Bijuva™ (estradiol/progesterone) – New drug approval

- On October 29, 2018, TherapeuticsMD announced the FDA approval of Bijuva (estradiol/progesterone), for the treatment of moderate to severe vasomotor symptoms due to menopause in women with a uterus.

- Vasomotor symptoms (commonly known as hot flashes or flushes) occur as the ovaries stop producing hormones and levels of circulating estrogen decrease. Hot flashes (including night sweats) are the most common symptoms, occurring in up to 80% of women, and can be debilitating and last years after menopause.

- The efficacy of Bijuva was demonstrated in a 12-week, placebo-controlled substudy of a 52-week safety study enrolling 726 postmenopausal women. The co-primary efficacy endpoints included the mean weekly reduction in frequency of moderate to severe vasomotor symptoms and mean weekly reduction in severity of moderate to severe vasomotor symptoms at weeks 4 and 12.

    - Bijuva statistically significantly reduced the frequency of moderate to severe vasomotor symptoms from baseline vs. placebo at weeks 4 (-40.6 for Bijuva vs. -26.4 for placebo; $p < 0.001$) and 12 (-55.1 for Bijuva vs. -40.2 for placebo; $p < 0.001$).
    - Bijuva statistically significantly reduced the severity of moderate to severe vasomotor symptoms from baseline vs. placebo at weeks 4 (-0.48 for Bijuva vs. -0.34 for placebo; $p = 0.031$) and 12 (-1.12 for Bijuva vs. -0.56 for placebo; $p < 0.001$).
    - In addition, in the 52-week safety study, endometrial biopsy assessments revealed 1 case of endometrial hyperplasia and no cases of endometrial cancer in women who received Bijuva, and no cases of hyperplasia or endometrial cancer in women who received placebo.

- Bijuva carries a boxed warning for cardiovascular disorders, breast cancer, endometrial cancer, and probable dementia.

- Bijuva is contraindicated in women with undiagnosed abnormal genital bleeding; known, suspected, or history of breast cancer; known or suspected estrogen-dependent neoplasia; active deep vein thrombosis, pulmonary embolism, or history of these conditions; active arterial thromboembolic disease (for example, stroke and myocardial infarction), or a history of these conditions; known anaphylactic reaction or angioedema with Bijuva; known liver impairment or disease; and known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders.

- Other warnings and precautions of Bijuva include malignant neoplasm, gallbladder disease, hypercalcemia, visual abnormalities, addition of a progestogen when a woman has not had a hysterectomy, elevated blood pressure, hypertriglyceridemia, hepatic impairment and/or past history of cholestatic jaundice, hypothyroidism, fluid retention, hypocalcemia, exacerbation of endometriosis, hereditary angioedema, exacerbation of other conditions, laboratory tests, and drug laboratory test interactions.

- The most common adverse reactions (≥ 3% of women and > placebo) with Bijuva use were breast tenderness, headache, vaginal bleeding, vaginal discharge and pelvic pain.

- The recommended dose of Bijuva is one capsule, 1 mg/100 mg, orally each evening with food.

    - Use of estrogen, alone or in combination with a progestogen, should be limited to the lowest effective dose available and for the shortest duration consistent with treatment goals and risks for the individual woman.

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    - Postmenopausal women should be reevaluated periodically as clinically appropriate to determine if treatment is still necessary.

- TherapeuticsMD plans to launch Bijuva in the second quarter of 2019. Bijuva will be available as 1 mg of estradiol and 100 mg of progesterone in a single capsule.