WAYS TO REDUCE THE IMPACT OF CANCER TREATMENT ON THE VULVA & VAGINA

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This handout is offered as a communication aid for patients and their providers. It is not a substitute for professional medical examination, diagnosis, or treatment.

Contents

To further your knowledge and comfort, After Cancer recommends also reading the following patient handouts:

Managing Sexual Dysfunction with Pelvic Floor Physical Therapy
Let's Slide Into Lubricant
Sensate Focus: Touching Exercise to Rediscover Intimacy
Practical Solutions for Low Libido

INTRODUCTION

Pain with sex is a powerful inhibitor of sexual response; it affects the quality of life and is a common and expected problem for females impacted by cancer. The medical approach to sexual problems after cancer is to prevent or address pain first.

Even after overcoming pain, low interest in sex, also known as low libido, may still be a problem. Studies indicate that emotional and psychological factors are just as important as the prevention and treatment of pain and addressing fatigue and low interest, and the quality of the couple's relationship.

Ongoing support from a therapist, social worker, sex therapist, sexologist, or oncosexologist, starting at diagnosis and continuing into survivorship, can reduce anxiety and help couples stay connected. An oncology or primary care provider can point toward qualified professionals. Health insurers may help find an in-network behavioral health provider for anxiety.

Sensate Focus, a series of progressive intimate touch exercises for intimate partners, has successfully reduced anxiety and vaginal pain related to intimacy.

Yoga, massage therapy, and mindfulness exercises have all been shown to reduce stress and improve well-being related to cancer treatment.

VAGINAL MOISTURIZERS

Why Use a Vaginal Moisturizer

Keeping delicate vaginal tissue well-moisturized may go a long way toward maintaining vaginal health and decreasing pain with sexual activity.

Menopause is a frequent cause of vaginal dryness.

Some cancer treatments lead to menopause:

- Hormonal cancer treatment
- Surgical removal of the ovaries
- Radiation - If radiation therapy includes the lower abdomen and or pelvis, the ovaries will likely be irradiated, bringing on menopause.

Radiation can lead to inflammation, thinning, and scarring of vaginal tissue, with or without menopause.

The natural aging process also brings menopause.

While estrogen is the most effective way to reverse the changes of menopause, it is not appropriate for or recommended for all patients.

Non-hormonal options thicken the vagina, making it more elastic and reducing pain with penetration. Vaginal moisturizers are a primary non-hormonal option to resolve vaginal dryness and thinning tissue.

Recommended Vaginal Moisturizers

Packaging on the moisturizers often recommends insertion every 2-3 days. There is some evidence to suggest that daily use may be more effective in females impacted by cancer. Consider trying the product for 6 weeks to decide if it is helpful. Vaginal moisturizers are intended for regular use, regardless of the frequency of vaginal penetration. These products are safe and should be used on an ongoing basis.

Here are three vaginal moisturizers our practice recommends to patients:

- **Hyalo Gyn** – can be found on Amazon.com
- **Replens™ Long-lasting Moisturizer** can be found at many pharmacy retailers such as CVS, Walgreens, Target, and Walmart. Often, there is a manufacturer coupon available online at http://www.replens.com/Products/Replens-Long-Lasting-Moisturizer/

- **Revaree®** Vaginal Inserts at https://try.hellobonifide.com. The active ingredient is hyaluronic acid, which is close to the natural acidic pH of the vagina

- **Natural oils, such as Vitamin E or coconut oil, may be used as vaginal moisturizers**

If you try other vaginal moisturizers, ensure they are free of parabens, chlorhexidine gluconate, glycerin, propylene glycol, or scents.

How to apply vaginal moisturizers

- Ensure hands are clean
- Some vaginal moisturizers come with disposable applicators
    - Some applicators are pre-filled
    - Other applicators will need to be filled
- Vaginal moisturizers may be inserted with a clean finger

Vaginal moisturizers work best when applied when going to bed; if used when up and moving, the moisturizer will leak out of the vagina.

- If vaginal estrogen is prescribed, don't apply vaginal moisturizer the same night as the vaginal estrogen.

Vaginal moisturizers may also be applied to the labia. Apply a grape-sized amount at the vaginal opening and over the labia with clean fingers.

VAGINAL LUBRICANTS

Please see the *After Cancer Patient Handout on lubricants* for more in-depth information on choosing and using lubricants.

Vaginal lubricants are a valuable tool. They can help prevent small tears in vaginal tissue with penetration. They also help to make penetration more enjoyable and less anxiety-provoking.

Types of Vaginal Lubricants

In our practice, we have found that plant-based oils, like coconut or olive oil, used with every episode of vaginal penetration are the most kind to your vaginal tissue. The Centers for Disease Control (CDC) states that plant-based oils may break down condoms, potentially exposing you to Sexually Transmitted Diseases (STDs), Sexually Transmitted Infections (STIs), or unintended pregnancy. Oil can cause staining of your sheets and clothing.

Water-based lubricants may dry out quickly. If this happens, reapply. Water-based lubricants often contain ingredients that can irritate vaginal tissue.

Silicone-based lubricants last longer than water-based.

