Prescription Writing : Module 3

Prescription Writing Of MHT
References

• Clinical Practice Guidelines on Menopause 2012, updated 2015, Indian Menopause Society

• Clinical Practice Guidelines on Post Menopausal Osteoporosis 2012, Indian Menopause Society

• North American Menopause Society 2012, Indian Menopause Society

• NICE 2015

• Endocrine Society 2015

• 2016 IMS Recommendations on women’s midlife health and menopause hormone therapy
Grades Of Evidence And Recommendations:

- High Quality: A
- Moderate Quality: B
- Low Quality: C
- Very Low Quality: D

Strength of Recommendations:

- Strong Recommendations: “Recommend”
- Weak Recommendations: “Suggest”
Take Home Message

- Target population for initiation of HT is usually within 10 yrs of menopause
- HT initiated in early postmenopausal period in healthy women is safe
- Like all medicines, HT needs to be used appropriately, but it is essential that women in early menopause who are suffering menopausal symptoms should have the option of using HT

Right woman, Right Age, Right HT, Right dose, Right route
Agenda

• Concepts and counseling in Hormone Therapy

• Therapeutic Lifestyle Management

• Calcium and Vitamin D

• Regimes of HT, duration, starting and stopping HT

• Contraindications of HT
Agenda

• Use of HT in special situations

• Side effects of HT and their management

• Tibolone

• Raloxifene

• Guidelines
Therapeutic Lifestyle Management

3-Step Management of Menopause

Eat Right

Exercise

Medication
Therapeutic Lifestyle Management

• Physical Activity, Targeted Exercise
• Nutrition
• Avoid alcohol, tobacco
• Stress reducing strategies
• Meditation, Paced respiration

• Massage, Hobbies Nutrition
• Emotion stability
• Positive attitude
• Family involvement
• Spiritual Attitude
• Sleep
Living With Menopause - Physical Fitness

Mind Your Body

- Aerobics
- Weight Bearing
- Flexibility
- Balance
Benefits Of Exercise

- Helps to maintain a healthy weight
- Increase in metabolic rate
- Improves bone density
- Coordination and balance
- Muscle strength and joint mobility
- Improves lipid profiles, reduces CVD risk
- Improves genitourinary problems
- Relieves depression

- Induces sleep
- Improves quality of life
Physical Activity Vs. Exercise

• Physical activity is any bodily movement, produced by your muscles

• Exercise is a type of physical activity that is planned, structured, repetitive and purposeful to improve or maintain some component of your fitness or health

• Both are important for health
Intensive Counseling On Therapeutic Lifestyle Management

• Physical Activity
• Exercise—Aerobic—CVS
• Strengthening, Resistance training—Muscle
• Flexibility, Range of motion—Muscle, Joints

• Balance and Posture—prevention of falls
• Breathing—Respiratory system
• Kegels—pelvis
Exercise Prescription

Recommendations for Physical activity and Exercise

• Exercise should include aerobic, muscle strengthening, breathing and balance
• 30 minutes of moderate-intensity physical activity mostly 5 days a week
• Muscle-strengthening activities should be included at least 2 days/week
• 30 minutes/day - For fitness and reduced risk of chronic disease
• 60 minutes/day - For prevention of weight gain
• 60–90 minutes/day - To avoid regain of weight loss
Living With Menopause - Balanced And Nutritious Diet

Mind Your Food
BALANCED DIET FOR ADULT WOMAN

- Fats Oil: 20 gm
- Sugar: 20 gm
- Milk & Milk Products: 300 gm
- Pulses: Vegetarian - 30 gm, Non-vegetarian - 60 gm
- Vegetables: 300 gm
- Fruits: 100 gm
- Cereals and Millets: 270 gm
- Non-Veg: 30 gm
Recommendation

• Sugar 6 tsp/day
• Salt 1.5 tsp or 3-5 gms/day
• Oil 2 level tbs /day
• Fruit- 100 gms/day
• Vegetables- 300 gms/day
• Drink 8 glasses of water every day
• Add powdered flaxseed, cinnamon, fenugreek, saunf in salads and curds
Recommendation

- Snack on two to four nuts like almonds, walnuts or dried-fruit like dates, figs, apricot and seeds like pumpkin, sunflower

- Foods that are rich in phytoestrogens include lentils, kidney beans, and Bengal gram and soybean
Tea, Coffee And Diary Products

- Avoid more than 200 mg/day of caffeine
- Limit intake of tea and coffee to 3 cups a day
- 1 cup (150 mL) of brewed coffee is equal to 120 mg of caffeine
- 65 mg for 1 cup of instant coffee and tea
- Consume a minimum of 500-600 mL of milk or curds (low fat) to build on calcium bank in bones
- Support it with lots of vitamin C-rich fruits/vegetables to favor calcium absorption
Mind Your Sleep

- Go to bed and get up at the same time each day
- Sleep in a dark quiet room at a comfortable temperature
- Avoid large meals, exercise, caffeine, nicotine, and liquid two hours before sleep
- Maintain dim light bedroom environment with no gadgets around
Living With Menopause - Mental Well Being

Mind Your Mind

- Be a Learner
- Pursue a Hobby
- Continue working
- Read, Converse
The greatest mistake in the treatment of diseases is that there are Physicians for the body and Physicians for the soul although the two cannot be separated

- Plato
Living With Menopause: Spirituality

Mind Your Soul

- Prayer
- Meditation
- Be Positive
- Live without expectation
Living With Menopause - Emotional Well Being

Mind Your Emotions

• Bond with Family and Friends
• Participate in Social Activity
• Enjoy Conversation
• Be Happy and Contended
Living With Menopause - Nutrition

The Recommended Dietary Allowance (RDA) of calcium and Vitamin D for Adult Indian

- Calcium — >800 mg/day— 1,200mg/day
  - Upper limit of normal —2,500mg/day

- Vitamin D — 1500-2000 IU
  - Upper limit of normal—10,000 IU
Prescription Writing - Nutrition

- Assess the total calcium intake from dietary sources and if needed, supplements are used to correct the deficient balance. The intake should exceed >800 mg/day (Grade B)

- Risk of CV events, calculi are not observed with the recommended doses of calcium

- Prevention of kidney stones is possible if calcium is taken in the prescribed dose with sufficient fluids and prefer citrate
**Healthy Balanced Diet—Calcium Deficiency**

- Lactose intolerance and limited use of dairy products
- Consume large amounts of protein or sodium, it increases calcium excretion
- High oxalate diets
- Aging
- Vitamin D deficiency

