What’s New in Management of Menopause and Peri-menopausal Symptoms?

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I have no disclosures relevant to this talk

General Disclosures

• Bayer: litigation consultant
• Sebela Pharmaceuticals:
  – Investigator proctor in phase III trial of a copper IUD (VeraCept)
Learning Objectives

- List 4 non-hormonal prescription medications that decrease vasomotor symptoms (hot flashes)
- List 5 steps in the management of VMS not initially responsive to treatment
- Describe 4 symptoms or signs of genitourinary syndrome of menopause (GSM)
- List 4 medication categories that are FDA approved for the treatment of GSM

Menopause Terms

- **Menopause**
  - *The date* of a woman’s final menstrual period (FMP)
  - After the FMP, 12 months of amenorrhea is required
- **Menopausal Transition (MT)**
  - Variability in menstrual cycles before FMP
- **Perimenopause**
  - Onset of symptoms ➔ one year after FMP
Stages of Reproductive Aging Workshop (STRAW)

Reproductive phase: Menopausal Transition - Post-Menopause

Early Stage-2 Late Stage-1

Average age: 47 y.o. 49 y.o

Perimenopause

Stages of Reproductive Aging Workshop +10

Menopause 2012;19:1-9

<table>
<thead>
<tr>
<th>Stage</th>
<th>Menarche</th>
<th>FMP (0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td>-4</td>
<td>-3b</td>
</tr>
<tr>
<td>-3a</td>
<td>-2 Stage</td>
<td>-1</td>
</tr>
<tr>
<td>+1</td>
<td>a</td>
<td>+1b</td>
</tr>
<tr>
<td>+1c</td>
<td>+2</td>
<td></td>
</tr>
</tbody>
</table>

Terminology

REPRODUCTIVE MENOPAUSAL POSTMENOPAUSE TRANSITION

<table>
<thead>
<tr>
<th>Duration</th>
<th>variable</th>
<th>variable</th>
<th>1-3 years</th>
<th>2 years (1+1)</th>
<th>3-6 years</th>
<th>Remaining lifespan</th>
</tr>
</thead>
</table>

PRINCIPAL CRITERIA

Menstrual Cycle

Variable to regular Regular Regular Subtle changes in Flow/Length Variable Length Persistent 7 day difference in length of consecutive cycles Interval of amenorrhea of >60 days

SUPPORTIVE CRITERIA

Endocrine

FSH AMH Inhibin B Low Low Variable Low Low Low Low Variable Stabilizes Very Low Very Low

↑ Variable Low Low 25 IU/L **
Effects of Menopausal Estrogen Deficiency

• Vasomotor symptoms (VMS)
• Neuro-behavioral changes
• Bone loss
• Genitourinary syndrome of menopause (GSM)
• Acceleration of ASCVD → increased risk of heart attack, stroke (compared to premenopause)

Duration of Menopausal VMS

• 3302 females 7 US sites; 1996-2013 (17 Yrs), median 13 visits
• Findings
  – Median VMS duration (unadjusted) 7.4 years
  – Median post-FMP persistence 4.5 years

<table>
<thead>
<tr>
<th>Group</th>
<th>Median Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>10.1 years</td>
</tr>
<tr>
<td>Hispanic American</td>
<td>8.9 years</td>
</tr>
<tr>
<td>Non Hispanic white</td>
<td>6.5 years</td>
</tr>
<tr>
<td>Chinese American</td>
<td>5.4 years</td>
</tr>
<tr>
<td>Japanese American</td>
<td>4.8 years</td>
</tr>
</tbody>
</table>

Avis NE, JAMA Intern Med. 2015
Duration of Menopausal VMS

- **Findings (continued)**
  - Postmenopausal onset of VMS: 3.4 years
  - Premenopausal or early perimenopausal when first VMS
    - Total VMS duration: 11.8 years
    - Post-FMP persistence: 9.4 years
  - Additional factors related to VMS duration or persistence
    - Younger age
    - Lower educational level
    - Greater perceived stress and symptom sensitivity
    - Higher depressive symptoms and anxiety at first report

Neuro-behavioral Changes

- Restful **sleep disturbances**
  - Insomnia, easy awakening
  - Less deep (REM) sleep due to awakening from hot flashes
- **Irritability, fatigue, poor concentration**
  - Probably due to sleep disturbances
Neuro-behavioral Changes

