

VULVODYNIA & DYSPAREUNIA THERAPY

Gabapentin · Lidocaine · Amitriptyline · Estradiol / Testosterone

Prescriber Reference Guide · The Medicine Shoppe, York PA

Neuropathic Pain · Local Analgesia · Central Sensitization · Hormonal Atrophy · Topical · Custom Formula

Program Overview

Vulvodynia (chronic vulvar pain without identifiable cause) and dyspareunia (painful intercourse) are among the most underdiagnosed and undertreated conditions in women's health. Estimated prevalence of vulvodynia is 8-16% of women across the lifespan; dyspareunia affects a substantial additional population, particularly in peri- and post-menopausal women and those with a history of hormonal suppression. Commercial treatment options are limited and rarely address the multiple overlapping mechanisms driving chronic vulvovaginal pain. Compounded topical therapy enables the prescriber to construct a personalized, multi-ingredient formulation targeting neuropathic pain, local sensitization, and hormonal tissue changes simultaneously -- applied directly at the site of pathology.

Key Clinical Advantages

- Multi-mechanism targeting -- neuropathic modulation (gabapentin, amitriptyline), local analgesia (lidocaine), and tissue restoration (estradiol/testosterone) in a single application
- Topical delivery -- concentrates active ingredients at the site of pathology with substantially lower systemic absorption than oral equivalents; critical for gabapentin and amitriptyline in sensitive patients
- No commercial equivalent -- no single FDA-approved topical product addresses the full spectrum of vulvodynia/dyspareunia mechanisms; compounding is the only source for this combination
- Vulvar-compatible base -- formulated without common irritants (propylene glycol, parabens, fragrances) that can exacerbate vulvar hypersensitivity; base selection is clinically important in this patient population
- Customizable to presentation -- prescriber selects ingredients and concentrations based on whether the primary mechanism is neuropathic, atrophic, inflammatory, or mixed
- Non-controlled ingredients -- gabapentin is Schedule V in some states but generally low-restriction; no DEA concerns for topical amitriptyline, lidocaine, estradiol, or testosterone

Pathophysiology & Classification

Vulvodynia is a diagnosis of exclusion -- defined by the ISSVD as vulvar pain lasting at least 3 months without a clearly identifiable cause. Its mechanisms are multifactorial and frequently overlap, which is why multi-ingredient compounded therapy is conceptually well-suited to its management.

Classification

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| Generalized Vulvodynia | Diffuse, unprovoked vulvar pain affecting the entire vulvar region; often described as burning, stinging, or rawness; not limited to vestibule; more likely to have central sensitization component |
| Localized Vulvodynia (Vestibulodynia) | Pain localized to the vestibule, provoked by touch, pressure, or penetration; includes provoked vestibulodynia (PVD) and unprovoked vestibulodynia; most common subtype in reproductive-age women |
| Mixed (Provoked + Unprovoked) | Both spontaneous and contact-triggered pain; often reflects combined peripheral sensitization and central processing abnormalities |
| Dyspareunia -- Atrophic | Painful intercourse driven primarily by vulvovaginal atrophy (VVA) -- thinning, dryness, and loss of elasticity from estrogen deficiency; most common in post-menopausal women and those on hormonal suppression (aromatase inhibitors, GnRH agonists, hormonal contraceptives) |
| Dyspareunia -- Mixed | Atrophic structural changes combined with neuropathic sensitization; common in patients with long-standing dyspareunia where pain has become centrally maintained even after tissue restoration |

Key Pathophysiological Mechanisms

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| Peripheral Sensitization | Upregulation of nociceptors in vulvar tissue -- increased density of intraepithelial nerve fibers, lowered pain thresholds, and allodynia (pain from non-painful stimuli). Inflammatory mediators (substance P, NGF, mast cell degranulation) contribute to peripheral sensitization in vestibulodynia. |
| Central Sensitization | Altered central pain processing -- amplified pain signals, expanded receptive fields, and descending inhibitory pathway dysfunction. Explains why vulvodynia persists and generalizes even after peripheral triggers resolve. Addressed by amitriptyline and, secondarily, gabapentin. |
| Neuropathic Component | Aberrant pudendal nerve and vestibular nerve signaling; increased voltage-gated sodium and calcium channel activity in afferent nociceptors. Gabapentin (calcium channel modulation) and lidocaine (sodium channel blockade) directly target this mechanism. |
| Hormonal Tissue Atrophy | Estrogen deficiency causes vulvovaginal epithelial thinning, reduced glycogen, altered vaginal pH, decreased lubrication, and loss of submucosal collagen and elastin -- creating structural vulnerability to microtrauma and inflammation. Estradiol restores tissue architecture; testosterone supports additional trophic effects. |
| Pelvic Floor Dysfunction | Hypertonicity of the levator ani and bulbospongiosus muscles is common in provoked vestibulodynia and dyspareunia -- creates a pain-spasm cycle that perpetuates symptoms. Compounded topical therapy addresses tissue and nerve contributions; pelvic floor PT is recommended as a concurrent intervention. |
| Inflammatory / Immune Factors | Increased mast cell density in vestibular tissue, elevated pro-inflammatory cytokines, and possible low-grade neurogenic inflammation contribute in some subtypes. Amitriptyline has anti-inflammatory properties at the tissue level beyond its central effects. |

