ran sixteen weeks and measured hormones and sperm counts, not pregnancies or anything about the heart or bone.[5] No study reports testicular size in men taking testosterone with hCG; the study that followed those men reported semen measurements, hormones and pregnancies. [17] The one randomized trial of hCG on its own, in 40 men over 60, raised testosterone and estradiol by 150 percent and lean mass by about 2 kg, but strength and physical function did not improve and testis volume fell by about 5 mL. [20] For gonadorelin we found no published study of its use alongside testosterone therapy; the human work is in congenital hypogonadotropic hypogonadism, where a pump delivering pulses brought sperm into the semen at a median of six months against fourteen for injected gonadotropins in a comparison of 28 men. [10]

HUMAN STUDIES IN MEN RCT means randomized controlled trial. Doses are as given in each study.

STUDY	N	DESIGN AND TREATMENT	MAIN FINDING
Finkelstein 2013, 2016[2] [1]	400	RCT, healthy men 20 to 50, production suppressed then testosterone replaced at graded doses, aromatase blocked in half, 16 weeks	Estrogen loss accounted for most of the fat gain; spine density fell whenever aromatization was blocked
Burnett Bowie 2009[7]	69	RCT, men 60 and older, anastrozole 1 mg daily, 1 year	Testosterone 319 to 524 ng/dL, estradiol 15 to 12 pg/mL; spine density fell against placebo
Mauras 2003[15]	12	Crossover, healthy males 14 to 26, exemestane 25 or 50 mg daily, 10 days	Estradiol down 38 percent and testosterone up 60 percent at 25 mg
Helo 2015[8]	26	RCT, infertile hypogonadal men, clomiphene 25 mg or anastrozole 1 mg daily, 12 weeks	Testosterone rose 571 against 408 ng/dL; no change in semen measurements in either arm
Hohl 2025[16]	meta	Meta analysis of RCTs of clomiphene or enclomiphene	Testosterone up 273.76 ng/dL against placebo; no difference against testosterone gel
Kim 2016[5]	2 trials	Phase III RCTs, overweight men 18 to 60, enclomiphene at two doses against testosterone gel, 16 weeks	Sperm concentration held on enclomiphene and was markedly reduced on the gel
Krzastek 2019[3]	400	Retrospective, clomiphene citrate for low testosterone, mean 25.5 months	Beyond 3 years, 88 percent normal testosterone, 77 percent better symptoms, 8 percent side effects
Coviello 2005[9]	29	RCT, testosterone enanthate 200 mg weekly with placebo or hCG 125, 250 or 500 IU every other day, 3 weeks	Testosterone inside the testis fell 94 percent; hCG restored it in proportion to dose
Hsieh 2013[17]	26	Retrospective, testosterone with hCG 500 IU every other day	No azoospermia, semen measurements unchanged beyond a year, 9 pregnancies
Boccardo 2005[4]	114	RCT, men on bicalutamide, tamoxifen 20 mg or anastrozole 1 mg or placebo, 48 weeks	Gynecomastia 10, 51 and 73 percent; tamoxifen effective, anastrozole not
Zhang 2019[10]	28	Congenital hypogonadotropic hypogonadism, pulsatile gonadorelin pump against injected gonadotropins	Sperm appeared at a median of 6 against 14 months

SUMMARY

Aromatase inhibitors and estrogen receptor modulators both raise a man's own testosterone, and the modulators do it without the fall in sperm counts that testosterone therapy causes. What no trial has shown is that either makes a man feel or function better, and blocking aromatase has a measurable cost to the spine. Chorionic gonadotropin keeps the testis making testosterone while testosterone therapy is given, on the strength of two small studies. Gonadorelin has no evidence in this setting and no marketed product.

§ 05

How these medicines are given

Only one of them has an FDA label dose for a man. For the others the label covers a different patient, so the dose comes from published studies and from the ranges the AUA records for use in men, and your physician sets it. The AUA marks clomiphene, tamoxifen and anastrozole each as not FDA approved for use in males, and advises waiting at least four weeks after starting anastrozole, clomiphene or hCG before checking blood work.[21]

By mouth

Every trial in men described above used anastrozole 1 mg daily,[7] [14] and exemestane 25 mg or 50 mg daily in the only study in males. [15] Clomiphene citrate was given as 25 mg daily in the comparison with anastrozole and 50 mg daily in the comparison with hCG, and tamoxifen as 20 mg daily in the prostate cancer trial. [8] [18] [4] The enclomiphene reports describe two daily doses without stating them, so we quote no number, and no regulator has set one. [5]