- Short-term memory compromise
  - Forgetfulness, reduced computational skills
- Emotional swings; anxiety
  - But, depression is not related to estrogen deficiency
- Changes in sex-drive
  - Often less: reduced testosterone, sexual pain
  - Can be more: no pregnancy risk, new partner

Treatment of Vasomotor Symptoms
## Position Statement

The 2017 hormone therapy position statement of The North American Menopause Society

### Abstract

The 2017 Hormone Therapy Position Statement of The North American Menopause Society (NAMS) updates the 2012 Hormone Therapy Position Statement of The North American Menopause Society and identifies future research needs. An Advisory Panel of clinicians and researchers expert in the field of women’s health and menopause was recruited by NAMS to review the 2012 Position Statement, evaluate new literature, assess the evidence, and reach consensus on recommendations, using the level of evidence to identify the strength of recommendations and the quality of the evidence. The Panel’s recommendations were reviewed and approved by the NAMS Board of Trustees.

### NAMS Definitions

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full name</th>
</tr>
</thead>
<tbody>
<tr>
<td>ET</td>
<td>Estrogen (E) therapy</td>
</tr>
<tr>
<td>EPT</td>
<td>Combined E+P therapy</td>
</tr>
<tr>
<td>HT</td>
<td>Hormone therapy (ET, EPT)</td>
</tr>
<tr>
<td>MHT</td>
<td>Menopausal hormone therapy</td>
</tr>
<tr>
<td>P</td>
<td>Progestogen (progesterone or progestin)</td>
</tr>
<tr>
<td>CC-EPT</td>
<td>Continuous-combined E+P therapy</td>
</tr>
<tr>
<td>CS-EPT</td>
<td>Continuous-sequential E+P therapy</td>
</tr>
</tbody>
</table>

NAMS position statements
# NAMS Definitions

<table>
<thead>
<tr>
<th>Abbrev</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>VMS</td>
<td>Vasomotor Symptoms</td>
</tr>
<tr>
<td>VVA</td>
<td>Vulvovaginal Atrophy</td>
</tr>
<tr>
<td>GSM</td>
<td>Genitourinary syndrome of menopause</td>
</tr>
<tr>
<td>T</td>
<td>Testosterone</td>
</tr>
<tr>
<td>SHBG</td>
<td>Sex hormone binding globulin</td>
</tr>
</tbody>
</table>

# MenoPro by the North American Menopause Society (NAMS)

The MenoPro app from The North American Menopause Society (NAMS) has 2 modes: one for clinicians and one for women/patients, to support shared decision making.

Are you a Health Care Provider or Woman/Patient?

Available for iPad, iPhone and android
Moderate-Severe Hot Flashes
(inadequate response to lifestyle modifications)

GSM sx?
Yes No

Free of CI?
Yes No

Avoid HT
Try vaginal E₂ or ospemiphene

Intimate lubricants + moisturizers

* Consider transdermal hormone therapy

Wants HT? No CI?
Yes No

CV risk
Low (5%)<5Y HT OK* HT OK* Avoid
Mod (5-10%) HT OK* HT OK* Avoid
High (>10%) Avoid Avoid Avoid

Wants SSRI? No CI?
Yes No

Try
• SSRI
• SNRI

CI: Contra-Indication
HT: Hormone therapy


Case Study: Dolores

• 48 year old female
• Cycles are 27-35 days apart
• C/o mild-moderate hot flashes, especially at night
• Occasionally feels depressed, but not treated
• Non-smoker; no medications; generally healthy
• PE: BP 122/78, BMI 26 kg/m²
• Would like treatment for hot flashes, but “scared of hormones”
Nonhormonal Management of Menopause-associated Vasomotor Symptoms (VMS)

Key points from the 2015 NAMS Position Statement

Recommend: Prescription Therapies

- FDA-approved low-dose paroxetine salt
- Gabapentin and pregabalin
- Other SSRIs and SNRIs yielding significant VMS reductions in large RCTs

Choice of Medication

Depends upon
- Coexistence of mood disorder
- VMS more bothersome day or night
- Medication sensitivity
- Pharmacogenetic testing
- Patient preference

Prescription Therapies: Considerations

- Start lowest dose first
  - Then titrate up to effect, tolerance
  - Onset of action usually within 2 weeks
- When stopping, taper therapy over 1-2 wk
- Re-evaluate carefully and regularly (Q 6-12 mo.)