Active Ingredients -- Mechanisms of Action

1. Gabapentin

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| Mechanism | Alpha-2-delta subunit ligand -- binds to voltage-gated calcium channels on presynaptic nociceptive afferents, reducing calcium influx and decreasing release of excitatory neurotransmitters (glutamate, substance P) at the peripheral synapse. Reduces ectopic discharge from sensitized nociceptors. |
| Target in Vulvodynia | Peripheral sensitization and neuropathic pain component -- particularly effective for burning, stinging, and allodynia. Topical application delivers gabapentin directly to vulvar nociceptors, achieving relevant local concentrations without significant systemic absorption. |
| Topical vs. Oral | Oral gabapentin is used systemically for neuropathic pain but causes significant CNS side effects (sedation, dizziness, cognitive impairment) that limit dose escalation. Topical gabapentin achieves peripheral nociceptor concentrations directly, with substantially lower plasma levels -- supporting a markedly improved tolerability profile. |
| Evidence | Multiple open-label studies and clinical series support topical gabapentin (2-6%) for vulvodynia and vestibulodynia. Used in established vulvodynia treatment protocols at academic vulvodynia centers. Oral gabapentin RCT evidence for vulvodynia also supports the mechanism; topical route provides localized delivery with fewer systemic effects. |
| Typical Concentration | 2-6% in a vulvar-compatible cream or gel base; 6% is commonly used for more severe neuropathic symptoms |

2. Lidocaine

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| Mechanism | Voltage-gated sodium channel blocker -- stabilizes nociceptor membranes, raising the threshold for action potential generation. Provides local anesthesia by reversibly blocking sensory nerve conduction at the application site. |
| Target in Vulvodynia | Immediate local analgesia -- rapid onset makes it appropriate for use before intercourse, gynecological examination, or other provoked pain triggers. Reduces the provoked pain component of vestibulodynia by blocking the afferent signal at the point of contact. |
| Role in Desensitization | Extended-contact lidocaine protocols (overnight application) have been studied as a desensitization strategy in provoked vestibulodynia -- repeated blockade of afferent nociceptor firing may reduce peripheral sensitization over time. Clinical evidence supports overnight 5% lidocaine for PVD. |
| Evidence | RCT (Zolnoun et al.) demonstrated significant improvement in vestibulodynia pain scores with overnight topical lidocaine application over 7 weeks. Widely used as adjunct in vulvodynia protocols for pre-coital analgesia and procedural (colposcopy, vaginal exam) pain reduction. |
| Typical Concentration | 2-5% in cream, gel, or ointment base; 5% for overnight desensitization protocols; lower concentrations for daily or pre-activity use |
| Note on Timing | For pre-intercourse use: apply 20-30 minutes prior, then wipe excess before contact to avoid transferring lidocaine to partner (may cause penile numbness) |

3. Amitriptyline

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| Mechanism | Tricyclic antidepressant with multiple analgesic mechanisms at topical doses: (1) sodium channel blockade -- similar to lidocaine but with different kinetics; (2) norepinephrine and serotonin reuptake inhibition at peripheral nerve terminals -- enhancing descending inhibitory tone locally; (3) NMDA receptor antagonism -- reduces central sensitization contribution; (4) anti-inflammatory effects at tissue level via mast cell stabilization and cytokine modulation. |
| Target in Vulvodynia | Central sensitization and neuropathic pain -- particularly effective for the burning, spontaneous pain component that persists independent of contact (generalized vulvodynia). Oral amitriptyline is a first-line systemic agent for vulvodynia in major guidelines; topical delivery achieves local tissue concentrations with less systemic anticholinergic burden. |
| Topical vs. Oral | Oral amitriptyline for vulvodynia requires 4-12 weeks for therapeutic effect and causes significant systemic side effects (dry mouth, constipation, sedation, weight gain, cardiac conduction effects) that limit tolerability, particularly at the doses needed for pain modulation (25-75 mg/day). Topical amitriptyline provides local neuromodulation with substantially reduced systemic exposure. |
| Evidence | Multiple clinical series and case studies support topical amitriptyline (1-2%) alone and in combination with baclofen or ketamine for vulvodynia. Amitriptyline/baclofen combination has case-controlled evidence; amitriptyline/ketamine topical formulations are also used in specialist centers. |
| Typical Concentration | 1-2% in a vulvar-compatible base; often combined with gabapentin in the same preparation |

