"Women's Health" is also available at www.squarepharma.com.bd

WOMEN'S HEALTH

Vol-5 No-1 Jan-Mar 2012

Editorial Note:

Dear Doctor,

It's our immense pleasure to inform you that we have published our newsletter, "Women's Health". In this issue we are focusing on Hormone Replacement Therapy (HRT). Your comments and suggestions will enrich our upcoming issues. Please participate in quiz competition and win prizes.

Estrogen and progestogen use in postmenopausal women: 2010 - position statement of The North American Menopause Society

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH

SQUARE

WOMEN'S HEALTH

Estrogen and progestogen use in postmenopausal women: 2010 position statement of The North American Menopause Society (Concised)

BENEFITS AND RISKS OF HT

Confusion can arise among healthcare providers, the lay public, and the media when general concepts of risk are discussed. Understanding HT risks in particular is critical to clinical decision making around menopause and beyond.

Use of HT should be consistent with treatment goals, benefits, and risks for the individual woman. The benefit-risk ratio for an individual woman continually changes with her age and her menopause-related symptoms (e.g., vasomotor symptoms, sleep disturbance, vaginal atrophy, dyspareunia, or diminished libido), any of which may have an adverse impact on quality of life (QOL). Risk factors are related to: a woman's baseline disease risks, her age, age at menopause, cause of menopause, time since menopause, and prior use of any hormone including type, route of administration, dose, and medical conditions that emerged during treatment. Potential benefits and risks are described below for the relevant clinical outcomes.

Vasomotor symptoms

ET, with or without a progestogen, is the most effective treatment for menopause-related vasomotor symptoms (i.e., hot flashes and night sweats) and their potential consequences (e.g., diminished sleep quality, irritability, and reduced QOL). Treatment of moderate to severe vasomotor symptoms remains the primary indication for HT. Every systemic ET and EPT product has regulatory agency approval for this indication.

Vaginal symptoms

ET is the most effective treatment for moderate to severe symptoms of vulvar and vaginal atrophy (e.g., vaginal dryness, dyspareunia, and atrophic vaginitis). Many systemic ET and EPT products and all local vaginal ET products have regulatory agency approval for treating these vaginal symptoms. Lower doses than previously used, and less frequent administration, often yield satisfactory results. Some systemic ultralow dose regimens may be inadequate for relief of vaginal symptoms. When HT is used for systemic vasomotor symptoms, enquiry about the adequacy of therapy for urogenital atrophy is important. When HT is considered solely for urogenital atrophy, local vaginal ET is generally recommended.

Sexual function

Relief of moderate to severe vaginal atrophy with systemic or local HT can be effective in relieving dyspareunia, a common cause of intercourse avoidance. Local estrogen may improve coital satisfaction by improving lubrication and increasing blood flow and sensation in vaginal tissues. One oral systemic ET product is approved in the United States for the treatment of pain with intercourse. HT is not recommended as the sole treatment of other problems of sexual function, including diminished libido.

Urinary health

Local ET may benefit some women with urge incontinence who have vaginal atrophy. Whether ET by any route is effective in treating overactive bladder is unclear. There is controversy as to whether local ET can improve certain cases of pure stress incontinence. On the other hand, systemic HT may worsen or provoke stress incontinence. Local ET may help reduce the risk of recurrent urinary tract infection (UTI) by a direct proliferative effect on the urethra and bladder epithelia, helping to restore the acidic environment and normal lactobacillus-predominant flora of the vagina, and thus discouraging colonization of the vagina by pathogens associated with UTI. Clinically, only ET administered by the vaginal route has been shown in an RCT to be effective in reducing the risk of recurrent UTI. However, no ET/EPT product has regulatory agency approval for any urinary health indication.

TABLE 1. NAMS menopausal hormone therapy terminology

EPT - Combined estrogen-progestogen therapy
ET - Estrogen therapy
HT - Hormone therapy (encompassing both ET and EPT)
Local therapy - Vaginal ET administration that does not result in clinically ignificant systemic absorption
Progestogen - Encompassing both progesterone and progestin
Systemic therapy - HT administration that results in absorption in the blood high enough to provide clinically significant effects; in this paper, the terms ET, EPT, HT, and progestogen are presented as systemic therapy unless stated otherwise
Timing of HT initiation - Length of time after menopause when HT is initiated

Change in body weight / mass

Body mass index (BMI) increases with age in midlife, with the peak BMI occurring between ages 50 and 59. No statistically significant difference in mean weight gain or BMI has been demonstrated between women who use HT and those who do not.

