Duavive is a new oral HRT formulation containing conjugated oestrogens and the selective oestrogen-receptor modulator bazedoxifene and is indicated for the treatment of oestrogen deficiency symptoms in postmenopausal women with a uterus who cannot take progestogen-containing therapy.

This article discusses its properties, efficacy and adverse effects.

KEY POINTS

- Duavive is an oral HRT formulation combining a low dose of conjugated oestrogens and the selective oestrogen-receptor modulator bazedoxifene.
- It is licensed for the treatment of oestrogen deficiency symptoms in postmenopausal women with a uterus when progestogen-containing therapy is not appropriate.
- It relieves vasomotor symptoms associated with the menopause but is less effective for vaginal symptoms.
- Common adverse effects include headache, muscle and joint pain, and gastrointestinal symptoms but in clinical trials these were similar in frequency with placebo.
- A month’s treatment with Duavive costs £15.

Duavive HRT: conjugated oestrogens with bazedoxifene

STEVE CHAPLIN

NICE recommends HRT for up to five years to relieve vasomotor symptoms associated with the menopause; it should also be considered for alleviating associated low mood.1 A combined oestrogen/progestogen formulation is recommended for women with a uterus. However, combined HRT may increase the risk of breast cancer and stroke and may not protect against cardiovascular disease; transdermal administration is preferred for women at risk of venous thromboembolism.

There are currently over 20 oral combined HRT preparations available for sequential or continuous use; most contain estradiol but two (Premique, Prempar-O) contain conjugated oestrogens in combination with a progestogen. Duavive combines conjugated oestrogens with the selective oestrogen-receptor modulator (SERM) bazedoxifene.

Properties

Duavive is a modified-release combined therapy containing conjugated oestrogens 0.45mg and bazedoxifene 20mg, taken as a single oral tablet once daily. Duavive is licensed for the treatment of oestrogen deficiency symptoms in postmenopausal women with a uterus (with at least 12 months since the last menses) for whom treatment with progestogen-containing therapy is not appropriate.

Bazedoxifene has oestrogen agonist activity in bone and antagonist activity in breast and uterine tissues. The rationale for this combination is that bazedoxifene should inhibit the proliferative effects of conjugated oestrogens on the endometrium and prevent stimulatory effects in breast tissue. In one 12-month trial, the incidence of endometrial hyperplasia and bleeding with Duavive was similar to that observed with placebo and it was not associated with breast tenderness.2

There is little clinical experience of Duavive in women aged over 65 years, it is not recommended for women with renal impairment and it is contraindicated in those with hepatic impairment. Other prescribing cautions and contraindications are similar to those of other HRT preparations. The metabolism of bazedoxifene may be increased by rifampicin, phenobarbital, carbamazepine and phenytoin, potentially leading to decreased concentrations of bazedoxifene and increased risk of endometrial hyperplasia.

Duavive should only be used to treat symptoms that impair quality of life.
and the risks and benefits should be assessed at least annually.

**Clinical trials**

Two phase 3 trials provide the key data for the efficacy of Duavive (conjugated oestrogens 0.45mg/bazedoxifene 20mg) for vasomotor symptoms (SMART-2)\(^3\) and vulvovaginal atrophy (SMART-3).\(^4\) Both also included a treatment arm with a higher dose of conjugated oestrogens (conjugated oestrogens 0.625mg/bazedoxifene 20mg), which was not subsequently licensed.

SMART-2 included healthy postmenopausal women with an intact uterus aged 40–65 years, who were seeking treatment for hot flushes and reporting at least seven moderate to severe hot flushes per day (baseline about 10 per day) or 50 per week. Participants were randomised to receive placebo (n=63) or treatment with Duavive (n=127) for 12 weeks. The primary endpoints were the change in frequency and severity of hot flushes.

Duavive significantly reduced the mean daily number of moderate to severe hot flushes at four weeks compared with placebo (by about six vs three; \(p<0.001\)) and 12 weeks (by about eight vs five; \(p<0.001\)) (see Table 1) and also reduced their average daily severity. The proportion of patients with ≥75 per cent reduction in number of hot flushes at week 12 was 67 per cent with Duavive (odds ratio vs placebo 5.23; CI 95% 2.57–10.64).\(^5\)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Time slot</th>
<th>No. of pairs</th>
<th>Mean change</th>
<th>SE</th>
<th>(p) value vs placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duavive</td>
<td>Week 4</td>
<td>122</td>
<td>-5.90</td>
<td>0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Week 12</td>
<td>122</td>
<td>-7.63</td>
<td>0.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Placebo</td>
<td>Week 4</td>
<td>63</td>
<td>-2.84</td>
<td>0.56</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Week 12</td>
<td>63</td>
<td>-4.92</td>
<td>0.48</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1. Mean change from baseline in average daily number of moderate and severe hot flushes at weeks 4 and week 12 (last observation carried forward) with Duavive (conjugated oestrogens 0.45mg/bazedoxifene 20mg) vs placebo\(^5\)

Adverse events

The overall frequency of adverse events associated with Duavive reported in clinical trials was similar to that with placebo.\(^6\) The most frequent adverse effects included headache, muscle and joint pain, and gastrointestinal symptoms. Approximately 8–10 per cent of women discontinued treatment due to adverse events in studies lasting up to two years in both Duavive and placebo groups.\(^6\) There are insufficient data to determine the long-term risks of venous thromboembolism, cerebrovascular and cardiovascular disease, and cancer.

**References**


**Declaration of interests**

None to declare.

**Steve Chaplin is a pharmacist who specialises in writing on therapeutics**