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Estradiol Today

The latest news from the **Estradiol Initiative**

Estradiol Initiative
A New Standard of Care

Welcome to the second issue of ***Estradiol Today***. Your comments and suggestions are appreciated, including topics you would like to see in future editions. Please email Bob Watson at **janebob99@lobo.net**.

The mission of the **Estradiol Initiative** non-profit organization is to educate patients and clinicians about the benefits and risks of using transdermal estradiol (tE2) for men receiving Androgen Deprivation Therapy (ADT) for prostate cancer. Our main goal is to secure FDA and NCCN approval for tE2 ADT (eADT) as a Standard of Care (SoC) for these patients.

As members of the **Estradiol Initiative's** research team, we receive many questions about how to get doctors to prescribe transdermal estradiol (tE2). Increasingly, these questions come from people who have heard about tE2 as an alternative to the standard agents for ADT.

Often these patients have been burdened by the side effects of standard ADT drugs and are looking for something less likely to degrade their quality of life. They may have already approached one or two doctors, but have been told that the doctors don't prescribe off-label medicines. Or, they may have been told that their employer doesn't permit it.

Fortunately, we know that some doctors are willing to prescribe off label. Here are some of our thoughts on how get an off-label prescription for tE2.

Richard Wassersug, PhD
Paul Schellhammer, MD
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→ **Please visit our website at estradiolinitiative.org**

Overcoming the Challenges of Getting a Prescription for tE2 when it is Off-Label

by Richard Wassersug

Transdermal estradiol has not yet been officially approved as a "Standard of Care" by the National Comprehensive Cancer Network for treating prostate cancer. Getting that approval would allow doctors to prescribe it "on-label". However, when a drug is "off-label", that is a legitimate reason for a doctor to decline to prescribe it to you.

The doctor might also point out that off-label medications are generally not covered by insurance. They may also point out that all effective cancer treatments, including tE2, have some side effects. If you do find that your doctor is willing to prescribe tE2 off-label, you can expect that they will discuss with you their opinion of the risks and benefits of tE2. That is their responsibility, as part of the informed consent process.

• ***Financial Concerns***

On a positive note, we have learned that insurance companies are increasingly willing to pay for tE2, particularly when they find out how much cheaper it is than the standard ADT drugs. We recommend checking with your insurer ***before*** approaching a doctor for a tE2 prescription. It doesn't help your case to expect a doctor to do all the communications with an insurer who has previously refused to cover tE2. If you expect that you'll need a letter from your physician, we've provided a draft letter below, that you can offer your doctor.

Coincidently, out-of-pocket costs for tE2 currently are about $150-300 /month for patches and about $30-100/month for gel/cream products.

• ***Side Effects of tE2***

The major side effects of tE2 are *gynecomastia* (breast growth) and *mastalgia* (breast/nipple sensitivity). Although nipple sensitivity is sometimes transient, it seems to be the most bothersome side effect of tE2.

Our research indicates that the amount of breast growth you are likely to experience from tE2 should be relatively small (i.e., less than a bra cup size of "**A cup**"). This is documented in the Estradiol Initiative's recent publication about gynecomastia: [Click Here to Access our Gynecomastia Paper]. Treatments exist for managing the expected symptoms of breast/nipple pain from tE2, as discussed in that paper.

• ***Core Benefits of tE2***

The core benefits of tE2 are extensively covered in the recent Langley et al. paper in the *New England Journal of Medicine (2026).* [Click Here for the NEJM Paper] You should bring a copy of that paper to your appointment.

The core benefits (relative to standard ADT drugs), include: reduced or eliminated hot flashes, reduced or eliminated osteoporosis, reduced risk of fractures (by 50% less), less fatigue, less loss of libido, lower blood pressure, lower blood glucose, and improved lipid profiles.

Recognize that doctors, generally, don't have time to read full research papers. So, use a highlighter pen to mark a half dozen or so of the major findings in the paper and offer to "*leave that copy of the paper, if they would like*."

• ***Presenting your Case to the Doctor***

This gets back to the question of how to persuade a doctor to prescribe tE2 off label.

It's important to realize that you won't win your argument for tE2 solely by pointing out how miserable you felt from previous ADT drugs (regardless of whether they are LHRH agonists, like Lupron, Eligard or Zoladex, or LHRH antagonists, like Firmagon and Orgovyx). The doctor's responsibility includes trying to do "no new harm"—so they need a better argument than how miserable you felt, or that you feel that a new treatment will be better.

It is <u>not</u> helpful to start a consult with a long presentation about how bad your life was on your previous ADT drugs. You do not want to project an image of yourself as an unconsolably miserable person. That won't help your case.