Quality of life

Although no HT product has regulatory agency approval for enhancing QOL, an improvement in health-related quality of life (HQOL) can result with HT use because of decreased menopause symptoms and

perhaps other mechanisms, including improved sleep and a possible elevation of mood that leads to a feeling of well-being. Whether HT improves HQOL in asymptomatic women is unknown, nor are data available to determine the effect of HT on global QOL.

Osteoporosis

There is RCT evidence that HT reduces postmenopausal osteoporotic fractures, including hip fractures, even in women without osteoporosis, although no HT product has regulatory agency approval for treatment of osteoporosis. Many systemic HT products, however, have regulatory agency approval for prevention of postmenopausal osteoporosis through long-term treatment. Extended use of HT is an option for women who have established reduction in bone mass, regardless of menopause symptoms; for prevention of further bone loss and/or reduction of osteoporotic fracture when alternate therapies are not appropriate or cause side effects; or when the benefits of extended use are expected to exceed the risks. The optimal time to initiate HT and the optimal duration of therapy have not been established, but HT would largely be used in the early years after menopause. The benefits of HT on bone mass dissipate quickly after discontinuation of treatment.

Cardiovascular effects

HT is currently not recommended as a sole or primary indication for coronary protection in women of any age. Initiation of HT by women ages 50 to 59 years or by those within 10 years of menopause to treat typical menopause symptoms (e.g., vasomotor, vaginal) does not seem to increase the risk of CHD events. There is emerging evidence that initiation of ET in early postmenopause may reduce CHD risk.

Diabetes mellitus

Although no HT product has regulatory agency approval to prevent DM, large RCTs demonstrate that HT reduces the new onset of T2DM. There is inadequate evidence to recommend HT as the sole or primary indication for the prevention of DM in peri- or postmenopausal women. Some data suggest that postmenopausal women with T2DM who use oral ET may require lower doses of medications for glycemic control.

In women with T2DM, measures to reduce CHD risk are probably of greatest concern. Transdermal ET administration may offer advantages over the oral route. Serum triglyceride levels and thrombotic factors, which are often increased in patients who have DM, are not increased further with transdermal HT. Moreover, adverse alterations in blood pressure in both nonhypertensive and hypertensive women have been reported only with oral therapy.

Endometrial cancer

Unopposed systemic ET in postmenopausal women with an intact uterus is associated with increased endometrial cancer risk related to the ET dose and duration of use. Standard-dose therapy (0.625 mg/d CE or the equivalent), when used for more than 3 years, is associated with up to a fivefold increased risk of endometrial cancer; if used for 10 years, the risk increases up to tenfold. This increased risk persists for several years after ET discontinuation. To negate this increased risk, adequate concomitant progestogen is recommended for women with an intact uterus when using systemic ET. HT is not recommended in women with a history of endometrial cancer.

Breast cancer

Estrogen-progestogen therapy

Diagnosis of breast cancer increases with EPT use beyond 3 to 5 years. In the WHI, this increased risk, in absolute terms, was 8 total breast cancers per 10,000 women using EPT for 5 or more years. Studies have not clarified whether the risk differs between continuous and sequential use of progestogen, with observational studies suggesting risk may be great er with continuous use of progestogen. It is also not clear whether there is a class effect from the progestogen or whether the specific agent used influences breast cancer risk. Early data from a large observational trial suggest that EPT with micronized progesterone may not be associated with an increased risk of breast cancer if used for up to 5 years, but these findings should not be overemphasized and require confirmation.

EPT and, to a lesser extent, ET, increase breast cell proliferation, breast pain, and mammographic density, and EPT may impede the diagnostic interpretation of

TABLE 2. NAMS menopause terminology

Early menopause - Natural or induced menopause that occurs well before the average age of natural menopause (51 y), at or under age 45
Early postmenopause - The time period within 5 years after the final menstrual period (FMP) resulting from natural or induced menopause
Induced menopause - Permanent cessation of menstruation after bilateral oophorectomy (i.e., surgical menopause) or iatrogenic ablation of ovarian function (e.g., by chemotherapy or pelvic radiation therapy)
Natural/spontaneous menopause - The FMP, confirmed after 12 consecutive months of amenorrhea with no obvious pathologic cause
Perimenopause/menopause transition - Span of time when menstrual cycle and endocrine changes occur a few years before and 12 months after an FMP resulting from natural menopause
Premature menopause - Menopause reached at or under age 40, whether natural or induced
Premature ovarian insufficiency - loss of ovarian function before age 40, leading to permanent or transient amenorrhea (often described as premature ovarian insufficiency or premature menopause)

mammograms. Evolving but not conclusive evidence suggests that the increased risk of breast cancer with EPT may be a result of promotion of preexisting cancers that are too small to be diagnosed by imaging studies or clinical examination. Modest trends suggest that the risk of breast cancer dissipates somewhat over the 3 years after cessation of EPT.