Vaginal Lubricant Ingredients to Avoid

If an over-the-counter water-based or silicone-based lubricant is preferred, ensure it is free of any of these irritants: baby oil, capsaicin, chlorhexidine gluconate; flavors, fragrance; glycerin, lidocaine, menthol, mineral oil, parabens; petroleum (Vaseline); polyquaternium 7, 10, or 5; and or propylene glycol.

Avoid animal-based substances, such as butter, egg whites, fish oil, or yogurt, as these can lead to a vaginal infection.

Also, avoid using mineral oil, baby oil, and petroleum (Vaseline), as they may lead to vaginal irritation and infection.

VAGINAL DILATORS

Why Use Vaginal Dilators

Dilators are simple, smooth devices used to stretch the vagina gently. They come in various sizes and are used to prevent and treat problems with vaginal penetration related to less elasticity in the vaginal from radiation therapy, surgery, or menopause. Dilators can be helpful with painful vaginal penetration. Plastic dilators are smoother and less irritating than silicone.

Instructions for Vaginal Dilator Use

OncoLink by *Penn Medicine* has clear vaginal dilator instructions, particularly for vaginal health after radiation therapy.

Vaginal Dilators for Women Treated with Radiation Therapy

Talk with your radiation oncologist and or gynecologist about your vaginal health after radiation therapy. *Penn Medicine's Oncolink* explains that women having radiation to the pelvic area for cancer, such as bladder, anal, colorectal cancer, and gynecologic cancer, are at risk for developing vaginal elasticity issues, leading to issues, such as sexual dysfunction, pain with vaginal penetration, and vaginal discomfort.

Frequency of Vaginal Dilator Exercises

Dr. Alessandra Graziottin and her colleagues have published recommendations for dilator use in Chapter 27, *Sexual Rehabilitation After Gynecologic Cancers,* p. 205-222 of *Cancer, Intimacy, and Sexuality: A Practical Approach*, by Reisman & Gianotten, eds., Springer International Publishing AG, Switzerland, 2017. The authors recommend:

- Pelvic floor physical therapy after radiation treatment (see After Cancer's handout on Pelvic Floor Therapy)
- Dilator use starting four weeks after treatment, 2-3 times per week for 1-3 minutes, and continued for 9-12 months
- In their practice, however, they suggest "earlier start and twice daily [dilator] use for 5 minutes."
- Starting vaginal estrogen therapy as soon as possible, before treatment-related menopause affects vaginal tissues.
- Continuing vaginal estrogen, "such as estriol in gel," lifelong.

See your surgical or radiation oncologist or your gynecologist to discuss when it is safe to start using vaginal dilators.

After 12 months of practicing vaginal dilation, per Oncolink from Penn Medicine, talk with your radiation oncologist and or gynecologist about continuing vaginal dilation, possibly for the rest of your life.

- Continuing vaginal dilation will help maintain vaginal elasticity of the vagina, essential for pelvic exams and later-in-life sexual function.

Recommended Vaginal Dilator Sets

Radiation oncology providers may have vaginal dilators for patient use. If vaginal dilators are not offered, do not hesitate to ask about them.

Dr. Veronika E. B. Kolder, MD, former Medical Director, Menopause and Sexual Health Clinic, recommends the following over-the-counter vaginal dilators:

- **Dr. Laura Berman® Dilator Set** by CalExotics, 4 hollow plastic dilators with vibration, $20, can be purchased on www.amazon.com. AA batteries are sold separately.
- **Femmax® Vaginal Dilators** by Myaid, 4 hollow plastic dilators, $35, can be purchased on www.amazon.com
- **MiddlesexMD®**: a set of 7 plastic dilators, which can be sterilized, $109, at www.middlesexmd.com

OTHER NON-PRESCRIPTION OPTIONS FOR PELVIC PAIN

Pelvic Floor Physical Therapy

Treatment is most effective and less painful when vaginal tissues are well moisturized and, if OK'd by your oncologist, well-estrogenized before pelvic floor physical therapy starts. Pelvic Floor Physical Therapy can help with:

- Support for learning how to use dilators

- Treatment of tight or painful pelvic floor muscles (hypertonus)
- Treatment of involuntary contraction of the vaginal muscles with penetration (vaginismus) due to trauma and/or pain

See After Cancer's handout on Pelvic Floor Therapy for detailed information on this helpful and often life-changing treatment.

Yoga for Pelvic Pain

Consider yoga if tense pelvic muscles are contributing to pelvic pain. Here is a link to the Mayo Clinic 2019 guide for yoga to help relieve pelvic pain.

Websites

- Ergoerotics®: Comfortable sexual solutions related to pain, disability, and aging, www.ergoerotics.com
- A Women's Touch Sexuality Resource Center, https://sexualityresources.com/
- www.AdamEve.com and www.TooTimid.com for vibrators and sex toys

Additional Options for Pain Due to Radiation Therapy

- Barrier creams and ointments
- Examples include A&D Ointment®, Zinc Oxide Ointment, and Desitin®, all available over the counter. **They are not meant for internal vaginal use** but can be used on the vulvar and the skin around the anus.
- Cool Water Cones-Post Surgical Dilators https://www.cmtmedical.com/product/cool-water-cones-post-surgical-dilators/, $15, available in 3 sizes.