Of course, you need to say that your previous drug "X "was bothersome! But keep it brief. Focus on presenting the positive case *for* tE2, not the negative case against other drugs.

The starting point for a positive case is the 5-year Overall Survival data for tE2 compared to the LHRH agonists (as was reported in the Langley et al. 2026 *NEJM* paper). You can point out that Overall Survival with tE2 is as good as for Lupron (called Lucrin in the UK). Additionally, you can point out that tE2 is equally as safe as standard ADT drugs (i.e., there are no increased risks of cardiovascular events comparing tE2 to Lupron).

If asked "***Why do you want to try tE2?"***, focus on the better quality of life. The quality-of-life improvements with tE2 include: a lower risk of hot flashes, lower risk of osteoporosis and bone fractures, and better cardiac and metabolic profiles (i.e., less risk of hypertension and lower blood glucose, respectively).

Then, in a clear and dispassionate way, ask the doctor, "***May I try it*?**"

By asking that question, you are showing respect for the doctor. That is part of "Shared Decision-Making" (SDM). SDM can be rewarding for both you and the doctor. SDM is far more likely to get you the doctor's tE2 prescription than simply asserting that it is your choice. That kind of assertion is called "Self-Directed Medicine" (the other SDM). You may feel that you have the right to self-directed medicine, but that kind of display of dominance is *not likely* to get you an off-label script for tE2. You will more likely succeed by being soft-spoken, kind, respectful, and concise with your request.

In our experience, every patient who has followed this strategy has eventually managed to get a prescription for tE2.

Additional Strategies for Getting Estradiol

by Bob Watson

You may find that your Primary Care Physician (PCP) is more willing to prescribe tE2 than your Urologist or Medical Oncologist. Because tE2 is not yet an approved "Standard of Care", your PCP may be more likely to prescribe tE2 either as a: (1) low-dose adjunct tE2 for treating symptoms of standard ADT drugs, or (2) as high-dose tE2 for replacing standard ADT drugs with estradiol ADT.

Alternatively, there are many doctors who are comfortable prescribing hormones to both men and women. The problem is finding them. Fortunately, you can ask your local compounding pharmacist for a list of their doctors who routinely prescribe hormonal treatment. Those doctors will be much more likely to read the NEJM paper, and, hopefully, feel comfortable prescribing tE2 for either symptom management using low-dose tE2, or as a primary treatment for ADT using high-dose tE2.

Getting Estradiol Patches

by Paul Schellhammer

For patients who cannot get aid with insurance coverage, they should be aware that Mark Cuban's Cost Plus pharmacy delivery program provides the 0.1 mg estradiol patch at a cost of just under $5 per patch and will ship to you when provided with a physician's prescription. The patient must sign up on the Cost Plus website prior to requesting the physician's office to forward the script to Cost Plus.

In the USA, for Vietnam veterans receiving an agent orange disability, discussion with your VA provider (together with the NEJM paper) may provide them documentation to approve a prescription. When transdermal estradiol is included in the NCCN guidelines, this process will be facilitated.

Sample Insurance Letter

by Paul Schellhammer

Here is a sample letter of support that can be written by your doctor, if reimbursement for tE2 requires a letter to an insurance company.

> I am writing this letter in support of my prescription for transdermal estradiol patches for patient _____.
>
> Peer-reviewed medical literature supports its use as an alternative to LHRHa drugs for androgen deprivation therapy (ADT). The transdermal delivery through the skin avoids a first pass exposure of estrogen to the liver, and the related cardiovascular and blood clotting side effects associated with oral estrogens.

The appropriateness of transdermal estradiol for ADT is supported by the best medical science; i.e., level 1 evidence via a large multicenter, well controlled randomized clinical trial reported in the premier peer-reviewed medical journal, the *New England Journal of Medicine*. (See below)

Of note is the improvement in lipid profile, insulin sensitivity, bone health and reduced hot flashes and blood pressure when transdermal estradiol is compared to standard ADT drugs. Furthermore, the cost of estradiol patches is multiple times less than LHRHa injections or oral ADT drugs.

Please advise if you disagree with my prescription and presentation.

(Doctor's signature)

Reference:

Langley RE, Gilbert DC, Mangar S, et al. Transdermal Estradiol Patches in Locally Advanced Prostate Cancer. N Engl J Med. 2026;394(16):1595-1607. doi:10.1056/NEJMoa2511781

- **Please let us know if these strategies work for you. Also, if you have some other strategies that you have found to be effective. We would be happy to post them in a future issue of *Estradiol Today.***

- **Thank you for reading *Estradiol Today*. For more information, check out the Patient and Clinician FAQ's at: https://estradiolinitiative.org/.**

→ **Please consider making a tax-deductible donation to the Estradiol Initiative!**