- Long-term treatment with corticosteroids, thyroid hormone excess, thiazide diuretics
- Bowel or digestive diseases that decrease ability to absorb calcium, such as inflammatory bowel disease or celiac disease
Choosing Calcium Supplements—Factors To consider

• Amount of calcium
  - Elemental calcium is the actual amount of calcium in the supplement that the body absorbs for bone growth and other health benefits
• Tolerability
• Absorbability
• Cost
• Relation to meal
## Types Of Calcium Supplements

<table>
<thead>
<tr>
<th>Common Calcium Supplements</th>
<th>% of Elemental Calcium</th>
<th>Calcium mg/ 1000 mg of salt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Carbonate</td>
<td>40</td>
<td>400</td>
</tr>
<tr>
<td>Calcium Citrate</td>
<td>21</td>
<td>241</td>
</tr>
<tr>
<td>Calcium Gluconate</td>
<td>9</td>
<td>93</td>
</tr>
<tr>
<td>Calcium Lactate</td>
<td>13</td>
<td>184</td>
</tr>
<tr>
<td>Calcium Phosphate Tribasic</td>
<td>38</td>
<td>388</td>
</tr>
</tbody>
</table>

Naturally derived calcium forms like dolomite, oyster shell, bone meal may contain lead and other toxic minerals.
# Calcium carbonate Vs. Calcium citrate

<table>
<thead>
<tr>
<th>Calcium Carbonate</th>
<th>Calcium Citrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needs acid to dissolve and for absorption</td>
<td>Doesn’t require stomach acid for absorption</td>
</tr>
<tr>
<td>Less stomach acid as we age- need more may cause poor absorption</td>
<td>People over age 50- better absorbed</td>
</tr>
<tr>
<td>To be taken with meals</td>
<td>May be taken anytime</td>
</tr>
<tr>
<td>Least expensive form of calcium</td>
<td>May cost more</td>
</tr>
</tbody>
</table>

Calcium gluconate, calcium lactate, and calcium phosphate have less calcium than the carbonate and citrate forms.
Calcium Supplements

- Limit 500 mg calcium at one time from food and/or supplements
- Spread calcium sources throughout the day
- Start supplements with 500 mg calcium daily for about a week, gradually adding more to reduce side effects
- Absorption of calcium is decreased when taken with foods rich in fires and fat, iron, zinc, spinach, coffee, alcohol and antacids
Calcium Supplements

• Thyroid medications, corticosteroids, tetracyclines and anticonvulsants and calcium should be taken separately
• Contraindicated in patients with hypercalcaemia, renal insufficiency and with caution in nephrolithiasis
• Excess amounts more than 2,500 mg a day - effect kidneys and can reduce the absorption of other minerals like iron, zinc and magnesium
Vitamin D

- Vitamin D and its active metabolite 1,25-dihydroxyvitamin D (1,25(OH)2D) have classical actions on calcium balance and bone metabolism.
- The intestine cannot absorb calcium and phosphate adequately due to insufficient 1,25(OH)2D, leading to secondary hyperparathyroidism and a lack of new bone mineralization.
- Individuals who have more vitamin D are able to absorb more calcium.
- In combination with adequate vitamin D, calcium levels of about 800 mg per day can be achieved by a healthy diet that includes daily intake of calcium rich foods.
Vitamin D - Sunlight

- Sunlight
  - 7-Dehydrocholesterol
    - Cholecalciferol (Vitamin D₃)
      - Liver
        - 25-hydroxyvitamin D₃
          - Kidney
            - 1,25-dihydroxyvitamin D₃
              - Maintains calcium balance in the body

Dietary Intake:
- Vitamin D3 (Fish, Meat)
- Vitamin D2 (Supplements)
Despite the sunny climate there is widespread vitamin D deficiency in Asian Indians of all age groups including children, pregnant women and adult males and females living in urban and rural areas in India.
Vitamin D Deficient Population

- Age 50 or older - the skin becomes less effective with advancing age as a source
- Dietary intake is low
- Low exposure to sun
- Dark skin
- Pollution
Vitamin D Deficient Population

- Overweight/ Obesity
- Gastric bypass surgery
- Milk allergy or lactose intolerance
- Liver or digestive diseases, such as Crohn's disease or celiac
Vitamin D From Sunlight Exposure

- Amount varies with time of day, season, latitude and skin pigmentation

- It is preferable to get vitamin D through sunlight by exposing 20% of body surface area at least 30 minutes between 10 am and 3 pm, depending on the season, latitude, altitude, pollution, and skin pigmentation
Vitamin D From Sunlight Exposure

• The sunlight between 11 am to 2 pm is preferably the best

• Clothing, sunscreen, window glass and pollution reduce amount produced
Vitamin D Necessary For Calcium Absorption

- Choose a supplement with vitamin D unless obtaining vitamin D from other sources
- Follow age group recommendation. Avoid going over a daily combined total of 2,000 IU from food and supplements
- It’s not necessary to consume calcium and vitamin D at the same time to get the benefit of enhanced calcium absorption
Management Of Vitamin D Deficiency

• Cholecalciferol (vitamin D3) tablet or powder 60,000 IU/once a week for eight weeks preferably with milk or

• One IM injection of 6,00,000 IU is given to correct the deficiency (not to be repeated before three months and may be given after confirmation of persisting low levels of vitamin D)

• Maintenance therapy(from natural sources or supplements) is advised after correction of the deficiency
Maintenance Therapy

- Cholecalciferol tablet or powder 60,000 IU once a month in summer or twice a month in winter or
- Vitamin D supplements by oral spray or oral tablets of 2,000 IU/day, or
- Injection of Cholecalciferol 3,00,000 IU IM, twice a year or 6,00,000 IU IM once a year
- Cholecalciferol, 1,000 IU daily, will raise blood levels, on average, by approximately 10 ng/mL
Hormone Therapy Terminology

- HT/MHT—Hormone therapy
- HRT- Hormone replacement therapy as in premature menopause
- ET - Estrogen therapy
- EP - Estrogen Progesterone therapy
- AT- Androgen therapy
Menopausal Hormone Therapy

Wide range of hormonal products:

- Natural Estrogens
- Progestogens
- Androgens
- Tibolone
Types Of Estrogens

Natural Estrogens - Menopausal HT

• Native Estrogen - 17 beta Estradiol, Estrone, Estriol
• Conjugated Equine Estrogen