Dosing Ranges for Nonhormonal Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand name</th>
<th>Range (mg/day)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxetine salt</td>
<td>Brisdelle</td>
<td>7.5mg</td>
<td>Single dose, no titration needed</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Paxil</td>
<td>10-25</td>
<td>Start with 10 mg/d</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Celexa</td>
<td>10-20</td>
<td>Start with 10 mg/d</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Lexapro</td>
<td>10-20</td>
<td>Start with 10 mg/d (for sensitive or older persons, start 5 mg/d)</td>
</tr>
<tr>
<td>Desvenlafaxine</td>
<td>Pristiq</td>
<td>100-150</td>
<td>Start with 25-50 mg/d and titrate up by that amount each day</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Effexor</td>
<td>37.5-150</td>
<td>Start with 37.5 mg/d</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Neurontin</td>
<td>900-2,400</td>
<td>300mg at night, then add 300 mg at night, then a separate dose of 300mg in the morning</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Lyrica</td>
<td>150-300</td>
<td></td>
</tr>
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</table>
VMS: Non-Hormonal Therapies

<table>
<thead>
<tr>
<th></th>
<th>% treated patients with &gt;50% ↓HF</th>
<th>% placebo patients with &gt;50% ↓HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine 75 mg</td>
<td>54-70%</td>
<td>30%</td>
</tr>
<tr>
<td>Paroxetine 10mg</td>
<td>50-76%</td>
<td>35-57%</td>
</tr>
<tr>
<td>Sertraline</td>
<td>40-56%</td>
<td>21-41%</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>55%</td>
<td>36%</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>46-84%</td>
<td>27-47%</td>
</tr>
</tbody>
</table>

J Clinical Oncology 2009

VMS: Do Not Recommend

Level I evidence: unlikely to alleviate VMS (but may have other health benefits)
- Exercise
- Yoga
- Paced respiration
- Acupuncture

VMS: Do Not Recommend at This Time
(No benefit or no studies)

- Over-the-counter supplements
- Herbal therapies
- Vitamins
- Relaxation
- Calibration of neural oscillations
- Chiropractic intervention
- Cooling techniques
- Avoiding “triggers”

Case Study: Nicki

- 46 year old G₂ P₂ female seen with a c/o of hot flashes and irregular menses for 2 years
  - Menstrual interval “3 weeks up to 3 months”
  - Bleeding is heavy for first 3 days
  - Has premenstrual molimina
- Sexually active, not using contraception
- Healthy; no cardiovascular risk factors

Would you …..

1. Prescribe low dose combined OCs
2. Prescribe progestin only pills
3. Recommend a progestin releasing IUD
4. Order pelvic ultrasound to evaluate EMS thickness
5. Recommend an endometrial biopsy before making a decision regarding treatment

Perimenopause: Estrogen’s Storm Season

- **Hormonal changes**
  - Follicle phase $E_2$ levels can be 20-30% higher
    - Greater variance: higher highs, lower lows
  - Luteal phase progesterone peaks are lower
- **Cycle changes**
  - Follicle phase shorter (cycle interval now 24-26 days)
  - Cycle intervals less predictable
- **Bleeding changes**
  - Flow can be heavier, longer because of more endometrial proliferation ($\uparrow E$), less endometrial maturation ($\downarrow P$)
Any 3 Define Onset of Perimenopause

- New heavy or longer flow
- Shorter menstrual cycle lengths (<25 days)
- Onset of night sweats, especially around menses
- New mid-sleep awakening
- New or increased premenstrual mood swings
- New breast tenderness or fibrocystic change (FCC)
- New or increased dysmenorrhea
- New or increased migraine headaches
- Weight gain without changes in exercise or food intake


Hormonal Contraceptives in Perimenopause

- Low-dose OCs (< 30 mcg EE) provide relief VMS and prevention of pregnancy
  - Other benefits: cycle control, fewer ovarian cancers
- Patch or ring may be helpful, but no studies
- LNg-IUS prevents endometrial hyperplasia in ET users
  - LNg-IUS and DMPA alone will not address VMS