4. Estradiol

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| Mechanism | Topical estradiol restores estrogen-depleted vulvovaginal tissue: increases epithelial thickness and maturation, restores glycogen content, normalizes vaginal pH, improves submucosal collagen and elastin, and enhances vascular supply. Directly reverses the structural changes of vulvovaginal atrophy (VVA / genitourinary syndrome of menopause, GSM). |
| Target in Dyspareunia | Atrophic dyspareunia -- addresses the tissue-structural component of pain that is driven by estrogen deficiency. Essential in post-menopausal patients, those on aromatase inhibitors, those with a history of oophorectomy, and premenopausal patients with relative hypoestrogenism from hormonal contraceptives. |
| Systemic Absorption | Topical vaginal/vulvar estradiol has low systemic absorption -- substantially less than oral or transdermal systemic estrogen. For patients with estrogen-sensitive cancers (breast, endometrial), discuss with the oncologist; evidence suggests local vaginal estrogens at low doses have acceptably low systemic exposure even in this population, but requires individualized risk-benefit discussion. |
| Evidence | Cochrane review and multiple RCTs support topical estrogens for GSM/atrophic vaginitis with high-quality evidence for improved vaginal maturation, lubrication, and dyspareunia. |
| Typical Concentration | 0.01-0.1% estradiol in a vulvar-compatible cream; concentration per prescriber specification based on degree of atrophy and patient hormone history |

5. Testosterone

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| Mechanism | Androgen receptors are expressed in vulvar skin, clitoral tissue, and vestibular glands. Topical testosterone supports vulvar tissue trophism, enhances clitoral sensitivity, supports libido and arousal, and may reduce vulvar nociception through androgen receptor-mediated pathways. Complements estradiol's effects on tissue architecture. |
| Target in Dyspareunia | Hormonal atrophy with androgen deficiency component -- particularly relevant in post-menopausal women (bilateral androgen and estrogen decline), women on aromatase inhibitors (suppressed androgen as well as estrogen), and women with low androgens from SHBG elevation (oral contraceptive-related androgen deficiency). |
| Evidence | Evidence base for topical testosterone in female sexual dysfunction and vulvar atrophy includes multiple RCTs. Particularly well-studied in post-menopausal women and in women with pill-induced SHBG elevation causing androgen deficiency dyspareunia. |
| Typical Concentration | 0.05-0.1% testosterone in a vulvar-compatible cream; some protocols combine estradiol and testosterone in the same preparation |
| Virilization Monitoring | At low topical doses, virilization is not expected; monitor for signs (clitoral enlargement, abnormal hair growth, acne) with prolonged use and adjust dose if needed |

Formulation Strategy & Base Selection

Base selection is clinically important in vulvodynia -- the vulvar epithelium is hypersensitive and reactive in most affected patients, and many commercial cream bases contain preservatives, fragrances, or excipients that trigger or worsen symptoms. The following principles guide base selection:

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| Avoid Propylene Glycol | Propylene glycol is a common sensitizer and irritant in vulvodynia patients; all compounded preparations for this indication should be PG-free unless the patient has documented tolerance |
| Avoid Parabens | Paraben preservatives can act as contact allergens in sensitized vulvar tissue; paraben-free bases are standard for this patient population |
| Avoid Fragrances | Fragrance-free base required; any scented component can provoke pain flares in sensitized patients |
| Preferred Bases | Lipoderm (PCCA), HRT base, VersaBase, or simple petrolatum-based ointments depending on consistency preference; aqueous gels may be preferable for some patients; prescriber and compounding pharmacist should collaborate on base selection |
| pH Consideration | Vulvar tissue has a different pH environment than vaginal tissue; bases should be pH-compatible with vulvar surface (closer to skin pH ~5.5) rather than vaginal pH formulations |
| Consistency | Cream or ointment for most applications; gel for pre-intercourse analgesia (easier application and less residue); prescriber specifies based on intended use timing |