Synthetic Estrogens - Oral contraceptives

• Ethinyl Estradiol
Natural Estrogens Used For Menopausal HT

17β-estradiol

- Minimal load on liver

Estradiol Valerate

- Metabolizes in the liver to 17β-estradiol + valeric acid

Conjugated Equine Estrogens

- A mixture of Estrone & Equilin Sulphate (200 compounds), thus 2-3 times extra load on liver

Estadiol hemihydrate is the 17 beta isomer of estradiol

$ As compared to CEE $ and EV $^\#$ Conjugated Equine Estrogens $^*$$ Estradiol Valerate


Synthetic Estrogens Used For Menopausal HT

- Synthetic estrogens: estrogenic synthetic molecules (ethinyl estradiol usually used in oral contraceptives)
- High potency with regard to adverse hepatic effects and potential secondary risks (hypertension and thromboembolic disease) but low doses used in HRT
- Hepatic potency is 4 to 18 times higher than native estrogens
Potency

• Estriol is least potent short acting estrogen

• Conjugated Equine estrogen contains mixture of estrogens

• Estradiol is 12 times more potent than estrone and 80 times more potent than Estriol
### Dosage of Estrogen

<table>
<thead>
<tr>
<th>Estrogens</th>
<th>Ultra low</th>
<th>Low</th>
<th>Standard</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated equine estrogens (mg)-oral</td>
<td>0.15</td>
<td>0.3, 0.45</td>
<td>0.625</td>
<td>1.25</td>
</tr>
<tr>
<td>17β-estradiol (mg) oral</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Estradiol valerate (mg)-oral</td>
<td>1</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Transdermal 17β-estradiol (µg)</td>
<td>14</td>
<td>25</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>
Low Dose Adjustive Therapy

• Biological variables with the sex steroid synthesis and function

• Variable response of an individual to estrogen deficiency

• Application of the pharmacodynamics of various hormones and regimes to suit an individual woman’s need

• Start with age appropriate low dose therapy
Lower HT Doses —Why?

- One type of HT cannot fit all populations of postmenopausal women

- Benefits of HT can be maintained with lower doses than previously used whilst minimizing risks and possibly side effects

- Improved continuance and compliance to achieve potential long-term health benefits

- Efficacy in prevention of osteoporosis is not compromised
Exceptions To Low Dose Therapy

• Premature ovarian failure

• Severe osteoporosis

• Predominance of psychological problems, e.g. climacteric depression
Non-oral Routes-Indications

Indications for use of the transdermal route first line:

Transdermal estrogen has a neutral effect on triglycerides, C-reactive protein, and sex hormone binding globulin

- Triglyceridemia, Hyperlipidemia
- Increased C-reactive protein
- Migraine
- Diabetes
Non-oral Routes - Indications

- Controlled hypertension
- Existing gall bladder disease
- Obesity
- Smoking
- Previous venous thromboembolism
- Varicose veins
- Personal preference
Synthetic Estrogens – Not Used For MHT

- Ethinyl estradiol, Mestranol
- 750-1000 times more potent than natural estrogens
- Enhances hepatic effects which increases synthesis of clotting factors, angiotensin, SHBG
Role Of Intrauterine Levonorgesterol System

- During perimenopause
- Contraception
- Control of bleeding - AUB
- Women with side effects for oral progestogens
Overcoming Side Effects Of Progesterone In HT

Natural Progesterones

- Choosing natural progesterone and Dydrogesterone which are metabolically friendly

- Early reports on neutral effect on breast
Overcoming Side Effects Of Progesterone In HT

Androgenic progesterones

• Implicated in increased risk of:
  • Breast cancer
  • CVD events
  • Blunt beneficial effect of estrogen on lipids
• Useful for hemostatic control in AUB
Progesterone After Surgical Menopause

- Residual ovarian tissue—Endometriosis, frozen pelvis

- Residual endometrium—Endometrial ablation, supracervical hysterectomy
Concepts In Prescribing HT

• Different routes of administration
• Potentially different effects
• Risks and benefits differ at different age group
• Response to HT may differ among individuals and also in the same individual over period of time

Individualization or Personalization of HT
Concepts In Prescribing HT

• Identify goal of treatment
  • Rule out contraindications
  • Counseling, Variable response of an individual to estrogen deficiency
• Timing (window of opportunity)
  • Early start
  • Maintenance of estrogenic benefits
Concepts In Prescribing HT

- Patient selection
  - Avoiding generalized prescribing
- Personalization
  - Tailoring dose to patient
  - Continuation and tapering the dose with age
Concepts In Prescribing HT

• Selection of type of estrogen, type of progesterone
• Route of therapy
• Dosage-minimum effective dose
• Risk/Benefit analysis
• Tailor Evaluate response
• No mandatory time limit
• Follow up annually
Benefits Of Hormone Therapy

- 3 most beneficial effect of estrogens - symptom relief, urogenital atrophy and bone
- The most effective treatment for vasomotor symptoms is HT (GRADE A)
- Progesterones or low dose oral contraceptive pills can be used in the menopause transition phase for relief of symptoms (GRADE A)
- Vaginal estrogen therapy - most effective in the treatment of urogenital atrophy (Grade A)
Benefits Of Hormone Therapy

• Chronic therapy for atrophic vaginitis requires the use of the smallest effective dose; treatment can be continued indefinitely although safety data from studies do not go beyond 1 year (GRADE C)

• Recurrent Urinary Tract Infection after ruling out other causes (GRADE A)
Benefits Of Hormone Therapy

• EPT/ET- for prevention and treatment of osteoporosis; reduces the risk of spine, hip and other osteoporotic fractures by 33-40% (GRADE A)

• HT for bone protection within ten years of menopause (GRADE B)
Benefits Of Hormone Therapy

- Improves quality of life. Estrogen can be prescribed to enhance mood in women with estrogen deficiency related depressive symptoms. The effect appears to be greater for perimenopausal symptomatic women than for postmenopausal women (Grade A)
Possible Benefits Of Hormone Therapy

- Decrease in the risk for Type 2 diabetes (GRADE B)
- Decreases the abdominal obesity (GRADE B)
- Estrogens - protective effect on OA (GRADE B)
- Estrogen benefits verbal memory over the short period after surgical menopause (GRADE B)
- Reduces the neovascular macular lesions (GRADE C)
Before Prescribing MHT

• Dialogue and documentation
• Medical conditions and risks should be identified
• Pre HT tests conducted
• Dose, duration and follow up is clearly indicated
• Addition of progestogens - Intact uterus, endometriosis, stage I & II endometrial CA and supracervical hysterectomy
• Offer hormone therapy, if not contraindicated
Communication