NAMS Position Statements
Case Study: Sara

- 53 year old female with moderate-severe hot flashes and difficulty getting to sleep
- Menses were regular until one year ago, became irregular, and then stopped 16 months ago
- Tried herbal remedies...each helped for a few months
- Medical history, BP, physical exam are normal
- Flashes affect work productivity; wants something else

Explaining HT Benefit and Risk

HT risk is related to
- A woman’s baseline disease risks
- Her age
- Age at menopause
- Cause of menopause
- Time since menopause
- Prior use of any hormone
- HT types, route of administration, doses used
- Emerging medical conditions during treatment

NAMS Position Statements
NAMS Recommendations For Clinical Care
Menopause 2014, 21 (10): 125

- Menopausal hormone therapy is the most effective treatment for vasomotor symptoms
- Options include
  - Estrogen alone
  - Estrogen-progestogen
  - Estrogen-bazedoxifene
  - Progestogen alone, or
  - Combined OCs in persons requiring contraception

Prescription HT Options: ET and EPT

<table>
<thead>
<tr>
<th>Oral</th>
<th>Transdermal</th>
<th>Intravaginal</th>
</tr>
</thead>
<tbody>
<tr>
<td>ET</td>
<td>Micronized estradiol</td>
<td>Patches</td>
</tr>
<tr>
<td></td>
<td>Conjugated equine estrogens (CEE)</td>
<td>Gels</td>
</tr>
<tr>
<td></td>
<td>Synthetic conjugated estrogens</td>
<td>Emulsion</td>
</tr>
<tr>
<td></td>
<td>Esterified estrogens</td>
<td>Spray</td>
</tr>
<tr>
<td></td>
<td>Estropipate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estradiol acetate</td>
<td></td>
</tr>
<tr>
<td>EPT</td>
<td>CC-EPT</td>
<td>E+P combination patches</td>
</tr>
<tr>
<td></td>
<td>CS-EPT</td>
<td></td>
</tr>
</tbody>
</table>
Hormone Therapy Regimens

Month 1

- Estrogen Therapy (ET)
  - Estrogen
    - Continuous combined (CC) EPT
  - Estrogen
    - Progestin
      - Continuous-sequential (CS) EPT
        - Estrogen
          - Progestin 14d
            - Off for 14 d
      - Progestin 14d
        - Off for 14 d
  - Progestin 14d
    - Off for 14 d

Month 2

- Estrogen
- Progestin
- Continuous-pulsed (CP) EPT
  - 3d 3d

Choice of HT Regimen

- If no uterus: estrogen only
- If uterus present
  - Goal is to avoid vaginal bleeding entirely, or, at least, to make it predictable
- Endometrial activity predicts bleeding pattern
  - Recent spontaneous or induced bleeding
    - Use continuous sequential
  - No bleeding for >2-3 cycles
    - Use continuous combined
HT: Routes of Administration

- No clear benefit of one route of administration
- **Transdermal ET** has lower DVT/PE risk than **oral ET**
- Local ET preferred when solely vaginal symptoms
- With either route, progestogen required for endometrial protection from unopposed estrogen

NAMS Position Statements

“First Line” Use: Transdermal Estrogen

- Underlying medical conditions
  - History of DVT or PTE
  - High triglyceride levels
- Need for “steady state” drug release
  - Daily mood swings (especially while on oral HT)
  - Migraine headaches
- Inability to use oral tablets
  - Stomach upset due to oral estrogen intake
  - Problems with taking a daily pill
Hormone Therapy Dosages

- Therapeutic goal is lowest effective estrogen dose (plus low dose P) c/w goals, benefits, risks
  - Lower doses better tolerated, may have more favorable benefit-risk ratio than standard doses
- Local ET may be needed for persistent GSM symptoms
- Lower doses may take 6-8 weeks to provide relief

NAMS Position Statements

HT Starting Dosages

- Typical lowest doses of estrogen
  - 0.5 mg oral micronized 17ß-estradiol
  - 0.3 mg oral conjugated estrogen (CE)
  - 0.014-0.025 mg transdermal 17ß-estradiol patch
- Typical lowest doses of progestogen
  - 1.5 mg oral MPA
  - 0.1 mg oral norethindrone acetate
  - 0.5 mg oral drospirenone
  - 50-100 mg oral micronized progesterone