Collision barriers for foreshortened vagina or pain with deep penetration

- Comfort Ring, $20, at www.ergoerotics.com
- Ohnut™ Rings, $65, 4stackable rings to limit depth of penetration, at www.betweenthesatinsheets.com

NON-HORMONAL PRESCRIPTION OPTIONS

Topical Aqueous Lidocaine

4%, screw-top, 50 ml, moisten 3 small or one large cotton ball. Place at the thin fold of skin at the back of the vulva (the fourchette), being sure to include the narrowest part of the vaginal opening (the hymenal ring). Leave in place for 3 minutes. Pat away excess lidocaine before penetration to limit partner numbness.

A word of caution about lidocaine: it will numb sensation and may mask injury occurring during intimacy.

Silver Sulfadiazine Cream

1% USP, a brand name Silvadene® Cream, is a burn cream recommended by some oncologists for radiation burns of the vulva and is sometimes recommended for vaginal use after completion of radiation therapy. It may reduce the absorption of other creams and moisturizers.

EROS Clitoral Therapy Device

$325, FDA-approved small handheld adjustable female suction devise for female sexual dysfunction at www.healiohealth.com. Similar devices are available for $35-49 at some online sex shops and at www.amazon.com, which carries a 'Sucking Vibrator for Women' for $49. The EROS device is included here for completeness' sake, as it is the only FDA-approved device for female sexual dysfunction and may increase natural lubrication and arousal.

HORMONE TREATMENTS

I. Introduction

The treatment of female sexual problems after cancer depends on the severity of symptoms and exam findings, like the degree of atrophy, size of the vaginal opening, and presence of other medical conditions. The lack of affordable FDA-approved treatment options leads some medical providers to recommend over-the-counter (OTC), Internet, or compounded options.

There are many reasons why vaginal and vulvar treatments, particularly hormonal treatments, may be challenging for females impacted by cancer. Putting any medication on or in the genital area can be difficult for females who have experienced sexual trauma. A family history of hormone-sensitive cancer can also cause mixed feelings about using hormonal products. Even if you have had a type of cancer that is not hormone-sensitive and have been told you could use hormonal products, hormone therapy can still trigger anxiety historically based reasons, making it hard to use hormone therapy consistently.

For some females, the loss of hormone function due to cancer treatment feels like a necessary sacrifice in the bargain for recovery from cancer. The use of hormone 'replacement' may have a complicated meaning, possibly even meaning that we have not honored a bargain we made with our Higher Power. For all these reasons, an honest and open discussion with your medical provider is important.

II. Vulvar and Vaginal Hormonal Products

Two types of commonly used vulvar and vaginal hormonal products are estrogens and dehydroepiandrosterone (DHEA). Both are used to reduce the symptoms of genitourinary syndrome of menopause, which include vulvovaginal dryness and irritation.

A hormone is a substance produced by a gland. It is transported through the blood to specific cells or tissues in other parts of the body, where it binds to specific receptors. During the childbearing years, the ovaries produce estradiol, the bio-identical form of estrogen. It travels to receptors in other tissues, like the genital area, bone, and brain, where it acts at estrogen receptors. While the adrenal glands produce DHEA and circulate in the blood, it is technically not a hormone because there are no DHEA receptors in the body. Instead, DHEA works within cells by activating estrogen and testosterone receptors.

Once begun, the time it takes for estrogen or DHEA to relieve vaginal dryness and pain with sexual penetration depends on the severity of the vaginal thinning and narrowing due to menopause or radiation therapy. In mild cases, you may feel better within 6 weeks. Or, you may need grit and perseverance for as long as 1.5 years, using a dilator and hormonal product, to reach your goal. In the most severe cases of scarring due to radiation therapy, pain with penetration and vaginal narrowing may be permanent, and only partial relief of symptoms may be possible.

Once you have inserted a vaginal estrogen product, wait 6-12 hours before penetration. This will keep more of the product in you and minimize the exposure of your partner. If you tend to have sex in the evening, insert the product in the morning. If you tend to have sex in the morning, insert the product at bedtime.

Once you need a vulvar or vaginal estrogen or DHEA product for genitourinary syndrome of menopause, you will likely need it indefinitely. This is particularly true if you continue to be sexually active with penetration. On the other hand, if estrogen cream is prescribed for a specific symptom, for example, spotting due to a urethral caruncle, your provider will instruct you on when you can stop.

In the following notes, 'Rx' means a prescription is needed for these products. Instructions are based on the package insert, where available.

ESTROGENS

Estradiol:

- **Estrace® Vaginal Cream** (Rx) 0.01% cream.

Sig: Initially, 2 -4 grams vaginally once daily for 1-2 weeks; then gradually reduce over 1-2 weeks. Usual maintenance 1 gram vaginally, 1-3 times per week. Treatment is cyclic, 3 weeks on, then 1 week off.