• Dialogue and documentation
• The physician should discuss with the woman about
  (a) the benefits, risks and side effects of HT
  (b) the types of HT available, and the options suitable for her
  (c) the way treatment will be monitored
  (d) how long HT might be used
  (e) economic consideration
  (f) other available options

This will improve compliance of treatment
WHI-E: Number Of Events Per 10,000 Women Per Year Of CEE Therapy
Interpretation Of Risk

- Rare = Rare  >1/10,000 and <1/1,000 women per year
- Very Rare = Less than or equal to 1 per 10,000 women per year
### Explaining HT: Benefits

**WHI- Number Of Less Events on Estrogen vs. Placebo per 10,000 Women per year of HT Use between the age group of 50-59 years R (GRADE A)**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number of Less Events with Estrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial Infarction</td>
<td>12</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>8</td>
</tr>
<tr>
<td>Total Deaths</td>
<td>10</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>18</td>
</tr>
<tr>
<td>Fractures</td>
<td>5</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>6</td>
</tr>
</tbody>
</table>
Based on WHI- Number Of Excess Events on HT vs Placebo per 10,000 Women per year of HT Use between the age group of 50-59 years - R (GRADE A)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Estrogen</th>
<th>WHO/ CIOMS definition of Risk</th>
<th>Estrogen + Progesterone</th>
<th>WHO/ CIOMS definition of Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE</td>
<td>4</td>
<td>Rare &gt;1/10,000 and &lt;1/1,000</td>
<td>11</td>
<td>Rare &gt;1/10,000 and &lt;1/1,000</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
<td>Rare &gt;1/10,000 and &lt;1/1,000</td>
<td>4</td>
<td>Rare &gt;1/10,000 and &lt;1/1,000</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td>5</td>
<td>Rare &gt;1/10,000 and &lt;1/1,000</td>
</tr>
<tr>
<td>CVD</td>
<td></td>
<td></td>
<td>5</td>
<td>Rare &gt;1/10,000 and &lt;1/1,000</td>
</tr>
</tbody>
</table>
## Absolute Risk Of Breast Cancer

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk per 1000 women</th>
<th>Extra Breast Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Risk</td>
<td>45</td>
<td>-</td>
</tr>
<tr>
<td>HT 5 Y (CEE + MPA)</td>
<td>47</td>
<td>2</td>
</tr>
<tr>
<td>HT 15 Y (CEE + MPA)</td>
<td>57</td>
<td>12</td>
</tr>
<tr>
<td>Menopause after 54</td>
<td>58</td>
<td>13</td>
</tr>
<tr>
<td>BMI &gt; 31</td>
<td>59</td>
<td>14</td>
</tr>
<tr>
<td>Lifetime Excess Alcohol</td>
<td>72</td>
<td>27</td>
</tr>
</tbody>
</table>
Being overweight can cause at least 7 types of cancer in women.

Obesity can increase their risk of 7 types of cancer in women by 41%.

- Oesophagus
- Breast
- Gallbladder
- Pancreas
- Kidney
- Bowel
- Womb

Larger circles indicate cancers with more UK cancer cases linked to being overweight or obese.

Healthy Weight:
BMI of 18.5 to 25
194 women in 1000 develop one of these cancers

Overweight:
BMI of 25 to 30
229 women in 1000 develop one of these cancers
36 more cancers per 1000 women

Obese:
BMI of 30 or more
274 women in 1000 develop one of these cancers
81 more cancers per 1000 women
**HT- Breast**

**Perception**
- All types of HT cause an increased risk of breast cancer within a short duration of use

**Evidence**
- The risk of breast cancer associated with MHT in women over 50 is complex (B)
- Any possible increased risk associated with MHT may be decreased by selecting women with lower baseline risk including low breast density and by providing education on preventive lifestyle measures (reducing weight, reducing alcohol intake, increasing physical activity) [D]
HT- Breast

Perception

• All types of HT cause an increased risk of breast cancer

Evidence

• WHI cohort showed a small increase in risk of breast cancer of about eight extra cases per 10,000 women per year. Risk was not increased in first-time hormone users [GRADE A] The MHT attributable risk is small and decreases when treatment stops [B]

• The increased risk is primarily associated with the addition of a synthetic progestogen to estrogen therapy and to duration of use [B]

• The risk may be lower with micronized progesterone or dydrogesterone [C]
There is a lack of safety data supporting MHT use in breast cancer survivors.
Cardiovascular System - HT

Perception

• HT increases the risk of coronary heart disease (CHD) throughout the whole postmenopausal period

Evidence

• HRT in women aged 50 - 59 years does not increase CHD risk in healthy women and may even decrease the risk in this age group and all-cause mortality. [Grade A]
• Data on daily continuous combined estrogen-progestin are less robust but other combined therapy regimens appear to be protective as shown in Danish and Finnish studies [A]

• Recent meta-analyses and WHI 13-year follow-up data all show a consistent reduction in all-cause mortality for MHT users [A]

• It is not recommended to initiate MHT beyond age 60 years solely for primary prevention of CHD [A]
CHD

- Women within 10 years of menopause 0.89, whereas it is 1.7 in women more than 20 years after menopause.

Breast

- In new users - hazard ratio > by year 5 and fails to be significant at any point during the trial.
- With estrogen alone no increase over a 7 year period.
Venous Thromboembolism

- Oral estrogen is contraindicated in women with a personal history of VTE [A]

- Transdermal estrogen should be first choice in obese women with VMS [B]

- VTE risk increases with age and with thrombophilic disorders

- The risk of VTE increases with oral MHT but is rare below age 60
Venous Thromboembolism

- Observational studies and biological plausibility point to a lower risk with low-dose transdermal therapy
- Some progestogens may be associated with a greater VTE risk [C]
- The incidence of VTE is less frequent amongst Asian women [C]
- Population screening for thrombophilia is not indicated prior to MHT use [C]
HT - Bone

Perception

• **HT** should not be used for bone protection because of its unfavorable safety profile

• Recommendations by health authorities (EMEA, FDA) limit the use of HT to a second-line alternative

• HT could only be considered when other medications failed, were contraindicated or not tolerated, or in the very symptomatic woman
HT - Bone

Evidence

• For the age group 50-59, HT is safe and cost-effective

• Overall, HT is effective in the prevention of all osteoporosis-related fractures, even in patients at low risk of fracture [GRADE A]
HT - Bone

Perception

• HT is not as effective in reducing fracture risk as other products (bisphosphonates, etc.)