Dosing Protocols & Timing

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| General Application | Small amount (pea-sized) applied to affected vulvar area with clean fingertip; gently spread without vigorous rubbing; wash hands after application |
| Neuropathic Formula (Gabapentin + Amitriptyline) | Applied once or twice daily at consistent times; morning and/or bedtime; neuropathic benefit builds over 4-8 weeks of consistent use -- not PRN |
| Pre-Activity Lidocaine | Applied 20-30 minutes before intercourse or examination; wipe excess before contact to prevent partner numbness; may be used as needed rather than scheduled |
| Overnight Desensitization (Lidocaine 5%) | Applied at bedtime to vestibule; worn overnight; wipe residue in morning; protocol typically 7+ weeks; evidence-based for provoked vestibulodynia |
| Hormonal (Estradiol / Testosterone) | Applied daily or every other day to vulvar tissue; effects on tissue architecture develop over 4-12 weeks; use smallest effective dose for maintenance |
| Combined Formula | When ingredients are combined in a single preparation, dosing follows the most conservative schedule (typically once or twice daily); prescriber specifies exact instructions |
| Onset Expectations | Lidocaine: immediate (minutes). Gabapentin/amitriptyline neuropathic benefit: 4-8 weeks. Hormonal tissue restoration: 4-12 weeks. Counsel patients on differential timelines to manage expectations and prevent early discontinuation. |

Evidence Summary & Guidelines

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| ACOG Guidelines | ACOG Practice Bulletin supports multimodal treatment of vulvodynia including topical agents, pelvic floor PT, and psychological support. Notes limited high-quality RCT evidence but consistent clinical benefit across multiple treatment modalities. |
| ISSVD Consensus | International Society for the Study of Vulvovaginal Disease consensus statement supports topical therapies including local anesthetics and compounded formulations as components of multimodal vulvodynia management. |
| Topical Gabapentin Evidence | Andrews et al. (2009) open-label study: significant improvement in vulvodynia VAS scores with topical gabapentin 6%. Multiple clinical series at academic vulvodynia centers report benefit. Mechanistic rationale is strong; RCT evidence is limited but consistent with oral gabapentin evidence for the neuropathic mechanism. |
| Topical Lidocaine Evidence | Zolnoun et al. RCT: 57% of patients with provoked vestibulodynia reported significant improvement with overnight topical lidocaine 5% vs. 25% placebo response. Multiple subsequent clinical series confirm benefit. |
| Topical Amitriptyline | Lynch et al. case series and clinical experience support amitriptyline 2% / baclofen 2% combination for vulvodynia; amitriptyline/ketamine combinations also reported. Level of evidence: consistent clinical series; RCT data limited. |
| Hormonal Therapy | Strong RCT evidence for topical estrogens in GSM/atrophic dyspareunia (Cochrane review). Testosterone evidence supports benefit in HSDD and androgen-deficiency dyspareunia. |

Patient Selection & Multidisciplinary Context

Appropriate Candidates

- Chronic vulvodynia (>3 months) -- generalized or localized/vestibulodynia -- with inadequate response to standard therapies
- Dyspareunia with atrophic component -- post-menopausal, on aromatase inhibitors, oophorectomy, or hormonal contraceptive-related androgen deficiency
- Provoked vestibulodynia -- lidocaine-based protocols for pre-activity analgesia or overnight desensitization
- Patients who cannot tolerate oral gabapentin or amitriptyline due to CNS side effects -- topical delivery substantially reduces systemic burden
- Patients seeking a single topical application targeting multiple mechanisms rather than multiple separate oral medications
- Patients in whom pelvic floor PT and/or cognitive behavioral therapy is also being pursued -- compounded topical therapy works best as part of a comprehensive, multimodal plan

Multimodal Treatment Context

Vulvodynia rarely responds optimally to pharmacotherapy alone. Compounded topical therapy is most effective as part of a comprehensive treatment plan that may include:

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| Pelvic Floor Physical Therapy | First-line intervention for provoked vestibulodynia and dyspareunia with hypertonicity component; addresses the muscular/fascial component that compounds the pain cycle |
| Cognitive Behavioral Therapy | Evidence-based for pain catastrophizing, fear-avoidance behaviors, and sexual dysfunction in vulvodynia; targets central sensitization and psychosocial amplifiers |
| Sex Therapy / Couples Counseling | Addresses relationship impact, sexual avoidance, and partner communication; important component particularly when dyspareunia has persisted for >6 months |
| Vestibulectomy | Surgical option for refractory localized vestibulodynia (PVD) with strong evidence; reserved for patients who have failed conservative multimodal treatment |
| Low-Oxalate Diet / Dietary Modification | Evidence is mixed; some patients with vulvodynia report benefit; discuss as adjunct in patients with food-related symptom triggers |