- **Vagifem® Tablets** (Rx); generic **Yuvafem® Tablets** (Rx) 10 mcg tablet.
  Sig: Insert 1 tablet vaginally once daily for 2 weeks into the upper third of the vaginal vault using the supplied applicator. After 2 weeks, insert 1 tablet vaginally twice weekly, e.g., every Tuesday and Friday. While doses as high as 25 mcg/dose were previously available, they were removed from the market because of patenting considerations. In my clinical experience, 1 in 4 postmenopausal females does not get enough relief with the 10 mcg dose.
- **Imvexxy® Vaginal Inserts** (Rx) 4 mcg, 10 mcg inserts.
  Sig: Insert 1 vaginal insert daily x 2 weeks, followed by 1 insert twice weekly, for example, every Monday and Thursday.
- **Estring® Vaginal Insert** (Rx) delivers 7.5 mcg estradiol/24 hours.
  Sig: Insert one vaginal ring deep into the upper third of the vaginal vault. Keep in place continuously for 3 months, then remove. If appropriate, insert a new ring.
  If the flexible Estring® is too large to insert or wear comfortably initially, try 6 weeks of a vaginal estrogen cream first. Some females who have had a hysterectomy with removal of the cervix or radiation therapy may have a vaginal vault that is too narrow for the Estring®.

- **Premarin® Vaginal Cream** (Rx) 0.625 mg conjugated estrogen per gram. Conjugated Equine Estrogen, a mix of 11 horse estrogens. Instructions depend on the indication. Per package insert:
  Sig: Insert 0.5 – 2 grams intra-vaginally, daily x 21 days, then off x 7 days, for atrophic vaginitis.
  Sig: Insert 0.5 grams intra-vaginally, daily x 21 days, then off x 7 days, for treatment of moderate to severe pain with penetration, a symptom of vulvar and vaginal atrophy, due to menopause.
  Sig: Insert 0.5 grams intra-vaginally, twice weekly, e.g., Monday and Thursday, for treatment of moderate to severe pain with penetration, a symptom of vulvar and vaginal atrophy, due to menopause.

  I interpret this to mean that doses higher than 0.5 grams should only be used if an examination to confirm the diagnosis has been performed, not just a report of symptoms.

- **Estriol Vaginal Cream** (Rx) 0.5 mg per gram.
  Sig: 1 gram vaginally twice weekly, e.g., Monday and Thursday. Estriol is a weak bio-identical estrogen normally produced by the placenta. Like estradiol, it is usually derived from a plant source and purified by a complicated chemical process. A compounding pharmacy puts it in a cream base. One example of a compounding pharmacy is the Women's International Pharmacy at 2 Marsh Court, Madison, WI, 53718. Phone: 1-608-221-7800 or 1-800-699-8144. Fax: 1-800-635-1229. Another example is Towncrest Pharmacy in Iowa City, IA 1-319-337-3526.

- **DHEA** (Prasterone)
  Although technically a prohormone, not a hormone, DHEA is produced by the adrenal glands and found in large amounts in the blood. When inserted in the vagina or applied to the vaginal entrance, small amounts of DHEA do not raise blood levels of estrone, estradiol, or testosterone.

Some females who don't get enough pain relief from vaginal estrogen products alone will get relief when a medication that also works at testosterone receptors is added or substituted.

- **Intrarosa® Vaginal Inserts** (Rx), 6.5 mg insert.
  Sig: Insert one insert vaginally daily at bedtime. Twenty-eight inserts cost $207 at most retail pharmacies. Coupons are available. For those with insurance, the tier of coverage can sometimes be improved by submitting a Prior Authorization request based on personal or family history of genetic risk of breast cancer or the fact that Intrarosa® does not have a black box warning, whereas vaginal estrogen products do.

- **Julva® Cream**, available online without a prescription, 1-ounce tube costs $70 at www.amazon.com. Here are my suggestions related to Julva® Cream if you and your medical providers feel this is a good option for you:
  - I suggest you first get the 7-day trial pack available for $4.95 shipping at www.drannacabeca.com. Julva® Cream has a unique smell, probably due to the imu oil (bird fat, non-vegan). If you find the smell acceptable, apply the cream to the vulva as directed using 1/8th of a teaspoon once a day.

    If you do not experience irritation, order the 1-ounce tube at www.amazon.com. This tube will last about 1.5 months. Some Walmart stores also carry Julva® Cream.

  - Apply 1/8th of a teaspoon (spoon comes with tube) starting above the clitoris and including the hymenal ring (the narrowest part of the vaginal opening) and inner labia minora daily.

  - If not effective after 6-8 weeks, increase to twice-daily application. If that is not effective within another 6-8 weeks, Julva® Cream will not work for you.

  - Please note Julva® Cream will not give you elasticity or comfort inside the vagina. It does not come with a vaginal applicator, and the dose is for **vulvar use,** not deep vaginal use (the dose may be too high for vaginal use).

  - You may need to use Julva® Cream together with a daily vaginal moisturizer or vaginal estrogen product.