Evidence

• Although no head-to-head studies have compared HRT to bisphosphonates in terms of fracture reduction, there is no evidence to suggest that bisphosphonates or any other antiresorptive therapy are superior to HRT
HT — Benefit Risk Analysis

Assess patient criteria
- Symptomatic woman with interest in MHT who is:
  - Age < 60 Y or
  - < 10 Y since menopause

If age > 60 or > 10 y since menopause
  → Consider other options

Consider circumstances where MHT should not be used
  (TABLE 4)
  Avoid if:
  - Unexplained vaginal bleeding
  - Stroke, TIA, MI, PE, VTE
  - Breast or endometrial cancer
  - Active Liver Disease

Present
  → Consider other options
Exercise caution in women with:
- Diabetes
- Hypertriglyceridemia
- Active gallbladder disease
- Increased risk of Breast cancer or CVD
- Migraine with aura

Consider other options

Evaluate Cardiovascular Risk

Present

Evaluate Breast Cancer Risk

ABSENT

ACCEPTABLE

High

High to Moderate

ACCEPTABLE

Consider other options
Evaluate Breast Cancer Risk

Yes

Estrogen plus Progestogen Tibolone

No

Estrogen Alone

ACCEPTABLE
Patient Characteristics That May Be Favorable For Estrogen/Androgen Combination

- Surgical menopause
- Continued VMS despite estrogen replacement
- Decreased well-being despite estrogen replacement
- Acquired sexual desire dysfunction
- In India, androgen formulations for use at menopause are unavailable. Tibolone is a good alternative
Prescribing HT

Important points to consider

• When to Start?
• What Therapy? Which route? Which regime?
• Tackling side effects
• How long to give?
• When to Stop?
Starting HT

- Explain to women

- To report at 1, 3-month review appointment, that unscheduled vaginal bleeding is a common side effect of HRT within the first 3 months of treatment

- It will take 3-4 weeks for control of symptoms
Menopausal Hormone Treatment

- Uterus Intact
  - Estrogen Progesterone Therapy
  - First Line Management

- Post Hysterectomy
  - Estrogen Therapy

HT should be limited to symptomatic patients without excess risk of heart disease, stroke or breast cancer.
Estrogen Progesterone Therapy

• Unopposed estrogen prescribed for postmenopausal women who have had a hysterectomy

• Estrogen and Progesterone is prescribed for a woman with uterus, this reduces the risk of Endometrial Hyperplasia and Cancer associated with unopposed estrogen therapy
Route Of Administration

Oestrogen

• Oral, Transdermal, Vaginal

Progestogen

• Oral, Vaginal, Intra-uterine
How HT Is Given?

Continuous Sequential MHT
- Estrogen
- Progestogen
- Day 14
- Sequential therapy without tablet break
- Regular bleeding at end of cycle

Continuous Combined MHT
- Estrogen
- Progestogen
- Day 14
- Combined therapy without tablet break
- No bleeding at end of cycle

Continuous Estrogen
- Estrogen
- No tablet break
- No regular bleeding
Prescription Writing For Menopausal Symptoms

Estrogen Therapy

- Tab CEE 0.3 mg, 0.625 mg
- 17 beta-estradiol 1,2 mg/ Estradiol valerate
  1,2 mg daily orally
- Transdermal 17 beta-estradiol 25 - 100 gms
- Tab Tibolone 2.5 mg daily
Estrogen progesterone therapy in women with uterus in the peri and early menopause

Continuous sequential EPT

- 17 beta-estradiol/Estradiol valerate 1 mg/2 mg or
- Oral CEE 0.3 mg/0.625 mg or estradiol valerate 1 mg/2 mg or
- Transdermal 17 beta estradiol 25-100 gms daily
- And 10 mg dydrogesterone or micronized progesterone 200 mg 10-14 days.
Continuous Sequential EPT

- Estrogen is used everyday, with progesterone added cyclically for 10-14 days during each month.
- Uterine bleeding occurs in about 80% of women when progestogen is withdrawn, although bleeding can begin 1-2 days earlier, depending on the type and dose of progestogen used.
- In a typical continuous-cyclic regimen, progestogen is started on day 1 or day 15 each month.
Estradiol/Dydrogesterone 1/10 Or Sequential regimen

- Estrogen deficiency symptoms in postmenopausal women ≥6 months since last menses
Prescription Writing For Menopausal Symptoms

Estrogen progesterone therapy in women with uterus in the post menopausal women

Continuous combined EPT

- 17 beta-estradiol and dydrogesterone 5 mg daily
- CEE 0.3 mg/0.625 mg, 17 beta-estradiol/estradiol valerate 1 mg/2 mg or transdermal
- 17-beta estradiol 25-100 µgms daily and micronized progesterone 100 mg daily
- Tibolone 2.5 mg daily
Continuous Combined EPT

- Continuous-combined EPT
- Fixed doses of estrogen and progesterone are administered everyday
- Approximately 40% incidence of irregular spotting or bleeding in the first six months
Estrogen/Dydrogesterone 1/5: Combined

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 |
|-----|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Estrogen | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Progestin | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |

No bleeding

Estrogen deficiency symptoms in postmenopausal women ≥12 months since last menses
Perimenopausal Women

- The options available are monthly cyclic and sequential regimens
- Continuous combined regimens should not be used in perimenopausal women because of the high risk of irregular bleeding
Postmenopausal Women

- Continuous combined therapy is the regime of choice and induces endometrial atrophy
Problems From HT

• Bleeding problems

• Insufficient symptomatic response

• Side effects
Questions To Ask?

• When does the bleeding occur with respect to the estrogen and progesterone phase?

• How long and how much?

• History to rule out poor compliance, drug interactions medical conditions
Bleeding- Problem Of Compliance

• Scheduled or withdrawal bleeding—with the cyclic, cyclic combined and sequential EPT

• Unscheduled or irregular bleeding with continuous combined EPT
Causes Of Abnormal Bleeding

• Poor compliance- missing tablets especially progesterone
• Poor gastrointestinal absorption- IBS, Coeliac disease, Crohn’s
• Asynchrony of endogenous and exogenous hormones (in pre and perimenopausal women)- in a regular cyclical woman add progesterone from the 11th day before her expected cycle to mimic her natural cycle length
• Premenopausal woman with erratic cycles- an OCP unless contraindicated is good option or adjust the dose and type of progesterone
Causes Of Abnormal Bleeding

• Atrophic endometrium —commonly seen with continuous combined regimes

• Coagulation defects—thrombocytopenia, von Willebrand’s disease, on warfarin or high dose aspirin

• Drug interactions- Broad spectrum antibiotics may cause intestinal hurry and effect the absorption of hormones
Gynecological disorders

- Endometrial hyperplasias, polyps, fibroids, adenomyosis, endometritis, endometrial cancer
- Cervical polyps, erosions cancer
- Atrophic vaginitis, cancer of the vagina or vulva
- Hypothyroidism
When To Investigate?