Drug Interactions & Safety

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| Lidocaine -- Systemic Absorption | At standard topical vulvar doses, systemic lidocaine absorption is low. Caution with large surface area application or abraded tissue. Avoid in patients with known lidocaine/amide anesthetic allergy. |
| Gabapentin -- Systemic Exposure | Topical gabapentin systemic absorption is substantially lower than oral; CNS side effects rare at topical doses. Use with caution in patients on high-dose oral gabapentin/pregabalin (additive effects possible). |
| Amitriptyline -- Cardiac | Oral amitriptyline has cardiac conduction effects (QTc prolongation, arrhythmia risk) at systemic doses. Topical absorption is low; clinically significant cardiac effects are not expected at compounded topical doses, but document cardiac history and concurrent QTc-prolonging medications. |
| Amitriptyline -- MAOIs | Theoretical serotonergic interaction with MAOIs; topical doses reduce but do not eliminate this concern. Avoid in patients on MAO inhibitors. |
| Estradiol / Testosterone -- Systemic | Topical vulvar hormones have lower systemic absorption than systemic formulations. For patients with hormone-sensitive cancers or contraindications to systemic estrogen/testosterone, consult oncologist/specialist; emerging evidence supports low-dose local hormones even in many of these patients, but requires individualized discussion. |
| Partner Exposure | Counsel patients about potential partner transfer -- particularly relevant for testosterone (virilizing effects in female partners) and lidocaine (numbness). Wipe excess before contact; consider timing of application to minimize transfer risk. |

Monitoring & Follow-Up

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| Baseline | Vulvar pain assessment (VAS or NRS), dyspareunia frequency and severity, sexual function questionnaire (FSFI recommended), pelvic floor assessment, hormonal status (FSH, estradiol, total/free testosterone, SHBG if hormonal component is included) |
| 4 Weeks | Assess tolerability -- local skin reactions, contact dermatitis, increased burning (may indicate base incompatibility or allergy); address application technique; set expectations for neuropathic timeline |
| 8 Weeks | Reassess pain scores; lidocaine pre-activity benefit should be apparent; neuropathic benefit (gabapentin/amitriptyline) building; adjust concentrations if partial response |
| 12 Weeks | Formal reassessment with standardized pain and sexual function measures; hormonal tissue assessment if estradiol/testosterone included; consider formula modification or addition of a missed mechanism component |
| Hormonal Monitoring | If testosterone included: check serum testosterone and SHBG at 3 months; monitor for virilization symptoms. If estradiol included: no routine serum monitoring required for local vaginal/vulvar estrogen at standard doses. |
| Pelvic Floor Coordination | Coordinate with pelvic floor PT if concurrent; share treatment response information to guide the multidisciplinary plan |
| Ongoing | Annual reassessment; step-down trials for neuropathic agents when well-controlled; maintain hormonal component as long as atrophic pathology persists (often indefinitely in post-menopausal patients) |

Formulation & Dispensing

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| Dosage Form | Topical cream or gel -- compounded at The Medicine Shoppe in vulvar-compatible base; propylene glycol-free, paraben-free, fragrance-free as standard |
| Available Ingredients | Gabapentin, lidocaine, amitriptyline, estradiol, testosterone -- any combination; concentrations per prescriber specification |
| Common Combinations | Gabapentin 6% + amitriptyline 2% (neuropathic); lidocaine 5% (analgesia/desensitization); estradiol 0.01-0.1% + testosterone 0.05-0.1% (atrophic/hormonal); full multi-ingredient formula combining all indicated agents |
| Base Selection | Standard: Lipoderm, HRT base, or VersaBase; prescriber may specify base preference; compounding pharmacist available to discuss base options for individual patient needs |
| Quantity | 30-day supply standard; 60-day available |
| Pricing | Cash pay -- contact pharmacy for current pricing by formula |
| BUD / Storage | Per USP compounding standards; store at room temperature unless hormonal component indicates refrigeration; labeled on each preparation |

Ordering & Contact Information

All preparations require a valid prescription specifying desired ingredients, concentrations, base, and dosing instructions. Patients fill directly at our pharmacy. No prior authorization required.

How to Order

- By phone -- call (717) 846-0500; ask for the compounding pharmacist; have patient name, DOB, ingredients, concentrations, base preference, quantity, and sig ready
- By fax -- send prescription to (717) 845-8767; list each ingredient and concentration; specify base (e.g., PG-free cream), quantity, and application instructions
- E-prescribe -- select 'Compound' as medication type; list all ingredients with concentrations in Sig/Comments (e.g., 'Gabapentin 6% / Amitriptyline 2% in PG-free cream -- apply small amount to vulvar area twice daily')

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