HT Standard Dosages

Estrogen
• 1.0 mg oral micronized 17ß-estradiol
• 0.625 mg oral conjugated estrogen (CE)
• 0.0375-0.050 mg transdermal 17ß-estradiol patch

Progestogen
• 2.5 mg oral MPA (CC) or 5.0 mg MPA (CS)
• 100 mg oral micronized progesterone (CC) or 200 mg PO at bedtime (CS)

Kaunitz AM, Manson JE. Obstet Gynecol 2015;126(4):859

HT: Adjusting Estrogen Dosage

• Start low dose transdermal or oral estrogen
• If suboptimal response, modify by...
  – Change the estrogen dose (upward)
  – Change the estrogen preparation
  – Change delivery systems (oral transdermal)
  – Consider an estrogen + androgen (Covaryx)
NAMS 2017: Progestin-Only Therapy Dosages

- P-alone may be used to treat hot flashes, but is not as effective as ET or EPT regimens
- P formulations effective in treating VMS (per day)
  - MPA 10 mg
  - Megestrol acetate 20 mg
  - Micronized progesterone 300 mg
- No long term studies have addressed the safety of P-only treatment on menopause symptoms

Bazedoxifene 10 mg + CE 0.45 mg
Duavee®

- Tissue selective estrogen receptor modulator (SERM)
- Progestin-free
- Reduces VMS frequency and severity
- Prevents loss of bone mass
- Treats GSM
- No increase in endometrial hyperplasia
- Amenorrhea, breast tenderness adverse event rates and overall safety similar to placebo

Taylor HS. Menopause; 2012; 19(4):479-485
Case Study: Marie

- 54 year old G$_2$ P$_2$ female
- 2 years post menopausal; no PMB. Non-smoker
- Severe hot flashes; impacts work and relationship with partner
- Has moderate HTN; controlled with ACE inhibitor
- BMI: 31 kg/m$^2$
- Recent labs
  - TC = 240 mg/dL, LDL = 165 mg/dL, HDL = 60 mg/dL
  - FBS: 95 mg/dL

---

**Moderate-Severe Hot Flashes**
(inadequate response to lifestyle modifications)

- No
- Yes

**Wants HT? No CI?**

- Yes
- No

**CV risk**

- Low (5%)<br>  - HT OK<br>  - HT OK*<br>  - Avoid
- Mod (5-10%)<br>  - HT OK<br>  - HT OK*<br>  - Avoid
- High (>10%)<br>  - Avoid<br>  - Avoid<br>  - Avoid

* Consider transdermal hormone therapy

* Prior hyst: E$_2$ alone
* Intact uterus: E+P or CEE + bazedoxifene

---

**Cl: Contra-Indication**
**HT: Hormone therapy**

HT OK

HT OK*

Avoid

Avoid
Case Study: Betty

- 53 year old G₄ P₃ female with vulvovaginal dryness and irritation
- Menopause 2 years ago; no history of post-menopausal bleeding
- Sexually active “one or twice a week”, but reports that sex is quite uncomfortable
- Intermittently uses water-based lubricant
- No complaint of hot flashes or sleep problems

Genitourinary Syndrome of Menopause (GSM)

- Vaginal changes
  - Vaginal spotting or bleeding; dryness
- Dyspareunia: poor lubrication, less vaginal elasticity, skin irritation, introital shrinkage
  - Negative impact on relationship(s), quality of life
- Bladder and urethra changes
  - Urgency, frequency, dysuria, urge incontinence
  - Often misdiagnosed as bladder infection; tests negative
  - No effect on stress incontinence or pelvic organ prolapse
Moderate-Severe Hot Flashes
(inadequate response to lifestyle modifications)

- No
  - GSM sxS?
    - Yes
      - Free of CI?
        - Yes: Try vaginal E₂ or ospemiphene
        - No: Intimate lubricants + moisturizers
    - No: Avoid HT

- Yes

CI: Contra-Indication
HT: Hormone therapy


GSM Treatment

- Vaginal lubricants often improve vaginal dryness and painful intercourse
- When HT is considered solely for this indication, vaginal estrogen is recommended
- Progestogen generally not indicated with low-dose, local vaginal estrogen