• Routine endometrial surveillance is not needed
• With cyclical regimes if bleeding starts at the start of progesterone therapy, or these change in the duration or intensity of blood flow which is normal for that woman with continuous combined regimes-if bleeding is heavy or continuous and continues after 6-12 months of use
• In women with a high risk for uterine cancer
Insufficient Response

Poor compliance

• Missed tablets, Vomiting
• Non-adherent patches

Poor absorption

• Check blood levels
Insufficient Response

Concomitant testosterone deficiency

- Especially BSO, Loss of libido, Fatigue

Other co-existing conditions
Other Co-existing Conditions

- Differential diagnosis for Vasomotor symptoms, Calcium channel blockers, nicotinic acid, anti estrogens like raloxifen & tamoxifen, GnRH analogues, aromatase inhibitors, bromocriptine, cephalosporins, calcitonin, metronidazole, alcohol
  - Thyroid disease
  - Pheochromocytoma
  - Carcinoid
  - Renal neoplasia
- TB
- Recurrent UTI
Dealing With ET/EPT Side Effects

Side Effects

Fluid Retention
• Restrict salt intake; maintain adequate water intake; exercise; try a herbal diuretic or mild prescription diuretic

Bloating
• Switch to low-dose transdermal estrogen; lower the progestogen dose a level that still protects the uterus; switch to another progestin or to micronized progesterone
Dealing With ET/EPT Side Effects

Breast Tenderness
- Lower the estrogen dose; switch to another estrogen; Restrict salt intake; switch to another progestin; cut down on caffeine and chocolate

Headaches
- Switch to transdermal estrogen; lower the dose of estrogen and/or progestogen; switch to a continuous combined regime switch to progesterone or 19 norpregnane derivatives; ensure adequate water intake; restrict salt, caffeine, and alcohol intake
Dealing With ET/EPT Side Effects

<table>
<thead>
<tr>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood changes</strong></td>
</tr>
<tr>
<td>• Lower the progestogen dose; switch progestogen; switch from systemic progestin to the progestin IUS; change to a continuous-combined EPT regimen; ensure adequate water intake; Restrict intake of salt, caffeine and alcohol</td>
</tr>
<tr>
<td><strong>Nausea</strong></td>
</tr>
<tr>
<td>• Take oral estrogen tablets with meals or before bed; switch to another oral estrogen; switch to transdermal estrogen; lower the estrogen or progestogen dose</td>
</tr>
</tbody>
</table>
Contraindications Of HT

- Active endometrial and gynecological hormone dependent cancers
- Active breast cancer, estrogen progestogen receptor positive cancers known or suspected pregnancy
- Undiagnosed, abnormal vaginal bleeding
- Severe active liver disease with impaired or abnormal liver function
- Previous personal or family history of venous thromboembolism
- Systematic lupus erythematosus
Use With Caution

- Migraine headaches
- Superficial thrombophlebitis
- Strong family history of breast cancer
- Uterine fibroids
- Endometriosis
- Gallbladder disease
Stop Treatment

• If migraine appears for the first time or if headache gets worsened

• Blurring of vision or any symptoms suggesting of vascular occlusion

• If jaundice appears

• If there is significant rise in blood pressure

• HT to be stopped 4-6 weeks before elective surgery
<table>
<thead>
<tr>
<th>Conditions</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Small increase risk, no worsening of pre-existing disease</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>Vaginal estrogen not contraindicated</td>
</tr>
</tbody>
</table>
| Coronary Heart     | • Should not be initiated for primary or secondary prevention  
| Disease            | • Transdermal route preferred and natural progesterones    |
## Hormone Therapy & Pre-existing Conditions

<table>
<thead>
<tr>
<th>Conditions</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>Increased risk of osteoporosis, not contraindicated</td>
</tr>
<tr>
<td>Fibroids</td>
<td>Can cause enlargement</td>
</tr>
<tr>
<td>Liver Disease</td>
<td>Transdermal route preferred, liaise with gastroenterologists</td>
</tr>
<tr>
<td>Gallbladder disease</td>
<td>Increased risk of gallbladder disease</td>
</tr>
<tr>
<td>Migraine</td>
<td>Not contraindicated, transdermal route preferred</td>
</tr>
<tr>
<td>Conditions</td>
<td>HT</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>Otosclerosis</td>
<td>Insufficient evidence to contraindicate</td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
<td>May reduce risk of Parkinson’s disease, not contraindicated</td>
</tr>
<tr>
<td>Post-transplant</td>
<td>Should be considered, increased risk of osteoporosis</td>
</tr>
<tr>
<td>Renal failure</td>
<td>Should be considered, increased risk of early menopause</td>
</tr>
<tr>
<td>Conditions</td>
<td>HT</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Increased risk of osteoporosis, Increase in ‘flares’</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Increased risk of osteoporosis, Increase in ‘flares’</td>
</tr>
<tr>
<td>Thyroid Disease</td>
<td>Increased risk of osteoporosis, not contraindicated</td>
</tr>
<tr>
<td>Venous Thromboembolism</td>
<td>Vaginal estrogens, Transdermal estrogens not contraindicated</td>
</tr>
</tbody>
</table>
## Hormone Therapy & Pre-existing Conditions

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Hormone Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous abnormal smears/cervical cancer</td>
<td>Not Contraindicated</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td></td>
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<tr>
<td>Hyperlipidemia</td>
<td></td>
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<tr>
<td>Hypertension</td>
<td></td>
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<tr>
<td>Ovarian cancer</td>
<td></td>
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<tr>
<td>Past history of benign breast Disease</td>
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<tr>
<td>Contact lens wearers</td>
<td></td>
</tr>
</tbody>
</table>
## Hormone Therapy & Pre-existing Conditions

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Hormone Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Not Contraindicated</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
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<tr>
<td>Melanoma</td>
<td></td>
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<tr>
<td>Obesity</td>
<td></td>
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<tr>
<td>Sickle cell anemia</td>
<td></td>
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<tr>
<td>Smoking</td>
<td></td>
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<tr>
<td>Valvular heart disease</td>
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</tbody>
</table>
Follow Up