Those starting EPT shortly after menopause experienced an increased risk of breast cancer over the next 5 years, whereas those with a gap time of greater than 5 years did not.

Estrogen therapy

Women in the ET arm of the WHI demonstrated no increase in risk of breast cancer after an average of 7.1 years of use, with 6 fewer cases of invasive breast cancer per 10,000 women per year of ET use, which is not statistically significant. The decrease in risk was observed in all three age groups studied. When ET was extended beyond 10 to 15 years in observational studies, breast cancer risk seemed to increase.

After breast cancer

Controversy surrounds the issue of safety of EPT in survivors of breast cancer. Observational studies suggest that EPT is safe and perhaps even protective against recurrence of breast cancer. However, these data have been questioned because of the potential bias from selection of women at low risk of recurrence using ET. ET use in breast cancer survivors has not been proven to be safe and may be associated with an increased risk of recurrence.

Ovarian cancer

Cancer of the ovaries causes more deaths than any other cancer of the reproductive system, primarily because it is usually detected in an advanced stage. Published data on the role of HT and risk of ovarian cancer are conflicting. Most epidemiologic studies have shown no association or a modest increase. There is a relatively large volume of observational trial data that points to an association between HT use and increased ovarian cancer risk.

The association between ovarian cancer and HT beyond 5 years, if any, would fall into the rare or very rare category. Women at increased risk of ovarian cancer (e.g., those with a family history) should be counseled about this rare association.

Lung cancer

In a post-hoc analysis of the EPT arm of the WHI that combined data from 0 to 4 years of follow-up, the incidence of non-small cell lung cancer (which accounts for about 80% of lung cancer) was not significantly increased , but the number of deaths and the number of poorly differentiated and metastatic tumors increased in the treatment group. The cases were essentially limited to past and current smokers and to women older than age 60. The overall data, including the WHI analysis, suggest that initiating EPT in older women with a history of smoking may promote the growth of existing lung cancers.

Mood and depression

Several small, short-term trials among middle-aged women suggested that HT improves mood, whereas other trial results showed no change. Progestogens in EPT may worsen mood in some women, possibly in those with a history of premenstrual syndrome, premenstrual depressive disorder, or clinical depression. HT might have a positive effect on mood and behavior, HT is not an antidepressant and should not be considered as such.

Cognitive aging and dementia

HT cannot be recommended at any age for the sole or primary indication of preventing cognitive aging or dementia. HT seems to increase the incidence of dementia when initiated in women age 65 and older. Similarly, HT should not be used to enhance cognitive function in younger postmenopausal women with intact ovaries, although very small clinical trials support the use of ET initiated immediately after menopause induced by bilateral oophorectomy. Available data do not adequately address whether HT used soon after menopause increases or decreases later dementia risk. Limited data do not support the use of HT as treatment of AD.

Premature menopause & premature ovarian insufficiency

Women experiencing premature menopause (<40 y) or premature ovarian insufficiency are medically a distinctly different group than women who reach menopause at the median age of 51.3 years. Premature menopause and premature ovarian insufficiency are associated with a lower risk of breast cancer and earlier onset of osteoporosis, CHD, Parkinson's disease; premature bilateral oophorectomy is possibly associated with cognitive decline as well. There are inadequate data regarding HT in these populations. Most observational reports suggest an increased risk of CHD with early natural or surgical menopause in the absence of HT and a protective effect of HT when HT is administered. The existing data regarding HT in women experiencing menopause at the median age should not be extrapolated to women experiencing premature menopause and initiating HT at that time. The risks attributable to HT use by these young women receiving HT may be smaller and the benefits potentially greater than those in older women who commence HT at or beyond the median age of menopause, although no comparative data exist.

Total mortality

The WHI trials are consistent with observational studies indicating that HT may reduce total mortality when initiated soon after menopause. The WHI suggests that both ET and EPT nonsignificantly reduce total mortality by 30% when initiated in women younger than age 60, and when data from the ET and EPT arms were combined, that reduction with HT use was statistically significant. In contrast, HT was not associated with mortality reduction

among women who initiated HT at age 60 or older.