More information

1. Vaginal estrogen products are all absorbed into the blood to varying degrees. This is important for several reasons. First, if you have had an estrogen-dependent tumor, like most breast cancers, you may be taking medication to keep your blood estrogen level as low as possible. This is because estrogen may increase the risk of cancer recurrence. Second, if you have a uterus, too much estrogen without enough progesterone (the other main female hormone produced by the ovaries) can cause the lining of the uterus to thicken abnormally, increasing the chance of

abnormal bleeding, overgrowth of the uterine lining (endometrial hyperplasia), and uterine cancer. While the amount of estrogen absorbed from vulvar and vaginal products is rarely a problem, generally, the goal is to use the lowest effective dose.[1],[2]

2. Although Premarin® Vaginal Cream and Estrace® Vaginal Cream are equally effective on vaginal tissues, Premarin® Cream is not approved by the equivalent of the Australian FDA because of the mix of 11 horse estrogens in the product; it is derived from pregnant mares' urine and is not vegan. Blood levels can't measure the actual estrogenic effect of Premarin® products. I prefer to prescribe estradiol vaginal products, for which serum levels have been measured, reported, and compared. This difference is especially important for females with breast cancer who are trying to use the lowest effective dose.

3. The vaginal entrance and vagina have different embryologic tissue origins. The vaginal entrance and bladder have estrogen and testosterone receptors. The vagina has mostly estrogen receptors. This provides theoretical support for a possible advantage of DHEA over estrogen alone, specifically at the vaginal entrance and for urethral and bladder tissues. DHEA can be delivered to these tissues with either vaginal inserts (Intrarosa®) or vulvar application (Julva® Cream).

4. Early studies of low-dose vaginal estrogen (Vagifem® equivalent) use in females impacted by breast cancer who were also taking an aromatase inhibitor (AI) (e.g., Tamoxifen, Anastrozole, Letrozole, Exemestane) raised concern. This was because a few females who were on both an AI and the equivalent of Vagifem® had blood levels of estradiol that were too high. More recent studies of vaginal DHEA in females taking AIs, done with better hormone tests, do not show any worrisome elevations of blood estrogens.[3] Blood DHEA-S and testosterone levels were elevated at the 6.5 mg/day dose (the dose in Intrarosa®) but not at a 3.25 mg/day dose. Further research on vaginal DHEA is needed in females with hormone-dependent cancers.

5. Females with cardiovascular disease can use standard vaginal estrogen products for painful penetration. This is because the low amounts of hormone absorbed from the vagina with standard dosing are insufficient to cause liver protein production, increasing the risk of blood clots in the circulation (thromboembolism).

6. Some patients with a history of breast cancer or BRCA genetic risk use daily vaginal moisturizers and daily Julva® Cream at the hymenal ring and vaginal entrance to increase elasticity.

7. The high cost of medications is why some medical providers prescribe compounded vaginal Estriol (E3) cream, which costs about $40 per month through the Women's International Pharmacy in Wisconsin and $30 per month through Towncrest Pharmacy in Iowa City, IA. Estriol

[1] See tables in University of Iowa Menopause and Sexual Health Clinic Protocols 2014, at www.aftercancer.co, Resources for Providers, Best Practices, or comparison of various products.

[2] Santen RJ, et al. Systemic estradiol levels with low dose vaginal estrogens. Menopause 2020;27(3):361-70.

[3] Barton DL, et al. Systemic and local effects of vaginal DHEA: NCCTG N10C1 (Alliance). Support Care Cancer 2018;26(4):1335-43.

is a low-potency estrogen normally produced by the placenta. It has the possible advantage that it can't be metabolized into higher-potency estradiol.

8. A vaginal estradiol insert/suppository (Imvexxy®) is now commercially available. It's a welcome improvement in the delivery system over reusable but difficult-to-clean plastic vaginal applicators (Premarin® and Estrace® creams) and the single-use plastic applicator (Vagifem® tablets). The inserts are still under patent, so that cost may be a concern.

9. Studies have looked at the possible benefits of vaginal testosterone. I have some experience prescribing a compounded vulvar estrogen plus testosterone cream for vulvar pain (vulvodynia) but stopped recommending this after commercial products like vaginal and vulvar DHEA became available, as these also work at testosterone receptors.

III. Systemic Estrogen, Estrogen & Progesterone, and Ospemifene

Hormone therapy that is given to control hot flashes, improve sleep, reduce aches and pains, or prevent or treat osteoporosis is called 'systemic' hormone therapy. This is because it relies on absorption into the blood to have its effect. It can be given by mouth (oral hormone therapy) or through the skin as a patch or gel (transdermal hormone therapy). Females with a uterus who take systemic estrogen also need to take some form of progesterone. Natural progesterone or a synthetic progestin will prevent overgrowth of the uterine lining and reduce the risk of cancer of the uterus. Females without a uterus who take systemic estrogen do not need progesterone or a progestin.

There are too many systemic estrogen options to list here, but you can learn more at www.aftercancer.co, Resources for Providers, 2014 Menopause and Sexual Health Clinic Protocols. Ospemifene® is an oral medication prescribed to treat the genitourinary syndrome of menopause. Testosterone is sometimes compounded in doses appropriate for females and applied to the skin to treat low sexual interest. Generally, it should only be considered once any sexual pain problems have been treated.

