AWMSG Secretariat Assessment Report – Limited submission

Levonorgestrel (Kyleena®) 19.5 mg intrauterine delivery system

Company: Bayer plc

Licensed indication under consideration: Contraception for up to five years

Marketing authorisation date: 23 December 2016

Comparator(s)

- The weighted average by level of use of all reversible contraceptive methods available in Wales. The submission includes a mixed comparator consisting of all reversible Welsh contraceptive options (including oral, transdermal and other methods).

Limited submission details

- Significant new formulation with a pro-rata or lower cost per treatment.
- Estimated small difference in cost compared to comparator(s).

Clinical effectiveness

- Kyleena® is the first low-dose levonorgestrel-containing intrauterine system (IUS) licensed for use for up to five years. A levonorgestrel-containing IUS (Jaydess®) has previously been recommended by the All Wales Medicines Strategy Group (AWMSG) for contraception for up to three years.
- AWMSG All Wales Prescribing Guidelines (2012) state that long-acting reversible contraceptives (LARC) should be considered as a first-line option as this is the most effective way to avoid pregnancy.
- A clinical guideline issued by the National Institute for Health and Care Excellence (NICE), updated in 2014, and a clinical service standard published by The Faculty of Sexual and Reproductive Healthcare (FSRH) in 2016, both recommend that women requiring contraception should be given information about and offered a choice of all contraceptive methods.
- The comparator included in the company submission is a mixed contraceptive comparator consisting of all Welsh reversible contraceptive options (including oral, transdermal and other methods). Clinical experts advised AWTTC that LARCs would be the most appropriate comparator.
- There is no UK/Wales clinical effectiveness evidence available for the mixed contraceptive comparator. Clinical effectiveness data for the mixed contraceptive comparator (based on failure rates) was reported from a survey in the United States involving 7,643 women aged 15 to 44 years. This data was compared with data from a phase III, international, open-label study of 2,885 nulliparous and parous women aged 18 to 35 years, who were randomised 1:1 to receive 19.5 mg levonorgestrel (Kyleena®) or 13.5 mg levonorgestrel (Jaydess®) for three years. After three years, women using Kyleena® were given the choice to continue with

treatment for up to an additional two years as part of an extension study. Of the 707 women entering the two-year extension study, 550 completed it.

- Based on the phase III study and real-world data, Kyleena® is more effective than the mixed contraceptive comparator. The five-year Pearl Index (the number of pregnancies per 100 woman-years) in the Kyleena® group of the phase III study was 0.29 (95% confidence interval [0.16 to 0.50]). The failure rates at Year 1 for Kyleena® versus the weighted average of all reversible contraceptive options was approximately 0.2% and 17.2%, respectively. The five-year cumulative failure rate for Kyleena® was 1.4%. Discontinuation rates after the first year of use for Kyleena® versus the weighted average of all reversible contraceptive options were equal to [commercial in confidence data removed] and 44.2%, respectively.
- The submission does not include a comparison with Jaydess®. However, FSRH reports a three-year Pearl Index of 0.31 for Kyleena® and 0.33 for Jaydess®, and a cumulative three-year failure rate of 1% for Kyleena® and 0.9% for Jaydess®.
- For all premature discontinuations of Kyleena®, there was a rate of 40.1% in the first three years of the phase III study and 22.2% in the two-year extension study. The most common reason for study discontinuation in the first three years was adverse events. Over the five-year study period, 13 women discontinued treatment due to pregnancy, eight of which were ectopic.
- The adverse event profile for Kyleena®, including the incidence of ectopic pregnancies, is in line with the current body of knowledge for other levonorgestrel-releasing IUS/devices.

Budget impact

- Prevalence was defined according to women being of reproductive age (16 to 49 years old) and percentage of women using non-surgical contraceptives.
- The company has provided a budget impact model comparing Kyleena® against a weighted average of all reversible Welsh contraceptive methods. The market shares dictate the weight each contraceptive method holds within the weighted average of all reversible contraceptive options. There is uncertainty with the budget impact model as clinical experts have advised that Kyleena® will displace other LARCs; therefore, the budget impact model might overestimate the costs as it assumes that Kyleena® will displace all reversible forms of contraception.
- The company's estimated uptake for Kyleena® is [commercial in confidence data removed] in Year 1 and [commercial in confidence data removed] in Year 5. This translates to [commercial in confidence data removed] women receiving Kyleena® in Year 1 and Year 5. The number of women eligible for contraception is kept constant and population growth is not considered, which might underestimate the net budget impact of Kyleena®.
- The company estimates that the net budget impact will range from £112,410 in Year 1, increasing to £371,339 in Year 5.
- In addition to a one-off acquisition cost per patient for the five-year use of Kyleena®, the budget impact estimates also include significant maintenance costs, ranging from £286,332 in Year 1 to £583,786 in Year 5. These costs include one initial consultation, one follow-up visit each year, one insertion and one removal consultation specific for LARC methods, and sterile packs. These additional costs are likely to be associated with other LARCs and, to a lesser extent, the mixed contraceptive comparator.

Additional information

- AWTTC is of the opinion that, if recommended, levonorgestrel (Kyleena®) may be appropriate for prescribing by all prescribers within NHS Wales for the indication under consideration. The Summary of Product Characteristics recommends that Kyleena® should only be inserted by physicians/healthcare professionals who are experienced in IUS insertions and/or have undergone training on the Kyleena® insertion procedure.

Evidence search

Date of evidence search: 4 May 2018.
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Levonorgestrel (Kyleena®) 19.5 mg intrauterine delivery system. Reference number: 3582. July 2018.