PRACTICAL THERAPEUTIC ISSUES

Class versus specific product effect

Estrogens and progestogens have some common features and effects as well as potentially different properties. However, the current gold standard for determining the net clinical outcome for any given agent (alone or in combination) is through RCTs. On a theoretical basis, there are likely to be differences within each family based on factors such as relative potency of the compound, androgenicity, glucocorticoid effects, bioavailability, and route of administration. Potential differences are addressed where appropriate in individual sections above.

Progestogen indication

The primary menopause-related indication for progestogen use is to negate the increased risk of endometrial cancer from systemic ET use. All women with an intact uterus who use systemic ET should also be prescribed adequate progestogen. Postmenopausal women without a uterus should not be prescribed a progestogen with systemic ET. A progestogen is generally not indicated when ET at the recommended low doses is administered locally for vaginal atrophy or transdermally at the ultralow dose approved for prevention of bone loss. Concomitant progestogen may improve the efficacy of low-dose ET in treating vasomotor symptoms. Some women who use EPT may experience undesirable side effects from the progestogen component. A combination of estrogen with an estrogen agonist/antagonist is currently under investigation and may become an alternate option to progestogen use.

Dosages

The lowest effective dose of estrogen consistent with treatment goals, benefits, and risks for the individual woman should be the therapeutic goal, with a corresponding low dose of progestogen added to counter the adverse effects of systemic ET on the uterus. Lower ET and EPT doses are better tolerated and may have a more favorable benefit-risk ratio than standard doses. However, lower doses have not been tested in long-term trials to support an assumed more favorable risk-benefit ratio. Among the lower daily doses typically used when initiating systemic ET are 0.3 mg oral CE, 0.5 mg oral micronized 17A-estradiol, and 0.014 to 0.025 mg transdermal 17A-estradiol patch. The progestogen dose varies based on the progestogen used and the estrogen dose, typically starting at the lowest effective doses of 1.5 mg MPA, 0.1 mg norethindrone acetate, 0.5 mg drospirenone, or 50 mg micronized progesterone. Different doses may have different health outcomes. Some women may require additional local ET for persistent vaginal symptoms while on systemic therapy.

Routes of administration

There is currently no clear benefit of one route of administration versus another for systemic ET. Nonoral routes of administration including transdermal and intrauterine systems may offer both advantages and disadvantages compared with the oral route, but the long-term benefit-risk ratio has not been demonstrated. With transdermal therapy, there is no significant increase in triglycerides, no change in C-reactive protein, no increase in sex hormone-binding globulin, and little effect on blood pressure. There is observational evidence that transdermal ET may be associated with a lower risk of deep vein thrombosis than oral administration, but no RCT evidence is available. Local ET administration is preferred when treating solely vaginal symptoms.

Systemic progestogen is required for endometrial protection from unopposed ET. Topical transdermal progesterone delivery is not recommended when EPT is prescribed. Intrauterine systems also cannot be recommended at this time. (For more, see Progestogen indication.)

Regimens

There are multiple dosing-regimen options for endometrial safety when adding progestogen to estrogen. Research is inadequate to endorse one regimen over another. Current data support the recommendation to minimize progestogen exposure through one of various options. There is insufficient evidence regarding endometrial safety to recommend as alternatives to standard EPT regimens the off-label use of long-cycle regimens, vaginal administration of progesterone, the contraceptive levonorgestrel-releasing intrauterine system, or low-dose estrogen without progestogen. If any of these approaches is used, close surveillance of the endometrium is recommended pending more definitive research, much of which is currently in progress. Tissue-selective estrogen complex- a combination of estrogen with an estrogen agonist/antagonist- may become an alternate option.

There are also multiple dosing regimen options from which to choose when using ET alone for women after hysterectomy. No data provide guidance on which regimen is best for all women.

Bioidentical hormones

NAMS recognizes that one area of confusion in clinical practice is so-called bioidentical hormone preparations. This term has been used to refer to many well-tested, regulatory agency- approved, brand-name HT products containing hormones chemically identical to hormones produced by women (primarily in the ovaries), such as 17b-estradiol or progesterone. However, the term is most often used to describe custom-made HT formulations (called "bioidentical hormone therapy" or BHT) that are compounded for an individual according to a healthcare provider's prescription.

Use of BHT has escalated in recent years, often with the dose determined by salivary hormone testing, a procedure that has not been proven accurate or reliable. There may be increased risks to the women using these products.