NAMS Position Statements
GSM: Treatment

- OTC lubricants
  - Water based: Astroglide®, KY Jelly®, Sliquid®
  - Silicone based: K-Y intrigue®, Astroglide X®
  - Oil based: Elegance®, olive oil, coconut oil
- Vaginal moisturizers: Luvena®, Vagisil®, Replens®
- Local estrogen therapy
  - Cream, vaginal tablet, vaginal ring
- Systemic HT (when prescribed for VMS)
- Oral ospemiphene
- Intravaginal DHEA

### Topical (Vaginal) Estrogen

<table>
<thead>
<tr>
<th>Composition</th>
<th>Brand Name</th>
<th>Dose and sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal cream 17β-Estradiol</td>
<td>Estrace® Vaginal Cream</td>
<td>Initial: 2.0-4.0g/d for 1-2 wk. Maint: 1.0g/d (0.1 mg/g)</td>
</tr>
<tr>
<td>Vaginal cream conj estrogens</td>
<td>Premarin® Vaginal Cream</td>
<td>0.5-2.0 g/d or twice/wk (0.625 mg/g)</td>
</tr>
<tr>
<td>Vaginal ring 17β-estradiol</td>
<td>Estring®</td>
<td>Ring contains 2 mg releases 7.5 mcg/d for 90 d</td>
</tr>
<tr>
<td>Vaginal ring E₂ acetate</td>
<td>Femring® (Systemic dose and indication)</td>
<td>Systemic dose ring for 90 d 12.4mg releases 50mcg/d 24.8mg releases 100mcg/d</td>
</tr>
<tr>
<td>Vaginal tablet E₂ hemihydrate</td>
<td>Vagifem® 10mcg</td>
<td>Initial: 1 tablet/d for 2 wk Maintenance: 1 tab 2x /wk</td>
</tr>
<tr>
<td>Estradiol vaginal insert</td>
<td>Imvexxy® 4 mcg and 10 mcg</td>
<td>Initial: 1 tablet/d for 2 wk Maintenance: 1 tab 2x /wk</td>
</tr>
</tbody>
</table>
GSM: Topical Vs. Systemic E$_2$

- Topical therapy is preferred when vaginal symptoms are the only complaint
  - Topical more effective than systemic oral ET
  - Presumed lower risk
- Systemic ET may worsen or provoke stress incontinence
  - Low dose transdermal ET has no effect on incontinence
- Only vaginal ET is effective for prevention of UTI

Cody JD. Cochrane Database Syst Rev. 2009

Ospemiphene (Osphena®)

- Selective estrogen-receptor modulator (SERM)
  - No direct estrogen effect
  - Only oral SERM approved in the US to treat moderate to severe dyspareunia
- Improvement in...
  - Dyspareunia
  - Vaginal maturation index
  - Vaginal pH
  - Vaginal dryness

NAMS, Menopause. 2013
Vaginal DHEA (Intrarosa®)

- Indicated for moderate to severe dyspareunia
- Vaginal Insert of 6.5 mg DHEA (prasterone)
  - Used daily at bedtime
  - Does not contain estrogen
  - Thought to work by converting to E and androgen
- Somewhat improved VVA and sexual function
- Postulated to improve sexual function beyond ameliorating vaginal symptoms

Urinary Tract Symptoms: Vaginal Estrogen

- Provides greater benefit than non-hormonal treatments
- Improves, may cure
  - Overactive bladder
  - Urge incontinence
  - Recurrent urinary tract infections
  - Urethritis (irritative) symptoms
- No effect on stress incontinence (oral ET may worsen it!)
- No HT product FDA approved for urinary health in US

HT Discontinuance

- After 2 years of use, recommend drug vacation to determine whether HT is still needed
- Vasomotor symptom recurrence similar whether tapered or abrupt discontinuance
  - 25-50% chance of symptoms recurring when HT discontinued
  - There is no consensus about whether stopping “cold turkey” or tapering is preferable (2017)
- Decision to resume HT must be individualized

