Estradiol/Norethindrone Acetate Tablets

AB Rated to Activella®

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Administration of Estradiol/Norethindrone Acetate Tablets 1.0 mg/0.5 mg with food did not modify the bioavailability of estradiol and norethindrone acetate.

The pharmacokinetic parameters of estradiol (E2), estrone (E1), and norethindrone (NET) following oral administration of Estradiol/Norethindrone Acetate Tablets are as follows:

- **Estradiol (E2)**: The oral bioavailability of estradiol is approximately 40%.
- **Estrone (E1)**: The oral bioavailability of estrone is approximately 20%.
- **Norethindrone (NET)**: The oral bioavailability of norethindrone is approximately 50%.

### Effects on Bone Mineral Density

<table>
<thead>
<tr>
<th>Estradiol/Norethindrone Acetate Tablets 1.0 mg/0.5 mg</th>
<th>Estradiol/Norethindrone Acetate Tablets 0.5 mg/0.5 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine BMD, % change from baseline</td>
<td>Lumbar spine BMD, % change from baseline</td>
<td>Lumbar spine BMD, % change from baseline</td>
</tr>
<tr>
<td>2 mg estradiol with 1 mg norethindrone acetate</td>
<td>2 mg estradiol with 1 mg norethindrone acetate</td>
<td>2 mg estradiol with 1 mg norethindrone acetate</td>
</tr>
<tr>
<td>Placebo</td>
<td>Placebo</td>
<td>Placebo</td>
</tr>
</tbody>
</table>

### Cardiac Events

- **Significantly different from placebo**
- **Not significantly different from placebo**

- **CHD events**: The rate of CHD events was comparable among women receiving Estradiol/Norethindrone Acetate Tablets compared to placebo.

### Breast Cancer

- **Significantly different from placebo**
- **Non-significantly different from placebo**

- **Incidence of breast cancer**: The incidence of breast cancer was comparable among women receiving Estradiol/Norethindrone Acetate Tablets compared to placebo.

### Osteoporosis

- **Significantly different from placebo**
- **Non-significantly different from placebo**

- **Lumbar spine BMD**: There was an increase in lumbar spine BMD in the US and European clinical trials for Estradiol/Norethindrone Acetate Tablets.

### Laboratory Tests

- **Significantly different from placebo**
- **Non-significantly different from placebo**

- **Changes in laboratory test results**: There were no significant changes in laboratory test results observed in women receiving Estradiol/Norethindrone Acetate Tablets compared to placebo.

### Adverse Outcomes

- **Global index**: The earliest occurrence of CHD, invasive breast cancer, non-invasive breast cancer, hip fractures, and lumbar spine fractures.

### Additional Information

- **Other adverse outcomes**: The rates of other adverse outcomes were not significantly different among women receiving Estradiol/Norethindrone Acetate Tablets compared to placebo.

### Study Populations

- **Estradiol-alone arm**: 4,943 women in the estrogen-alone substudy of WHI.

### Summary

Estradiol/Norethindrone Acetate Tablets 1.0 mg/0.5 mg are indicated for the treatment of menopausal symptoms in women who have undergone a hysterectomy.