By injection

The chorionic gonadotropin label is for intramuscular use only and gives two regimens for selected cases of hypogonadotropic hypogonadism in males: 500 to 1,000 USP units three times a week for three weeks followed by the same dose twice a week for three weeks, or 4,000 USP units three times weekly for six to nine months, reduced afterwards to 2,000 USP units three times weekly for three months.[24] Alongside testosterone therapy the AUA records a much smaller dose, 250 IU or 500 IU every other day, drawn from the single study that measured testosterone inside the testis. [21] [9]

Gonadorelin

There is no dose to give, because no human gonadorelin product is marketed in the United States and the studies that exist deliver it through a pump.[10] Your physician can talk through the options that are approved or supported by evidence.

DOSES IN THE SOURCES CITED HERE None of these is a treatment plan. Your dose is set by your physician.

MEDICINE	IN THE STUDIES	RECORDED BY THE AUA FOR MEN	FDA LABEL DOSE FOR MEN
Anastrozole	1 mg daily[7] [14]	0.05 to 1 mg every 1 to 3 days[21]	NONE
Exemestane	25 or 50 mg daily for 10 days[15]	Not listed[21]	NONE
Clomiphene citrate	25 to 50 mg daily[8] [18]	25 to 50 mg every 1 to 2 days[21]	NONE
Tamoxifen citrate	20 mg daily, or 10 mg twice daily[4] [19]	20 mg daily[21]	NONE FOR GYNECOMASTIA
Chorionic gonadotropin	250 to 500 IU every other day with testosterone[9] [17]	500 to 4,000 IU, 2 to 3 times a week[21]	YES[24]

§ 06

What to expect

The first weeks. Hormones move quickly and symptoms do not. Anastrozole brought testosterone to its highest point at three months in the one year trial.[7] Testosterone rose by the first month on clomiphene, hCG or both in the trial of 282 men, and symptom scores improved at one month and further at three. [18] Because these medicines act through your own production, the AUA advises that blood work be drawn no sooner than four weeks after starting. [21]

If the aim is fertility. Sperm production answers more slowly than hormones do. Sperm concentration held steady through sixteen weeks of enclomiphene and through more than a year of testosterone given with hCG.[5] [17] Semen testing is how this is followed, since blood levels say nothing about it.

If the aim is breast tenderness. One month of tamoxifen reduced breast size partially in seven of ten men in the crossover study, which its authors took to mean a longer course might be needed, and the prostate cancer trial ran 48 weeks.[19] [4] The AUA advises that breast symptoms appearing during testosterone therapy be watched for a period based on clinical judgment, since they sometimes settle on their own. [21]

DURING TREATMENT

- Report blurred vision, spots or flashes of light while taking clomiphene or enclomiphene, which the clomiphene label asks be taken seriously because they can last after the medicine is stopped.[25]
- Report leg pain or swelling, or sudden shortness of breath, while taking tamoxifen, because blood clots in the legs and lungs have occurred during tamoxifen treatment.[27]
- Report breast tenderness or swelling, which the chorionic gonadotropin label lists among its adverse reactions and which three of twenty men developed in the hCG trial in older men.[24] [20]
- Report low mood or a change in mood, the side effect most often recorded in long term clomiphene use.[3]

§ 07

Safety

Most of the safety record for these medicines was gathered in the patients their labels were written for: women with breast cancer for the aromatase inhibitors and tamoxifen, women having fertility treatment for clomiphene. What follows separates what is known in men from what comes from those settings.

Bone, with an aromatase inhibitor

Estradiol is the hormone that protects the adult male skeleton, and an aromatase inhibitor lowers it on purpose. Spine density fell substantially whenever aromatization was blocked in the controlled study, and estradiol above 10 pg/mL was generally enough to prevent that loss.[1] In the one year trial in older men, spine density fell on anastrozole while it rose slightly on placebo.[7] The anastrozole label records a mean fall in spine and hip density in women and advises considering bone density monitoring, and the exemestane label records lumbar spine density 3.1 percent lower at 24 months against 0.2 percent lower on tamoxifen in women.[22] [23] The AUA puts it directly: aromatase inhibitors "should in general not be used for extended periods of time due to concerns regarding loss of BMD," and with careful dose titration estradiol can often be held in the therapeutic range.[21]