NAMS Position Statements

Appendix
### ET: Oral Tablets

<table>
<thead>
<tr>
<th>Product</th>
<th>Brand</th>
<th>Standard dose</th>
<th>Low dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated equine estrogen (CEE)</td>
<td>Premarin</td>
<td>0.625 mg</td>
<td>0.3, 0.45 mg</td>
</tr>
<tr>
<td>Conjugated estrogen (synth)</td>
<td>Cenestin Enjuvia</td>
<td>0.625 mg</td>
<td>0.3, 0.45 mg</td>
</tr>
<tr>
<td>Esterified estrogen</td>
<td>Menest Estratab</td>
<td>0.625 mg</td>
<td>0.3 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product</th>
<th>Brand</th>
<th>Standard dose</th>
<th>Low dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estropipate</td>
<td>Ogen</td>
<td>0.625 mg</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>Ortho-est</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Generic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micronized $E_2$</td>
<td>Estrace</td>
<td>1.0 mg</td>
<td>0.5 mg</td>
</tr>
<tr>
<td></td>
<td>Generic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol acetate</td>
<td>Femtrace</td>
<td>0.9 mg</td>
<td>0.45 mg</td>
</tr>
</tbody>
</table>
## ET Transdermal: Patch*

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Mg/24 hr</th>
<th>Use/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alora</td>
<td>0.025, 0.05, 0.075, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Esclim</td>
<td>0.025, 0.0375, 0.05, 0.075, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Estraderm</td>
<td>0.05, 0.1 (reservoir)</td>
<td>2</td>
</tr>
<tr>
<td>Vivelle</td>
<td>0.05, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Vivelle-Dot</td>
<td>0.025, 0.0375, 0.05, 0.075, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Climara</td>
<td>0.025, 0.0375, 0.05, 0.06, 0.075, 0.1</td>
<td>1</td>
</tr>
<tr>
<td>Menostar</td>
<td>0.014 ☯</td>
<td>1</td>
</tr>
</tbody>
</table>

* All contain 17B-estradiol only

☯ Indicated only for prevention of osteoporosis

---

## ET Transdermal: Patch*

<table>
<thead>
<tr>
<th>Patch</th>
<th>Brand</th>
<th>Source</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>E₂ matrix</td>
<td>Alora, Climara, Vivelle, Vivelle-Dot, Menostar</td>
<td>Soy/Yams</td>
<td>0.05mg</td>
</tr>
<tr>
<td></td>
<td>E₂ is embedded in the adhesive layer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>applied directly to the skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E₂ reservoir</td>
<td>Estraderm</td>
<td>Soy/Yams</td>
<td>0.05mg</td>
</tr>
<tr>
<td></td>
<td>E₂ release is controlled by a co-polymer membrane; contains more layers than matrix patch</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**ET Transdermal: Gels, Emulsions, Sprays***

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Type</th>
<th>mg/24 hr</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divigel</td>
<td>Gel</td>
<td>0.25, 0.5, 1 mg/packet</td>
<td>1 packet daily</td>
</tr>
<tr>
<td>Elestrin</td>
<td>Gel</td>
<td>0.87 gm pump</td>
<td>1 pump daily</td>
</tr>
<tr>
<td>EstroGel</td>
<td>Gel</td>
<td>1.25 gm pump</td>
<td>1 pump daily</td>
</tr>
<tr>
<td>Estrasorb</td>
<td>Emulsion</td>
<td>1.74 gm/pouch</td>
<td>2 pouches daily</td>
</tr>
<tr>
<td>Evamist</td>
<td>Spray</td>
<td>1.53 mg/spray</td>
<td>1 spray daily</td>
</tr>
</tbody>
</table>

* All contain 17B-estradiol only

---

**ET Transdermal: Gels, Emulsions, Sprays***

<table>
<thead>
<tr>
<th>Transdermal</th>
<th>Brand</th>
<th>Source</th>
<th>Equivalents</th>
</tr>
</thead>
<tbody>
<tr>
<td>E&lt;sub&gt;2&lt;/sub&gt; gel</td>
<td>Divigel</td>
<td>Soy/Yams, Sunflower seeds, Rapeseed, Poppy seeds, Pine trees</td>
<td>1g packet</td>
</tr>
<tr>
<td></td>
<td>Elestrin</td>
<td>Soy, Rapeseed, Pine tree wood</td>
<td>2-3 pumps</td>
</tr>
<tr>
<td></td>
<td>EstroGel</td>
<td>Oil seed, Soy, Pine tree wood</td>
<td>.035mg</td>
</tr>
<tr>
<td>E&lt;sub&gt;2&lt;/sub&gt; emulsion</td>
<td>Estrasorb</td>
<td>Soy</td>
<td>2 packets</td>
</tr>
<tr>
<td>E&lt;sub&gt;2&lt;/sub&gt; spray</td>
<td>Evamist</td>
<td>Soy/Yams</td>
<td>3 sprays</td>
</tr>
</tbody>
</table>
**Progesterone/ Progestin Products**

