This policy statement is approved by Halton, Knowsley, Liverpool, Southport and Formby, South Sefton, St Helens, Warrington, West Lancashire, and Wirral CCGs

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NHS
Pan Mersey
Area Prescribing Committee

CONJUGATED OESTROGENS and BAZEDOXIFENE modified release tablets (Duavive®)

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of CONJUGATED OESTROGENS and BAZEDOXIFENE modified release tablets (Duavive®) for the treatment of oestrogen deficiency in postmenopausal women with a uterus.

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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 progestin-containing therapy is not appropriate.[1]

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of Duavive® because:

- There is a lack of evidence to support the use of Duavive® over established treatments.
- The available safety data does not allow for assessment of whether the incidence of rare but important adverse events (such as cardiovascular or cerebrovascular events, venous thromboembolism or cancer) is increased in women taking conjugated oestrogens and bazedoxifene when compared with placebo or historical data.[2]
- Experience of use in treating women over 65 years is limited.[1]
- There is a lack of data to determine the optimal duration of treatment.[2]

It was concluded that the clinical benefits did not outweigh the potential unknown risk of treatment and it is more expensive than other available standard hormone replacement therapy (HRT).

Prescribing information

- The Pan Mersey Area Prescribing Committee does not recommend the prescribing of Duavive® 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 progestin-containing therapy is not appropriate.
- Oestrogen deficiency in post-menopausal women with a uterus should be treated in line with NICE Guideline [NG23] Menopause: Menopause: diagnosis and management, November 2015.
- Standard treatment for vasomotor and psychological symptoms (in women with a uterus) is combination oestrogen and progestogen HRT.[3]

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

Supporting information

CONJUGATED OESTROGENS and BAZEDOXIFENE modified release tablets (Duavive®)

Effectiveness

Duavive® is a combination of conjugated oestrogens and bazedoxifene 0.45mg/20mg. Bazedoxifene is a selective oestrogen receptor modulator which reduces the oestrogen-induced risk of endometrial hyperplasia in non-hysterectomised women.[1]

The SMART 2 trial (RCT, n=332) showed that Duavive® statistically significantly reduced the average daily number of moderate and severe hot flushes from a baseline of 10.3 to 2.8 at week 12. In the placebo group, hot flushes were reduced from 10.5 hot flushes at baseline to 5.4 at week 12. The difference between the groups was statistically significant ($p<0.001$).[4]

Decreases in vaginal pH and changes in the severity of the most bothersome vulvar or vaginal symptom were not statistically significantly different between the Duavive® group and the placebo group in the SMART 3 trial RCT, n=664).[4]

Statistically significant improvements in total score of the menopause-specific quality of life questionnaire (secondary endpoint) were seen in both the SMART 2 and SMART 3 trials in the Duavive® group compared with the placebo group.[4]

There are no active comparator trials with standard HRT treatments.[4]

Safety

Very common adverse events include abdominal pain. Common adverse events include vulvovaginal candidiasis, constipation, diarrhoea, nausea, muscle spasms, and increased blood triglycerides.[1]

Due to the small number of women exposed and short duration of exposure; safety data does not allow for assessment of whether the incidence of rare but important adverse events such as cardiovascular, cerebrovascular, venous thromboembolism or cancer are increased compared with placebo or other treatments.[2]

Contraindications to using Duavive® include women with known, suspected, or history of breast cancer; known, past or suspected oestrogen-dependent malignant tumours (e.g. endometrial cancer); undiagnosed genital bleeding; untreated endometrial hyperplasia; active or history of venous thromboembolism; known thrombophilic disorders; active or history of myocardial infarction or stroke; acute liver disease or a history of liver disease as long as liver function tests have failed to return to normal; women of childbearing potential; and porphyria.[1]

Refer to SPC for full list of contraindications, adverse reactions and interactions.

Cost[5]

Drug	Patient cost per 12 months (ex VAT)
Conjugated oestrogens 0.45mg bazedoxifene 20mg tablets (Duavive®)	£180.00
Tibolone 2.5mg tablets	£103.44
Estradiol 2mg/norethisterone acetate 1mg tabs (Elleste Duet Conti)	£68.08
Conjugated oestrogens 300microgram / medroxyprogesterone 1.5mg M/R tablets (Premique Low Dose)	£26.08
Estradiol 1mg/dydrogesterone 5mg tablets (Femoston-conti)	£97.72
Estradiol 50microgram / norethisterone 170 microgram per 24 hours patch (Evorel Conti)	£156.00

Patient factors[1]

The experience treating women older than 65 years is limited. Duavive® has not been studied in women over 75 years of age.

Duavive® should not be taken by women of childbearing potential.

The pharmacokinetics of Duavive® have not been evaluated in patients with renal impairment. Use in this population is therefore not recommended.

The safety and efficacy of Duavive® have not been evaluated in patients with hepatic impairment. Use in this population is contraindicated.

Supporting information

References

1. Pfizer Limited. Summary of Product Characteristics Duavive 0.45mg/20mg modified release tablets, April 2019. Accessed online 23 April 2019.
2. European Medicines Agency. Committee for Medicinal Products for Human Use (CHMP) Assessment report. Duavive, Procedure No. EMEA/H/C/002314/0000, October 2014. Accessed online 23 April 2019.
3. NICE Guideline [NG23] Menopause: diagnosis and management, November 2015. Accessed online 19 July 2019.
4. NICE Evidence Summary [ES3] Oestrogen deficiency symptoms in postmenopausal women: conjugated oestrogens and bazedoxifene acetate, December 2016. Accessed online 23 April 2019.
5. NHS Business Services Authority. Dictionary of medicines and devices (dm+d) browser. Accessed online 19 July 2019.