Review:

• After one month for efficacy and side effects, check weight and blood pressure

• After 3 months to assess effects and compliance
Follow Up

• Then annually for efficacy, side effects and compliance, check weight and blood pressure, a physical examination, update of medical and family history, relevant laboratory and imaging investigations, a discussion on lifestyle, and strategies to prevent or reduce chronic disease. review regarding continuing /modifying HT

• Evaluation to rule out pelvic pathology (endometrial hyperplasia and cancer) For women with persistent unscheduled bleeding while taking HT

• Emphasizing importance of adhering to age-appropriate breast cancer screening
Duration Of Therapy

• Premature menopause – Hormone Therapy:

   Up to natural age of menopause; further continuation of therapy according to the indication and the need (Grade C)

• Natural menopause:

   Safety data of EPT therapy with CEE+MPA is 3–5 years with ET safety data for use is 7 years of treatment with 4 years follow-up
Indian Menopause Society 2013: Duration Of Therapy

- Role of extended use of Hormone Therapy is a shared decision between the woman and the physician (Grade A)

- Stopping HT: May be abrupt or the dose and duration may be tapered off gradually (Grade C)
Duration Of Therapy

Patients likely to consider continuing therapy include those who:

• Fail attempt to stop EPT

• Are at high risk for fracture, or

• Alternative therapies are not appropriate
Follow Up Investigations

• Baseline investigations annually or earlier:
  - Routine blood and urine examination
  - Blood sugar
  - Lipid profile
• Pelvic USG, Mammography
• Pap Smear every 3 years
• DXA once in two - five years [optional]
Switch Of Regimens

• From OCPs to HT

• Switch directly to MHT at the end of OCPs
  - Age of 45–50 years
  - Serum FSH:LH ratio of > 1, FSH > 30 IU/L
Switch Of Regimens

- Switching form sequential to continuous combined therapy / tibolone
- Natural age of menopause,
- Six months amenorrhea

Note: Dose of estrogen in OCPs in India- Ethinyl estradiol (EE) 20µg, 30µg, 50µg
Tibolone

- Oestrogenic action on bone, vagina, vasomotor symptoms and lipids
- Progestogenic & antiestrogenic action on endometrium and breast
- Androgenic action on mood and libido
Tibolone

Specific Indications:

• Mood & libido
• Adverse effects with conventional HRT
• Older women
• Family history of breast cancer
• History of endometriosis, fibroids
• Add back therapy with GnRH analogues
Tibolone

• 2.5 mg single daily dose orally
• 1.25 mg equally effective

Adverse Effects

• Nausea & weight gain
• No change in HDL level
• Increases risk of recurrence in breast cancer survivors
Tibolone

Not recommended within 1 year of menopause because of risk of irregular vaginal bleeding
Tibolone

Contraindications for Prescribing Tibolone

• Undiagnosed genital bleeding
• Women over 60 years, women with risk factors for stroke, e.g. Hypertension, smoking, diabetes and atrial fibrillation
• Known past or suspected breast cancer known or suspected estrogen-dependent malignant tumor, endometrial hyperplasia
Tibolone

Contraindications for Prescribing Tibolone

- Previous or current venous thromboembolism (VTE) [deep vein thrombosis (DVT), pulmonary embolism], known thrombophilic disorders (e.g. Protein C, protein S or antithrombin deficiency)
- History of arterial thromboembolic disease [e.g. angina, myocardial infarction, stroke or
- Transient ischemic attack (TIA)], acute liver disease or with abnormal liver function tests, porphyria
Tibolone Drug Interactions

• May enhance the effect of anticoagulants

• Rifampicin, antiepileptic medicines such as carbamazepine, phenytoin, phenobarbital, primidone and barbiturates such as amobarbital (amylobarbitone) may reduce the blood levels of tibolone

• Women with diabetes may need an increase in the dose of their antidiabetic medicine (insulin or oral antidiabetic medicine)
Tibolone

- Treatment should be discontinued if signs of thromboembolic complications occur, if results of liver function tests become abnormal, or if cholestatic jaundice appears.

- The occurrence of vaginal bleeding or spotting soon after starting treatment with tibolone may be due to the residual effects of endogenous or exogenous estrogens.
Tibolone

- Bleeding commencing after 3 months of treatment or persistent bleeding should be appropriately investigated. In most cases, no apparent cause of bleeding is found.

- As with all steroids with hormonal activity, yearly medical examination is advisable.
Non Hormonal Treatments for Relief of Menopausal Symptoms

- Gabapentin: 300 mg TID × 6 weeks-3 months
- Venlafaxine: 25-75 mg/day
- Paroxetine: 7.5-20 mg/day
- Fluoxetine: 10-20 mg/day
- Isoflavones: 70 mg-100 mg daily × 6 weeks-3 months (equal producer patients have to be identified)
- Lycopene: 18-24 mg daily
Prescription Writing For Menopausal Symptoms

Premature Menopause

• Cyclic sequential EPT regime till the age of natural menopause

• Low dose oral contraceptive pill may be used till the natural age of menopause if not contraindicated
Prescription Writing For Menopausal Symptoms

Sexual Dysfunction

• Tibolone 2.5 mg OD × 6 weeks- 3 months

• Vaginal estriol succinate cream 0.5 mg or Tab estriol 1 mg, 2 mg/
vaginal conjugated equine estrogen if urogenital atrophy is present
Urogenital Symptoms in Menopause

- Vaginal estriol succinate cream 0.5 mg or oral Tab estriol 1 mg, 2 mg or vaginal conjugated equine estrogen 0.625 mg daily for 2 weeks followed by biweekly application for 6-12 weeks at bedtime, may be continued for 1 year
- Lactic acid wash daily

No routine monitoring of endometrial thickness
Genitourinary Syndrome - Vaginal Estrogen Therapy

Indications in postmenopausal women

- Vaginal symptoms
- Recurrent urinary tract infections
- Overactive bladder
- Vaginal surgery---Pre and postoperative
- Pap’s smear---After a short course of therapy
Advantages/Disadvantages

- Avoids enterohepatic circulation
- No endometrial stimulation
- No progesterone
- No systemic side effects
- Mainly local effects
- Acceptable following estrogen dependent cancers after counseling
- Mode of administration
Vaginal Preparations- India

• Conjugated equine estrogen (Premarin) 0.3-2.5mg/day

• Estriol (Evalon) creams . 03mg-0.5mg/day

• Estriol (Evalon) Tablets1-2mg/day

• Estradiol tablet, 10-25mcg (E 2)
Recommendations

• Treatment should be started early and before irrevocable atrophic changes have occurred