<table>
<thead>
<tr>
<th>Oral Progestin</th>
<th>Equiv dose</th>
<th>Available doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPA (Provera®)</td>
<td>5-10 mg</td>
<td>1.2, 2.5, 5, 10 mg</td>
</tr>
<tr>
<td>Micronized progesterone (MP) (Prometrium®)</td>
<td>200-300 mg</td>
<td>100, 200 mg</td>
</tr>
<tr>
<td>Drospirenone (DRSP)</td>
<td>0.5 mg/d</td>
<td>0.5 mg/d</td>
</tr>
<tr>
<td>Norethindrone acetate (NETA)</td>
<td>1.0 mg/d</td>
<td>0.5, 1.0 mg/d</td>
</tr>
<tr>
<td>Norethindrone (NOR)</td>
<td>0.7-1.0 mg/d</td>
<td>0.35 mg</td>
</tr>
<tr>
<td>Norgestimate (NGM)</td>
<td>0.09 mg</td>
<td>0.09 mg</td>
</tr>
<tr>
<td>Norgestrel (LNg)</td>
<td>150 mcg/d</td>
<td>150 mcg/d</td>
</tr>
</tbody>
</table>

**EPT: Oral Tablets**

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Estrogen</th>
<th>Progestin</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activella</td>
<td>17β-E2 1 mg</td>
<td>NETA 0.5 mg</td>
<td>Once daily oral</td>
</tr>
<tr>
<td>Angeliq</td>
<td>17β-E2 1 mg</td>
<td>Drospirenone 0.5 mg</td>
<td>Once daily oral</td>
</tr>
<tr>
<td>FemHRT</td>
<td>EE 5 µg; EE 2.5 µg</td>
<td>NETA 1 mg; NETA 0.5 mg</td>
<td>Once daily oral</td>
</tr>
<tr>
<td>Prefest</td>
<td>17β- E2 1 mg</td>
<td>Micronized NGM 0.09 mg</td>
<td>E (alone) 3 days; E+P 3 days</td>
</tr>
<tr>
<td>Premphase 14 active/14 pbo</td>
<td>CEE 0.625 mg</td>
<td>MPA 5 mg</td>
<td>Once daily oral (CS-EPT)</td>
</tr>
<tr>
<td>Prempro 28 active</td>
<td>CEE 0.625 mg; 0.45 mg; 0.3 mg</td>
<td>MPA 5.0 mg; 2.5 mg; 2.5 mg; 1.5 mg</td>
<td>Once daily oral (CC-EPT)</td>
</tr>
</tbody>
</table>
### EPT: Transdermal Patches

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Estrogen</th>
<th>Progestin</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>CombiPatch</td>
<td>17(\beta)-E2 0.05 mg 0.05 mg</td>
<td>NETA 0.14 0.25 mg</td>
<td>Twice weekly</td>
</tr>
<tr>
<td>Climara Pro</td>
<td>17(\beta)-E2 0.045 mg</td>
<td>LNG 0.015 mg</td>
<td>Once weekly</td>
</tr>
</tbody>
</table>

### General References

NAMS References

- The 2017 hormone therapy position statement of NAMS. Menopause 2017; 24(7): 728–753.

NAMS References

- NAMS Statement on Continuing Use of Systemic Hormone Therapy After Age 65. Menopause 2015; 22(7): 693
- Kaunitz AM, Manson JE. Failure to treat menopausal symptoms: a disconnect between clinical practice and scientific data. Menopause. 2015 Jul;22(7):687-8
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• Avis NE, et. al, Duration of Menopausal Vasomotor Symptoms Over the Menopause Transition. JAMA Intern Med 2015; 175(4):531-539