WOMEN'S HEALTH

Custom-compounded formulations, including BHT, have not been tested for efficacy or safety; safety information is not consistently provided to women along with their prescription, as is required with commercially available HT; and batch standardization and purity may be uncertain. The US Food and Drug Administration (FDA) has ruled that compounding pharmacies have made claims about the safety and effectiveness of BHT unsupported by clinical trial data and considered to be false and misleading.

TREATMENT ISSUES

Pretreatment evaluation

HT should be considered only when an indication for therapy has been clearly identified, contraindications ruled out, and the potential individual benefits and risks adequately discussed with each woman so that an informed decision can be made. Before initiating HT, a comprehensive history and physical examination are essential. NAMS recommends assessment of risk factors for stroke, CHD, VTE, osteoporosis, and breast cancer and discussion of these results with each woman before initiating therapy. Mammography should be performed according to national guidelines and age, but preferably within the 12 months before initiation of therapy. Other specific examinations, such as bone densitometry, may be considered on a case-by-case basis.

Timing of initiation

Emerging data reveal that the timing of HT initiation in relation to proximity to menopause may be important. How soon treatment is begun after menopause seems to have an impact on long-term health outcomes (eg, early initiation may reduce total mortality rates and CHD risk; see Coronary heart disease and Total mortality).

Women older than age 60 who experienced natural menopause at the median age and have never used HT will have elevated baseline risks of CHD, stroke, VTE, and breast cancer, and HT should therefore not be initiated in this population without a compelling indication and only after appropriate counseling and attention to CVD risk factors.

Premature menopause and premature ovarian insufficiency are conditions associated with a lower risk of breast cancer and earlier onset of osteoporosis and CHD, but there are no clear data as to whether ET or EPT will affect morbidity or mortality from these conditions. Despite this, it is logical and considered safe to recommend HT for these younger women, at least until the median age of natural menopause. Younger women with premature menopause might also require higher doses of HT for menopause symptom relief than the doses currently recommended for women ages 50 to 59.

Duration of use

One of the most challenging issues regarding HT is the duration of use. Existing data do not provide a clear indication as to whether longer duration of therapy improves or worsens the benefit-risk ratio. Because the long-term effects of HT on risk of breast cancer, CHD, stroke, total CVD, and osteoporotic fracture in perimenopausal women with moderate to severe menopause symptoms have not been established in RCTs, the findings from trials in different populations should, therefore, be extrapolated with caution. For example, data from large studies such as WHI and HERS should not be extrapolated to symptomatic postmenopausal women who initiate HT younger than age 50, as these women were not studied in those trials. WHI and HERS involved predominantly asymptomatic postmenopausal women age 50 and older (with mean ages of 63 and 67, respectively), most of whom were 10 years or more beyond menopause; and HERS was conducted solely among women with known coronary artery disease. Results obtained from RCTs among women with established disease should not be extrapolated to women without such conditions. The data also should not be extrapolated to women experiencing premature menopause (<40 y) and initiating HT at that time.

Extending HT beyond the years around menopause may be a concern for healthcare providers and their patients. The benefits outweigh the risks in some women, whereas the reverse is true for others. Treatment recommendations are different for women experiencing premature menopause, those who are first users of HT, or women who are in their 60s and have previously used HT for several years.

Provided that the lowest effective dose is used, that thewoman is well aware of the potential benefits and risks, and that there is clinical supervision, extending HT use for an individual woman's treatment goals is acceptable under some circumstances, including: 1) The woman for whom, in her own opinion, the benefits of menopause symptom relief outweigh risks, notably after failing an attempt to stop HT, 2) The woman with established reduction in bone mass for whom alternate therapies are not appropriate or cause unacceptable side effects, or the benefit-risk ratio of extended use is unknown.

Symptom recurrence

Vasomotor symptoms have an approximately 50% chance of recurring when HT is discontinued, independent of age and duration of use. The decision to continue HT should be individualized on the basis of severity of symptoms and current benefit-risk ratio considerations, provided the woman in consultation with her healthcare provider believes that continuation of therapy is warranted.

Discontinuance

Current data suggest that the rates of vasomotor symptom recurrence are similar when HT is either tapered or abruptly discontinued. No recommendation can be made as to how to discontinue therapy. Regarding outcomes

after discontinuance, an initial analysis of data showed that the age-adjusted incidence rate of breast cancer in women in the United States fell sharply (by 6.7%) in 2003, as compared with 2002. The decrease was evident only in women who were age >50 and was more evident in cancers that were estrogen-receptor positive than that were estrogen-receptor negative. It was theorized that the drop could be related to the large number of women discontinuing HT after the termination of the EPT arm of the WHI. Caution must be exercised in comparing data before 2002 to data beyond 2002 because of a change in surveillance methodology.