Vision and mood, with clomiphene

The clomiphene label warns of blurring and other visual symptoms such as spots or flashes, which become more common with a higher total dose or longer treatment, are usually reversible, and have in some cases persisted after the medicine was stopped. The label also contraindicates clomiphene in liver disease.[25] In the review of 400 men treated for low testosterone, 8 percent of those taking it beyond three years reported a side effect, most often a change in mood, then blurred vision, then breast tenderness, with no serious adverse event recorded.[3]

Blood clots, with tamoxifen

The tamoxifen label warns of thromboembolic events including deep vein thrombosis and pulmonary embolism during treatment. In the prevention trial of 13,388 women, pulmonary embolism occurred in 18 on tamoxifen against 6 on placebo, three of them fatal, and deep vein thrombosis in 30 against 19; the boxed warning applies to women taking it to reduce breast cancer risk rather than to men.[27] The AUA lists thromboembolic events, liver enzyme changes and eye problems including cataracts among the adverse effects to expect in men.[21]

Chorionic gonadotropin

The label is contraindicated in precocious puberty, prostate cancer or another androgen dependent tumour, and a previous allergic reaction to hCG, and it advises caution in heart or kidney disease, epilepsy, migraine and asthma because androgens can cause fluid retention. Anaphylaxis has been reported with urinary derived hCG products. The label also states, in

capitals, that hCG has not been shown to help in the treatment of obesity and has no known effect on fat mobilization, appetite or body fat distribution.[24]

SIDE EFFECTS RECORDED FOR USE IN MEN From the AUA's table of these agents and from the FDA labels.

MEDICINE	WHAT IS LISTED
Anastrozole	Hot flashes, raised blood pressure, nausea, back pain, bone pain, breathlessness, swelling of the ankles[21]
Clomiphene citrate	Visual symptoms, flushing, headache, abdominal discomfort[21]; mood change in long term use [3]
Tamoxifen citrate	Liver abnormalities and enzyme changes, eye problems including cataracts, blood clots in the legs and stroke[21]
Chorionic gonadotropin	Headache, irritability, depression, fatigue, swelling, breast enlargement, injection site pain[21 24]

TELL YOUR PHYSICIAN BEFORE STARTING IF ANY OF THESE APPLY

- You have thin bones, a previous fracture from a minor injury, or a family history of osteoporosis, which matters most if an aromatase inhibitor is being considered.[21 22]
- You have had a blood clot in a leg or a lung, or an inherited tendency to clot, or you take a blood thinner.[27]
- You have liver disease or have been told your liver tests are abnormal, which the clomiphene label treats as a reason not to use it.[25]
- You have had prostate cancer or another tumour that depends on male hormones, or you have heart or kidney disease, epilepsy, migraine or asthma, where the hCG label advises caution or does not permit its use.[24]
- You have breast symptoms or a lump you have not yet shown anyone.[11]
- You are trying to conceive now, or hope to in the next year or two, so that the plan is built around it.[11 12]
- You take any other prescription medicine, over the counter product or supplement. Please bring the full list.

The long view is missing for all of these uses in men. The longest controlled trials of an aromatase inhibitor ran one year,[13 14] the enclomiphene trials sixteen weeks,[5] the hCG trial three months,[20] and the clomiphene work beyond three years is a records review rather than a trial.[3] Nothing of the size of the large testosterone trials has been done, so there is no answer yet on fractures, heart events or cancer risk with years of continuous use.

§ 08

Is this right for you

These medicines suit a particular question. The clearest use the guidelines support is fertility: the AUA recommends against prescribing testosterone to a man currently trying to conceive, the Endocrine Society recommends against starting it in a man planning fertility in the near term, and both allow these alternatives in men who want to keep that option.[11 12] The second is breast tissue, where the AUA asks for estradiol to be measured in a man with breast symptoms or gynecomastia before testosterone is started, and for a man whose estradiol is above 40 pg/mL to be referred to an endocrinologist.[11 21] Taking an aromatase inhibitor to push a number down, with no symptom attached, is the use the evidence does not support.

