Tablets containing 1 mg estradiol and 2 mg drospirenone (Angeliq®) No. (No:227/05)
Schering Health Care Ltd

New product for the indication: prevention of osteoporosis

9 December 2005

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

**ADVICE:** following a full submission

1 mg estradiol / 2 mg drospirenone (Angeliq®) is not recommended for use within NHS Scotland for prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or have contra-indications to, other medicinal products approved for the prevention of osteoporosis.

It maintains bone mineral density, relative to placebo, in post-menopausal women. However, no evidence of cost-effectiveness has been presented.

Overleaf is the detailed advice on this product.

Chairman
Scottish Medicines Consortium
**Indication**
Prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or contra-indicated for, other medicinal products approved for the prevention of osteoporosis.

**Dosing information**
One tablet daily, continuously

**UK launch date**
June 2005

**Comparator medications**
There are a wide range of preparations offering hormone replacement therapy and licensed for this indication.

**Cost of relevant comparators**
The following table gives costs for a year’s treatment (thirteen 28-day cycles) of preparations which offer continuous oral treatment with oestradiol 1 mg/day in combination with a progestogen, for Premique® which was a comparator in one trial and for tibolone which was the comparator in a health economic analysis for prevention of menopausal symptoms.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Progestogen</th>
<th>Cost per annum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angeliq®</td>
<td>Drospirenone 2 mg</td>
<td>£112</td>
</tr>
<tr>
<td>Femoston-conti®</td>
<td>Dydrogesterone 5 mg</td>
<td>£88</td>
</tr>
<tr>
<td>Indivina®*</td>
<td>Medroxyprogesterone acetate 2.5 mg</td>
<td>£93</td>
</tr>
<tr>
<td>Klovance®</td>
<td>Norethisterone acetate 0.5 mg</td>
<td>£64</td>
</tr>
<tr>
<td>Tibolone (Livial®)</td>
<td>Not applicable</td>
<td>£140</td>
</tr>
<tr>
<td>Premique®+</td>
<td>Medroxyprogesterone acetate 5 mg</td>
<td>£118</td>
</tr>
</tbody>
</table>

* May be titrated up to 2 mg ethinylestradiol
+ Contains conjugated oestrogens 0.625 mg
Summary of evidence on comparative efficacy

In a double-blind, placebo-controlled, randomised, 2 year study performed at one centre. 240 women, at least 1 year past a natural menopause and 45-65 years of age, were recruited by questionnaires sent out with the aid of social security numbers. Women were with or without oestrogen deficiency symptoms. Exclusion criteria were severe systemic disease, bone disease including osteoporosis, history of malignancy, or clinically abnormal blood or urine tests at baseline. All women had a clinically normal gynaecological examination including transvaginal ultrasound at baseline. None of the women received medications with significant effect on bone metabolism or the endometrium. The participants were randomly assigned to one of four oral treatment groups: 1mg estradiol, 1mg drospirenone (unlicensed) (n=60); 1mg estradiol, 2mg drospirenone (the licensed dose) (n=60); 1mg estradiol, 3mg drospirenone (unlicensed) (n=60) or placebo (n=60). Patients also received calcium tablets equivalent to a daily dose of 500 mg.

Bone mineral density (BMD) of the lumbar spine, hip and total body was measured by dual X-ray energy absorptiometry (DEXA). At baseline and at the end of the study, the scans at the spine and hip were performed twice, with the participant standing up before repositioning for the second measurement. The average values of BMD from the double measurements were used in the analyses. The percentage change from baseline was compared by analysis of variance (ANOVA).

After 2 years of treatment, the difference in BMD between the HRT-treated groups and the placebo group was 7% in the spine, 4% in the hip and 3% in the total body (all p<0.001).

Biochemical markers of bone turnover indicated beneficial effects on bone resorption and re-modelling.

Summary of evidence on comparative safety

In all studies drospirenone/estradiol was associated with an increase in the proportion of women who experienced bleeding and/or the proportion of time periods during which bleeding occurred and/or a decrease in the incidence of amenorrhoea. In general, bleeding was of low intensity and the frequency tended to increase during the early cycles after initiation and then to reduce. Both Premique and estradiol monotherapy showed slight advantages over drospirenone/estradiol in terms of bleeding, but these differences were not tested for significance.

Other data were also assessed but remain commercially confidential.*
Summary of clinical effectiveness issues

Bone-mineral density is widely recognised as a predictor of fracture risk. Otherwise, the clinical implications of the outcomes observed have not been shown. The results might have been easier to interpret if they had been presented as changes in the T-value, which takes account of the norm for healthy women, rather than as a percentage change. T-values were reported at baseline but not at end-point.

There are no comparative data for this indication, except vs placebo.

Other data were also assessed but remain commercially confidential.*

Summary of comparative health economic evidence

None presented for this indication.

Patient and public involvement

A Patient Interest Group Submission was not made.

Budget impact

None presented for this indication.

Guidelines and protocols

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

This assessment is based on data submitted by the applicant company up to and including 15 November 2005.

Drug prices are those available at the time the papers were issued to SMC for consideration.

* Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/

The undernoted references were supplied with the submission. Those shaded grey are additional to those supplied with the submission.