When followed for 3 years after stopping HT, women in the WHI who had been assigned to EPT had a rate of cardiovascular events, fractures, and colon cancers equivalent to that of women who had been assigned to placebo. The only statistical difference was an increase in the rates of all cancer in women who had been assigned to EPT, with an excess of 30 cancers per 10,000 women per year of EPT, including a number of fatal lung cancers. Women who smoke should be cautioned that additional surveillance may be prudent. Growing data indicate that discontinuance of HT will lead to expected complications such as increased incidence of bone fracture, including hip fracture. When HT is discontinued after several years of use, bone mineral density should be monitored and bone-preserving therapy initiated if indicated. The possible sequelae of urogenital atrophy can be treated, as per the section on Vaginal symptoms.

Hazard ratios for all-cause mortality, reflecting the balance of all of the above and other outcomes, tended to be neutral in both the EPT and ET arms of the WHI. During the 3-year postintervention phase of the EPT trial, mortality rates were borderline elevated due primarily to the aforementioned increase in cancer. Over the entire EPT follow-up period (active treatment plus post-stopping phases), the HR for all-cause mortality was 1.04.

Individualization of therapy is key

Each woman is unique, having her own risk profile and preferences. When HT is desired by patients, individualization of therapy is key to providing health benefits with minimal risks, thereby enhancing QOL.

SUMMARY

The potential absolute risks published thus far for use of HT are low, particularly for the WHI ET trial, which provided evidence of considerable safety for 0.625 mg/day of oral CE. The risks in the WHI EPT trial were rare by the criteria of the Council for International Organizations of Medical Sciences, except for stroke, which was above the rare category. For women younger than age 50 or those at low risk of CHD, stroke, osteoporosis, breast cancer, or colon cancer, the absolute risk or benefit from ET or EPT is likely to be even smaller than that demonstrated in the WHI, although the relative risk at different ages may be similar. There is a growing body of evidence that each type of estrogen and progestogen, route of administration, and timing of therapy has distinct beneficial and adverse effects. Further research remains essential.

Ref: Estrogen and progestogen use in postmenopausal women: 2010 position statement of The North American Menopause Society. Menopause: The Journal of The North American Menopause Society. Vol. 17, No. 2, pp. 242/255.

Congratulations !

The Winners of WOMEN'S HEALTH Quiz Competition Vol-4 No.-3 Oct-Deac, 2011

Dr. Rokhshana Khatun
FCPS (Gyane and Obs)
Super Clinic
Savar, Dhaka

Dr. Kaniz Fatema
MBBS, DGO
General Hospital
Barisal

Dr. Anisa Karim
MBBS
Gobindagonj Health Complex
Gaibandha

Renorma™

Tibolone 2.50 mg Tablet

Re-normalizes menopausal symptoms

- Provides relief of Climacteric Symptoms (hot flushes, sweating, fatigue etc.)
- Decreases the risk of osteoporosis by increasing Bone Mineral Density (BMD)
- Increases the concentration of β-endorphins which improves mood
- Increases libido & frequency of sexual activity
- Reduces breast tenderness & risk of breast cancer
- Improves vaginal atrophy

Femastin™

Estriol 1 mg Tablet

Lightens the life

- Effective approach for the management of urogenital symptoms
- Reduces recurrent urinary tract infections in postmenopausal women
- Restores normal Vaginal Flora & effective in the treatment of Atrophic Vaginitis
- Safe for long-term use & ensures endometrial safety
- Right choice for relieving the symptoms of natural or surgically-induced menopause

Stronel®

Strontium Ranelate 2 gm

Granules for oral suspension

Effective & Safer anti-osteoporotic agent with dual action

- Has unique dual mode of action
- Builds stronger bone compared to bisphosphonates
- Well tolerated at the upper gastrointestinal level and safer than bisphosphonates
- Provides sustained 5-year efficacy against vertebral, non-vertebral and hip fractures
- Confirms the anti-osteoporotic efficacy to prevent vertebral fractures, whatever the age of the patient is

Production:dhakahealth01715219808

SQUARE PHARMACEUTICALS LTD. BANGLADESH

AWARDED Superbrands BANGLADESH

www.squarepharma.com.bd

SQUARE