Before we begin

- [ ] A review of your medical history, your symptoms, every medicine and supplement you take, and your plans for having children
- [ ] Blood pressure, weight and an examination that includes the breast tissue and the testes, so we have a clear starting point
- [ ] Baseline bloodwork of the kind the guidelines describe: morning testosterone, luteinizing hormone, and estradiol where there are breast symptoms or an aromatase inhibitor is under discussion [11] [21]
- [ ] A written note of what you want to change, so we can judge progress together

Looking for the cause comes first, because some of these situations resolve without a new prescription. The AUA advises measuring luteinizing hormone in a man with low testosterone, and prolactin when that level is low or low normal, and a reproductive evaluation before treatment in men interested in fertility.[11] Carrying a lot of weight raises the amount of aromatase at work, and in the trial of severely obese men diet and exercise alone improved the hormone picture, with anastrozole adding a further change in the numbers but not in how the men felt. [6]

Reviewing your progress

The AUA asks for blood work no sooner than four weeks after starting anastrozole, clomiphene or hCG, and for estradiol to be measured in every man taking an aromatase inhibitor during the stable phase. If testosterone stays low on a modulator, luteinizing hormone measured at four weeks helps explain why: a low or normal level suggests the dose could go up, while a high level points to the testis rather than the pituitary, in which case a higher dose is unlikely to help. Some men who respond at first stop responding to clomiphene later, so testosterone keeps being measured.[21] Your physician will set your own schedule, and you are welcome to stop at any time.

> QUESTIONS TO ASK YOUR PHYSICIAN
>
> What are we treating, a symptom or a number? Is my estradiol actually causing the problem I came in with? If fertility is the reason, how will we measure whether it is working? What will this do to my bones over a year or two? What is the plan if it does not help? We are glad to answer all of these.

§ 09

Regulatory status

Anastrozole and exemestane are FDA approved aromatase inhibitors for breast cancer in postmenopausal women: anastrozole for adjuvant treatment of hormone receptor positive early breast cancer, first line treatment of locally advanced or metastatic disease and advanced disease after tamoxifen, and exemestane for adjuvant treatment after two to three years of tamoxifen and for advanced disease that has progressed on tamoxifen.[22] [23] Neither label contains an approved use or a dose in men, so prescribing either to a man is off label. **Clomiphene citrate** is approved "for the treatment of ovulatory dysfunction in women desiring pregnancy" and its label has no use in men, so that too is off label.[25] [21] **Tamoxifen citrate** is approved for metastatic breast cancer in women and men, for adjuvant treatment of breast cancer, and for lowering breast cancer risk in women with ductal carcinoma in situ or at high risk; treating gynecomastia is not among its approved uses.[27]

Enclomiphene citrate has never been approved in the United States, and a search of Drugs@FDA returns no enclomiphene product under that name or the brand name used in its trials.[26] It appears in Category 1 of the FDA's list of bulk drug substances nominated for compounding under section 503A, the category for substances the agency is still evaluating, which is where the compounded enclomiphene now sold gets its footing. That is not an approval, and the FDA does not review the safety, effectiveness or quality of a compounded medicine before it is sold. [28] [29]

Chorionic gonadotropin is approved for selected cases of hypogonadotropic hypogonadism in males, for prepubertal cryptorchidism not due to anatomical obstruction, and for inducing ovulation in certain infertile women.[24] Using it to protect fertility during testosterone therapy is off label, though the AUA records that use.[21] Since 23 March 2020 it has been licensed as a biological product rather than approved as a drug, and the FDA has stated that products that made that transition "will not be eligible for the exemptions for compounded drugs under sections 503A and 503B," naming human chorionic gonadotropin among the affected substances.[30][26] A compounded hCG therefore has no federal pathway, and a prescription is filled with the licensed product. A physician may prescribe a medicine off label when it suits the patient, and your physician will discuss that with you where it applies.

Gonadorelin has no marketed human product in the United States. The two that existed, Factrel and Lutrepulse, are listed in Drugs@FDA as discontinued, and the only gonadorelin labels now published are veterinary products for cattle.[26] Gonadorelin does not appear on the FDA's list of bulk drug substances nominated for compounding under section 503A, and it is not among the six peptides covered by the federal enforcement discretion policy published on 30 October 2026.[28]

For athletes, all of these medicines are prohibited. The World Anti Doping Agency 2026 Prohibited List puts aromatase inhibitors, including anastrozole and exemestane, in section S4.1, and anti estrogens and selective estrogen receptor modulators, including clomifene and tamoxifen, in section S4.2; everything in section S4 is prohibited at all times, in and out of competition, and the class covers other substances of similar structure or effect, which takes in enclomiphene as an isomer of clomifene. Chorionic gonadotropin, luteinizing hormone and gonadotropin releasing hormone, named on the list as gonadorelin, appear in section S2.2.1 as testosterone stimulating peptides prohibited at all times in males.[31] A tested athlete needs an approved therapeutic use exemption.