• Treatment needs to be continued to maintain the benefits

• All local estrogen preparations are effective and patient preference will usually determine the treatment used
Recommendations

- Delay in starting local treatment will reduce degree of response
- Initial loading dose to stimulate receptors followed by low maintenance dose once or twice per week
Length Of Therapy

- Vaginal ET should be continued as long as distressful symptoms remain
The method of use, benefits and adverse effects of systemic HT cannot be extrapolated to the low dose vaginal preparations.
SERM – Selective Estrogen Receptor Modulator

- Raloxifene is the first of a benzothiophene series of antiestrogens to be labeled a SERM
- Lasofoxifene
- Droloxifine
- Idoxifene and
- Toremifene are similar SERM agents (but they are still considered experimental)
Raloxifene

Tissue selectivity

- **Agonist** - Bone
  - Lipid Metabolism

- **Antagonist** - Uterine Endometrium
  - Breast Tissue
Place In Therapy

Treatment & Prevention of post-Menopausal osteoporosis

Role of Raloxifene is being evaluated in:

• Advanced breast cancer
• Chemoprevention of breast cancer
• Cardioprotection

Not for symptom control
Dosage And Administration

• Recommended dosage is Raloxifene 60 mg once daily, which may be administered any time of day without regard to meals.
Contraindications

- Pregnancy
- Active or past history of venous thromboembolic events, including deep vein thrombosis, pulmonary embolism, and retinal vein thrombosis
- Hypersensitive to Raloxifene or other constituents of the tablets
Assess The Profile Of The Woman To Individualize Treatment

Type and stage of menopause

- Surgical menopause - E only/Tibolone
- Perimenopause - Cyclical Progesterone/OCP/HT cyclical
- Early Menopause <12 months - EPT (More estrogens) sequential
- Late Menopause <12 months - EPT continuous combined/tibolone (Lowest estrogens/transdermal)
Assess The Profile Of The Woman To Individualize Treatment

• Premature Menopause-OCP/HT sequential regime
• Urogenital Atrophy- Local estrogens
• Evaluate women’s need and preference
• Evaluation of women’s individual risk factors
Review Of Treatment

Non- MHT

6 - 8 Weeks

No Symptom Relief or has Side Effects

Symptom Relief

6 - 8 Weeks

MHT

No Symptom Relief or has Side Effects

Change dose OR Therapy

Symptom Relief

6-12 months review

Recurrence of Symptoms

Review of:
- Efficacy
- Side-effects/ Risks

Vaginal Estrogen Therapy

Change dose OR Therapy

Specialist Review
Tips On HT Use

- Hysterectomy- Only Tibolone
- Perimenopause- Cyclical Progesterone/OCP
- Early Menopause- More Estrogens
- Late Menopause- Lowest Estrogens
- Postmenopause, low libido- Tibolone
- Premature Menopause- OCP/HT
- Urogenital Atrophy- Local estrogens
Tips On HT Use

• Women aged <50: benefits of HRT far outweigh the risks, HRT should be offered
• Women aged between 50 and 60 with menopausal symptoms: benefits of HRT outweigh the risks
• Women aged >60: benefits of HRT equal the risks, treatment should be individualized
• Women aged >70, the risks tend to outweigh the benefits
Management Of Osteoporosis

Postmenopausal Women (Asymptomatic)

>5 yrs postmenopause

<5 yrs postmenopause

1 major risk factor or any 2 other risk factors

BMD by DXA at Hip/Spine

Normal

Osteopenia

Osteoporosis

Severe Osteoporosis
Postmenopausal woman with fragility fracture

Immediate pain relief, surgical management, calcium, Vit. D supplementation
Investigation- essential, rule out secondary causes

Follow-up

BMD (spine, hip) by DXA (repeat after 1-2 years)
Bone markers for monitoring therapy

Multidisciplinary Management

Lifestyle Management
Pharmacotherapy
Teriparatide
Bisphosphonates
Calcitonin-pain relief in vertebral fracture

Physio-therapy

Rehabilitation
Emotional, Social Support
Identify factors for recurrence
Aim independence at home and work
Guidelines: Module 4

Guidelines Recommendations Of MHT
<table>
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<tr>
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<tbody>
<tr>
<td>• Begins within 10 years of menopause or &lt; 60 years of age - ‘Window of Opportunity’ (support safe use for at least 5 years in healthy women initiating treatment before age 60)</td>
<td>• Premature menopause: MHT upto natural age of menopause 3-5 years</td>
<td>• Continuation of therapy should be decided at the discretion of the well-informed woman and her health professional</td>
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### Monitoring

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<tr>
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<tbody>
<tr>
<td>Pre-HT work-up</td>
<td>• Pre-HT work-up (Indian MS)</td>
<td>• Initial follow-up at 3 months (NAMS)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Annual follow-up</td>
<td>• Annual follow-up - physical, laboratory/imaging (All)</td>
<td></td>
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<tr>
<td></td>
<td>• Discussion on lifestyle</td>
<td>• Discussion on lifestyle strategies to prevent or reduce chronic disease (All)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>strategies to prevent or</td>
<td>• Currently no indication for increased mammographic or cervical smear screening.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>reduce chronic disease (All)</td>
<td>• Annual mammograms should be proposed in case of high breast density in women using MHT.</td>
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</tr>
</tbody>
</table>
MHT, including tibolone, can be initiated in postmenopausal women at risk of fracture or osteoporosis before the age of 60 years or within 10 years after menopause.

Initiation of MHT after the age of 60 years for the indication of fracture prevention is considered second-line therapy and requires individually calculated benefit/risk, compared to other approved drugs. If MHT is elected, the lowest effective dose should be used.
**Guidelines: CV Risk**

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<tbody>
<tr>
<td>No/lower risk in healthy women &lt;60 years of age or within 10 years of menopause</td>
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<td>---------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Progesterone (eg, dydrogesterone) + estrogen may not increase risk if given for <5 years | • Breast cancer risk should be evaluated before MHT prescription.  
• Small increase in risk (incidence of <1.0/1000 women/year of use)  
• Risk is lower than increased risks associated with common lifestyle factors  
• MCP or dydrogesterone could be associated with a lower risk than synthetic progestogen | NAMS: Risk of events in younger women is lower than that for older women  
Endocrine Society: Observational data suggest that progesterone or dydrogesterone may be associated with a lower risk, but further studies are required to confirm this |