More information

1. Transdermal estradiol products at or below the 0.05 mg dose are not associated with increased risk of venous thromboembolism (VTE) risk, while all doses of oral estrogens increase VTE risk.

2. Transdermal products at or below 0.05 mg dose usually are not enough to relieve genitourinary syndrome of menopause, vaginal dryness and irritation, and pain with penetration associated with low estrogen levels. In order to have the lowest effective systemic levels of estrogen and relief of vaginal symptoms, some females use systemic and vaginal estrogen products, e.g., A 0.0375 mg. estradiol patch, 100 mg oral micronized progesterone, plus Juvafem® tablets or the Estring®.

3. There is no advantage to blood testing to determine hormone therapy dose for relief of hot flashes and body aches; use the lowest effective dose.

4. When starting to treat hot flashes in naturally menopausal females, I have noticed the following approximate clinical dose-dependent response. Similar information for females who reach menopause due to cancer treatment is not available.

Dose of transdermal estradiol (mg)	**Percent of new start patients who will get relief**
.05	75%
.0375	50%
.025	25%
.014 (Menostar®)	15% (a published study claims 50%)

5. A typical start doses for systemic hormone therapy for moderate to severe hot flashes in a female with a uterus would be 0.0375 mg estradiol patch plus 100 mg of oral micronized progesterone at bedtime.

6. Oral micronized progesterone, 300 mg at bedtime, has decreased hot flashes and improved sleep. It also reduces anxiety in some females. It can be considered in females whose cancer is not hormone sensitive but will not improve genitourinary syndrome of menopause/vulvovaginal atrophy.

7. There is no advantage to compounded oral hormone therapy over prescription oral hormone therapy, as all oral hormone therapy ends up predominantly Estrone (E1) in the blood once it passes through the liver in what is called first-pass metabolism. Estrone is a low-potency estrogen that is the main estrogen in post-menopausal females. In such females, estrone levels are directly proportional to body mass index (weight). If you want to increase estradiol (E2), the most potent estrogen during reproductive years, use transdermal doses of 0.05 mg or less.

8. The free Menopro™ app, created by the North American Menopause Society at www.menopause.org, provides a risk calculator for initiating systemic hormone therapy for managing hot flashes. It does not address specific cancer types. Most breast cancers, adenocarcinoma of the cervix, and uterine cancer are hormonally sensitive, so if you have one of these cancers, systemic hormone therapy may not be appropriate for you.

9. There is good evidence for not starting systemic hormone therapy more than 10 years out from menopause. This is because of increased cardiovascular risk.

10. There is no evidence that systemic estradiol improves libido; however, if serum levels are at or above 60 mg/mL, vaginal atrophy and resultant pain will be relieved. Unfortunately, this is also the blood level where the risk of venous thromboembolism (blood clot to the leg or lung) increases.

11. There is little data regarding the risks or benefits of discontinuing long-term low or ultra-low-dose hormone therapy at or after age 65.

12. **Ospemifene** (Osphena®) 60 mg daily, get 30 pills for $248 at retail pharmacies, coupons available. Ospemifene is a synthetic estrogen receptor agonist/antagonist. Ospemifene is taken by mouth once a day to treat genitourinary syndrome of menopause/vulvovaginal atrophy. There are not many females who are good candidates for this medication. It is intended for use in postmenopausal females without a uterus who are at low risk for blood clots to the leg or lung (known as venous thromboembolism (VTE)). Females at low risk for VTE are slender, non-smokers with normal blood pressure and an active lifestyle. If such a female can't or won't use vaginal or transdermal estrogen or DHEA products for genitourinary syndrome of menopause/ vulvovaginal atrophy, she might want to consider ospemifene. However, ospemifene increases the risk of VTE, while the other options listed above don't increase VTE risk.

IV. Navigating the Pharmacy Payer System

Here is a summary of my clinical experience in trying to get insurance to cover hormonal therapies.

- For **vaginal estrogen** products, if the female had a very narrow vaginal opening that is too small for insertion of the plastic applicator that comes with Estrace® and Premarin® Vaginal Creams, a letter from the medical provider to your insurance company can sometimes get a better tier of coverage for the comparatively narrower Vagifem® or Yuvafem® applicator and might work for the Imvexxy® Vaginal Inserts.
- For **females impacted by breast cancer**, some insurance companies will cover Intrarosa® at a better tier if provided with a letter of supporting rationale and a Prior Authorization form. This approach sometimes works for female carriers of BRCA mutations who prefer Intrarosa®, too.
- For **transdermal hormone therapy** (HT), I always prescribed the generic first. If the adhesive is poor or you have an adverse skin reaction, I would get a Prior Authorization form from your pharmacy, fill it out, send it back to the pharmacy, and they will forward it to your insurance company. Alternatively, a nurse would fill out the form, and I would dictate a letter of support regarding why a specific brand name patch is needed. This was the best way to get the smaller patches with better adhesives, like the Vivelle-Dot® or Sandoz brand patch.
- For females wishing to continue **hormone therapy beyond age 65**, who receive a notification from their insurance that hormone therapy will no longer be covered (due to Beer's Criteria List), I send letters stating that both NAMS[4] and ACOG[5] have come out with statements indicating that the decision regarding continuation of HT should be between the patient and her provider. If the

[4] North American Menopause Society Position Statement on Continued use of Systemic HT after age 65. Menopause 2015;22:693

[5] American College of Obstetrics and Gynecology, Committee Opinion 565, June 2013, reaffirmed 2020, Hormone therapy and heart disease.

patient is on estrogen alone (without a progestin or progesterone), I describe the better safety profile related to breast cancer risk for estrogen-only therapy[6].