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

§ 10

Common questions

Are these medicines FDA approved?

Chorionic gonadotropin is approved for selected cases of hypogonadotropic hypogonadism in males, and the AUA notes it is the only one of these agents with an approved use in men.[24][21] Anastrozole, exemestane, clomiphene and tamoxifen are approved medicines, but for conditions in women, so prescribing them to a man is off label, and no enclomiphene or human gonadorelin product is approved at all.[22][25][27][26]

Do I need something to block my estrogen while I am on testosterone?

Estradiol commonly rises on testosterone therapy, and the AUA asks for it to be measured when a man has breast symptoms or gynecomastia rather than as a routine. Symptomatic breast changes are an uncommon side effect in men on testosterone and were rarely reported in randomized placebo controlled trials.[21] No trial has tested treating a raised estradiol against leaving it alone, and the one place the guidelines positively support these medicines is in men who want to keep their fertility.[11]

Will clomiphene or enclomiphene protect my fertility?

These medicines raise your own pituitary hormones instead of replacing testosterone, and in the enclomiphene phase III studies sperm concentration stayed in the normal range over sixteen weeks while it fell markedly in the men using a testosterone gel.[5] Clomiphene raises testosterone by about as much as a gel does.[16] The trials did not report pregnancies, so semen testing is how we follow it in your case.

Is enclomiphene a newly approved drug?

No enclomiphene product has been approved in the United States, and Drugs@FDA holds no record of one.[26] Its clinical programme reached two phase III studies and reported hormone and sperm results at sixteen weeks, and no approval followed.[5] Enclomiphene citrate sits in Category 1 of the FDA's bulk substances list, under evaluation, so what is dispensed is a compounded preparation, which the FDA does not review before it is sold.[28] [29]

Can hCG keep my testicles working while I take testosterone?

Testosterone therapy cuts the testosterone inside the testis by about 94 percent within three weeks, and adding hCG restores it in proportion to the dose.[9] In the one study of men taking both, none became azoospermic, semen measurements held for more than a year and nine of 26 men contributed to a pregnancy.[17] Testicular size was not measured in that study, and in the only randomized trial of hCG given on its own to older men testis volume fell by about 5 mL, so we would not promise you anything about size.[20]

What about gonadorelin?

No human gonadorelin product is marketed in the United States, and we found no published study of gonadorelin used alongside testosterone therapy.[26] The hypothalamus releases this hormone in short bursts that the pituitary answers, which is why the human studies use a pump that imitates the rhythm.[10] Your physician can talk through the options that are approved or supported by evidence.

I compete in sport. Can I use any of these?

All of them are prohibited at all times under the World Anti Doping Agency 2026 list: aromatase inhibitors in section S4.1, anti estrogens and estrogen receptor modulators in section S4.2, and chorionic gonadotropin, luteinizing hormone and gonadorelin in section S2.2.1 for male athletes. Enclomiphene is covered by section S4.2 as an isomer of clomifene.[31] A tested athlete needs an approved therapeutic use exemption before taking any of them.

Where does my prescription come from, and how do I know it is made properly?

A compounded medicine is prepared by a licensed pharmacy, and federal law sets out two kinds. A pharmacy compounding under section 503A prepares a medicine for one named patient on a prescription, and its state board of pharmacy has day to day responsibility for overseeing it, with the FDA able to inspect as well.[32] An outsourcing facility compounding under section 503B registers with the FDA, follows federal manufacturing quality standards, reports side effects to the FDA, and is inspected by the FDA on a schedule set by risk.[33] We work with pharmacies of both kinds, and which one fills your prescription depends on the product.

Is a compounded medicine the same as something sold online?

No. Compounded medicines are not FDA approved, and the FDA does not review their safety, effectiveness or quality before they are sold, which is why your physician weighs them case by case.[29] What a licensed pharmacy gives you is a preparation made for you on a prescription, by a business a regulator licenses and inspects, with records of the ingredients and testing behind it. Material sold online as a research chemical has none of that. It is labelled as not for human use, its identity, strength, purity and sterility have not been established for a person, and no pharmacist or physician is answerable for what is in the vial.

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