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

Halton | Knowsley | Liverpool | Southport and Formby | South Sefton | St Helens | Warrington | West Lancashire

PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
REF: PS187 FINAL
APC BOARD DATE: 28 JUN 2017

NHS Pan Mersey Area Prescribing Committee

CONJUGATED OESTROGENS and BAZEDOXIFENE 0.45mg/20mg modified release tablets (Duavive®)

BLACK

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of CONJUGATED OESTROGENS and BAZEDOXIFENE 0.45mg/20mg modified release tablets (Duavive®) for the treatment of oestrogen deficiency in postmenopausal women with a uterus

Duavive® is a combination of Conjugated Oestrogens and Bazedoxifene 0.45mg/20mg. Bazedoxifene is a third-generation selective oestrogen receptor modulator. Duavive® is licensed for the treatment of oestrogen deficiency in postmenopausal women with a uterus (with at least 12 months since the last menses) for women whom treatment with progestin-containing therapy is not appropriate.

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.[1]
- Experience of use in treating women over 65 years is limited.[2]
- There is a lack of data to determine the duration of treatment.

It was concluded the clinical benefits did not outweigh the potential unknown risk of treatment and it is more expensive than other available standard HRT treatments.

Oestrogen deficiency in post-menopausal women with a uterus should be treated in line with NICE NG 23 Menopause; diagnosis and management. Standard treatment for vasomotor and psychological symptoms is combination oestrogen and progestogen hormone replacement therapy.[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.

CONJUGATED OESTROGENS and BAZEDOXIFENE 0.45mg/20mg modified release tablets (Duavive®▼)

EFFECTIVENESS[1,4]

- Bazedoxifene is a third-generation selective oestrogen receptor modulator. Bazedoxifene inhibits the proliferative effects of conjugated oestrogens on the endometrium, reducing the incidence of irregular uterine bleeding and prevents oestrogenic stimulatory effects of conjugated oestrogens in breast tissue and therefore does not induce breast pain, tenderness or changes in the breast density.
- 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 ($p<0.001$) (1 RCT, n=332).
- 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 (1 RCT, n=664).
- Statistically significant improvements in total score of the menopause-specific quality of life questionnaire (secondary endpoint) were seen in both trials in the Duavive® group compared with the placebo group.
- There are no active comparator trials with standard HRT treatments.

SAFETY[2]

- The SPC for Duavive®▼ MR tablets states that very common adverse events include abdominal pain.
- Common adverse events include vulvovaginal candidiasis, constipation, diarrhoea, nausea, muscle spasms, and increased blood triglycerides.
- Duavive® has not been evaluated in people with renal or hepatic impairment and so use in these populations is not recommended.
- Experience of using Duavive® in women aged over 65 years is limited.
- Contraindications to using Duavive® include women with known, suspected, or history of breast cancer; known, past or suspected oestrogen-dependent malignant tumours (for example, endometrial cancer); undiagnosed genital bleeding; untreated endometrial hyperplasia; active or history of venous thromboembolism; known thrombophilic disorders; and active or history of myocardial infarction or stroke.
- 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.[1]

COST

Drug	Patient cost per course/ per year (ex VAT)
Duavive®	£195.00
Tibolone 2.5mg tablets	£134.68
Conjugated oestrogens 0.625mg/norgestrol 0.15mg tabs	£25.00
Estradiol 2mg/norethisterone 1mg tabs	£36.80
Estradiol 3.2mg patch, estradiol 3.2mg plus norethisterone 11.2mg patch	£144.17

Costs based on MIMS list prices January 2017 and 28 days treatment.

PATIENT FACTORS

Duavive® should not be used in acute liver disease or a history of liver disease if liver function tests have failed to return to normal.

Must not be taken by women of childbearing potential. [2]

PRESCRIBING INFORMATION

Duavive® is not recommended for prescribing.

REFERENCES

1. Committee for medicinal products for human use, assessment report Duavive, procedure number. EMEA/H/C/002314/0000 23 October 2014 http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/002314/WC500181564.pdf
2. Electronic medicines compendium, summary of product characteristics for Duavive® (conjugated oestrogens and Bazedoxifene acetate) http://www.medicines.org.uk/emc/medicine/32127 accessed online 30th January 2017.
3. NICE Guideline (NG23), Menopause: diagnosis and management. November 2015. https://www.nice.org.uk/guidance/ng23 (accessed online 30th January 2017)
4. NICE Evidence Summary (ES3) Oestrogen deficiency symptoms in postmenopausal women: conjugated oestrogens and bazedoxifene acetate. December 2016. https://www.nice.org.uk/advice/es3 accessed online 19 June 2017.