- If the patient's insurance does not cover **oral micronized progesterone** (Prometrium®), sometimes a letter outlining the benefits of oral micronized progesterone over synthetic progestins (e.g., medroxyprogesterone acetate (Provera®) and norethindrone acetate (Aygestin®) will cause the insurance company to improve tier of coverage for oral micronized progesterone. Position statements from national academic organizations can be used to support coverage requests.[6, 7]
- I have not had luck getting insurance to cover compounded medications, like a 50mg dose of oral micronized progesterone or the estriol vaginal cream. Neither of these products is commercially available at standard retail pharmacies. However, the price of compounded products is usually fairly reasonable, especially when compared to over-the-counter options or if you need to meet a high deductible.
- Copay cards and patient assistance programs provided by the medication manufacturer can be used alone or in combination with insurance. These are typically a good starting point for insurance patients with high deductibles or copays, as they can save more money than a generic discount card. However, it is important to note the restrictions on these offers. Some cannot be used with government-sponsored insurance like Medicare, and some have specific benefit limits. These are typically only available for brand-name-only medications.

  Current manufacturer savings options (in alphabetical order by product brand name)
  - Estrace® cream patient assistance program: https://www.abbvie.com/patients/patient-assistance/allergan-patient-assistance-program.html
  - Estring® copay card: https://www.estring.com/save-on-estring?gclid=57ec1652a43d1ae4f363760ce4fa64e4&gclsrc=3p.ds. Patient assistance program is also available: https://www.pfizerrxpathways.com/
  - Imvexxy® inserts copay card: https://www.imvexxy.com/savings-information
  - Intrarosa® inserts copay card: https://us.intrarosa.com/savings-and-support
  - Osphena® copay card: https://www.osphena.com/savings
  - Premarin® cream copay card: https://www.premarinvaginalcream.com/savings-and-support
- Discount cards, like GoodRx, may make medication more affordable. They are a good option for patients who do not have prescription insurance coverage or who do not have insurance coverage for specific products. Unfortunately, these cannot be used in combination with insurance. Medication price will vary by pharmacy. The best way to find the lowest price is to go to the discount card's website (e.g., goodrx.com) and search by the specific medication to see a list of available pharmacies and their contracted prices.
- Sometimes, price checking at different pharmacies can also result in a more economical price. This is especially true for a cash-paying patient. A cash-paying patient can call the pharmacy with the specific medication, strength, and quantity to get a quote. If a patient has insurance and wants to find the best cost, usually the best strategy is to call the Member Benefits number listed

[6] Stuenkel CA et al. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2015;100(11):3975-4011

on the back of the insurance card. The insurance company can list preferred contracted pharmacies and their copay structures.

SURGICAL TREATMENT OF VAGINAL STENOSIS AFTER PELVIC RADIATION THERAPY

Surgical treatment may be possible when patients are referred early before scarring is permanent.

VULVAR SKINCARE GUIDELINES

Department of Obstetrics and Gynecology, UI Women's Health Center
Developed by Dr. Colleen Stockdale, Vulvar and Vaginal Disease Clinic

NOTE: The goal is to promote healthy vulvar skin. This is done by decreasing and removing chemicals, moisture, or rubbing (friction). The products listed below have been suggested for use because of their past success in helping to decrease or relieve vulvar/vaginal burning, irritation, or itching.

Laundry Products

1. Use the detergent brand ALL FREE CLEAR on all laundry that goes into your washer, every load, every time. NO SUBSTITUTIONS. Use 1/3 to ½ the suggested amount per load. If you have a high-efficiency washer, use the smallest amount of detergent possible and double rinse.
2. Do not use fabric softeners or dryer sheets in the washer or dryer, even those advertised as "free." You can use wool dryer balls to help soften clothes.
3. If you use a shared washer or dryer, such as a Laundromat, apartment, or dorm, hand wash your underwear in ALL FREE CLEAR, then line dry.
4. Remove stain-removing products (including bleach): Soak and rinse in clear water all underwear and towels on which you have used a stain-removing product. Then wash in your regular washing cycle using ALL FREE CLEAR. This removes as much of the product as possible.
5. White vinegar or lemon juice (1/4 to 1/3 cup per laundry load) can freshen clothing and remove oils. Check with the washing machine manufacturer if lemon juice or vinegar is safe.

Clothing

1. Wear white, all-cotton underwear, not nylon, with a cotton crotch. Cotton allows air in and moisture out. Do not wear underwear when sleeping at night. Do not wear thongs. Loose-fitting cotton boxers or cotton pajama bottoms are fine.

2. Avoid pantyhose. If you must wear them, cut out the diamond crotch (if you cut out the crotch, be sure to leave about 1/4 inch of fabric from the seam to prevent running) or wear thigh-high hose. Many stores now carry thigh-high hose.
3. Avoid tight clothing, especially clothing made of synthetic fabrics. Remove wet bathing and exercise clothing as soon as you can.

Bathing And Hygiene

1. Do not use bath soaps, lotions, gels, etc., which contain perfumes. These may smell nice but can be irritating. This includes many baby products and feminine hygiene products marked "gentle" or "mild." DOVE FOR SENSITIVE SKIN™, NEUTROGENA™, BASIS™, AVEENO™, OR PEARS ™ are the soaps we suggest. Your partner needs to use one of these soaps, also. Do not use soap directly on the vulvar skin. Warm water and your hand will keep the vulvar area clean without irritating the skin.
2. Do not use bubble baths, bath salts, and scented oils. After getting out of the bathtub or shower, you may apply an unscented oil or lotion to damp skin. Do not apply lotion directly to the vulva.
3. Do not scrub vulvar skin with a washcloth; washing with your hand and warm water is enough for good cleaning.
4. Pat dry rather than rubbing with a towel. Or, use a hair dryer in a cool setting to dry the vulva.
5. Baking soda soaks - Soak in lukewarm (not hot) bath water with 4-5 tablespoons of baking soda to help soothe vulvar itching and burning. Soak 1 to 3 times a day for 10 minutes. If you are using a sitz bath, use 1 to 2 teaspoons of baking soda.
6. Use white, unscented toilet paper. Do not use toilet paper with aloe. Pat dry instead of wiping.
7. Do not use feminine hygiene sprays, perfumes, or adult or baby wipes. You can use Tucks (Witch Hazel) hemorrhoid pads. If urine causes burning of the skin, pour lukewarm water over the vulva while urinating. A clean, plastic condiment bottle works great for gently pouring water over the vulva.
8. Do not use deodorized pads and tampons.
9. Tampons may be used when the blood flow is heavy enough to soak one tampon in four hours or less. Tampons are safe for most women, but wearing them too long or when the blood flow is light may result in vaginal infection, increased discharge, odor, or toxic shock syndrome.
10. Use only pads with a cotton liner, not nylon mesh weave, that comes in contact with your skin. Nylon traps moisture and keeps blood and discharge against your skin longer. We recommend STAYFREE™, CAREFREE™, or 7th GENERATION™ (for urine leakage, use a pad specifically designed to collect urine).

11. Do not use over-the-counter creams or ointments until you ask your healthcare provider. When buying ointments, be sure they are paraben and fragrance-free.
12. Apply small amounts of extra virgin olive oil, vegetable oil, coconut oil, or zinc oxide ointment may be applied to the vulva as often as needed to protect the skin. It also helps to decrease skin irritation during your period and when you urinate.
13. Do not douche. Baking soda soaks or rinsing with warm water will help rinse away extra discharge and help with odor.
14. Do not shave or use hair removal products on the vulvar area. You may use scissors to trim the pubic hair close to the vulva. LASER hair removal is an option.
15. Some women may have problems with chronic dampness. Keeping dry is important.
16. Do not wear pads on a daily basis.
17. Choose cotton fabrics whenever you can.
18. Keep an extra pair of underwear with you and change if you become damp.
19. GOLD BOND™ or ZEASORB (AF) ™ powder may be applied to the vulva and groin area 1 to 2 times per day to help absorb moisture. Do not use powders that contain cornstarch.
20. It may be helpful to use a non-lubricated, non-spermicidal condom, which will help keep the semen off the skin, which can increase burning and irritation after intercourse. We suggest olive oil. The CDC does state that plant-based oils can cause the breakdown of condoms. Oils can stain sheets and clothing.

    If a water-based or silicone lubricant is chosen, ensure it is free of irritants: capsaicin, chlorhexidine gluconate; flavors, fragrance; glycerin, lidocaine, menthol; mineral oil, parabens, petroleum (Vaseline); polyquaternium 7, 10, or 5; and or propylene glycol.

    Please see the *After Cancer Patient Handout* on lubricants for more in-depth information on choosing and using lubricants.

BIRTH CONTROL OPTIONS

1. The new low-dose oral birth control pills do not increase risk of yeast infections.
2. Lubricated condoms, contraceptive jellies, creams, or sponges may cause itching and burning.
3. The use of latex condoms with a non-irritating lubricant is suggested to protect your skin. Our practice suggests all-natural plant-oil-based lubricants. Our experience has not found this to be a problem with vegetable-based oils. However, the Centers for Disease Control recommends that condoms not be used with any oil-based lubricants for birth control or prevention of sexually transmitted diseases (STDs) or sexually transmitted infections (STIs).

   If a water-based or silicone lubricant is chosen, ensure it is free of irritants: capsaicin,

chlorhexidine gluconate, flavors, fragrance, glycerin, lidocaine, menthol, mineral oil, parabens, petroleum (Vaseline), polyquaternium 7, 10, or 5; and or propylene glycol.

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