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AWMSG Secretariat Assessment Report – Limited submission

Lopinavir/ritonavir (Kaletra®) 80 mg/20 mg oral solution

Company: AbbVie Ltd.

Licensed indication under consideration: In combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infected children aged from 14 days to less than 2 years old.

Date of licence extension: 26 July 2017.

Comparator(s)

- No comparator was included in the company submission.

Limited submission details

The limited submission criteria were met based on:

- a minor licence extension
- anticipated usage in NHS Wales is considered to be of minimal budgetary impact.

Clinical effectiveness

- This submission covers a licence extension for lopinavir/ritonavir oral solution in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infected children aged from 14 days to less than 2 years old. Lopinavir/ritonavir oral solution is already licensed for use in patients aged 2 years and over in the same indication and is included on Welsh health board formularies. Marketing authorisation for this older age group was granted before 1 October 2010, and was not appraised by the All Wales Medicines Strategy Group (AWMSG) as it did not meet the criteria for appraisal at this time.
- The company does not specify a comparator in their submission. Lopinavir/ritonavir is the only ritonavir-boosted protease inhibitor licensed for children aged from 14 days to 2 years old. The Paediatric European Network for Treatment of AIDS guidelines for treatment of paediatric HIV-1 infection (2015) recommend combination therapy including either a ritonavir-boosted protease inhibitor or a non-nucleoside reverse transcriptase inhibitor (NNRTI) as first-line antiretroviral therapy in children aged less than three years. The NNRTI nevirapine is licensed for the treatment for HIV-1 in children of any age, and therefore could represent an alternative option to lopinavir/ritonavir for the indication under consideration. In response to queries from the All Wales Therapeutics and Toxicology Centre (AWTTC), the company clarified that they believe differences in the minimum licensed age between lopinavir/ritonavir and nevirapine mean the two treatments are not always comparable: in circumstances where treatment is initiated before 14 days of age nevirapine but not lopinavir/ritonavir will be a treatment option.

- An open-label, dose-finding trial (P1030) evaluated the safety, efficacy and tolerability of lopinavir/ritonavir oral solution in combination with two nucleoside reverse transcriptase inhibitors in children (n = 31) starting treatment between the ages of two weeks and six months. After 48 weeks of follow up, 22 of 31 patients had HIV-1 RNA < 400 copies/ml. While on study treatment, 29 of 31 children achieved an HIV-1 RNA < 400 copies/ml; 19 had durable viral suppression over a median follow up period of 123 weeks (range 4–252 weeks).
- A randomised trial (P1060) assessed the effectiveness of nevirapine or lopinavir/ritonavir (both given in combination with zidovudine and lamivudine) tablets in HIV-1-infected children (n = 451) aged 2–36 months. The percentage of children who experienced virologic failure or discontinuation of treatment was significantly higher in the nevirapine group than in the lopinavir/ritonavir group (40.8% versus 19.3%; p < 0.001), irrespective of prior nevirapine exposure. The incidence of virologic failure or death remained significantly greater in the nevirapine group compared to the lopinavir/ritonavir group at 6 months to 60 months follow-up.
- Patients treated with lopinavir/ritonavir in studies P1030 and P1060 had similar outcomes to an earlier study (M98-940) that supported the licence of lopinavir/ritonavir in children aged two years and older.
- The safety profile of lopinavir/ritonavir in children aged from 14 days to less than 2 years old is consistent with the known safety profile in adults and older children. Lopinavir/ritonavir contains propylene glycol and ethanol: the Committee for Medicinal Products for Human Use highlights that chronic exposure to these excipients in the youngest children should be monitored.

Budget impact

- In their submission the company estimated the cost of lopinavir/ritonavir oral solution per patient based on the estimated body surface area (0.51 m^2) and dose (230/57.5 mg/m^2 twice daily) for a two year old child.
- The company estimated that 12 patients in Wales would be eligible for lopinavir/ritonavir treatment each year, based on the number of children who acquired HIV infection through mother-to-child transmission in the UK in 2015. However, because lopinavir/ritonavir is not licensed for use in children aged less than 14 days, the company estimate that only 1–3% of eligible patients will be treated with lopinavir/ritonavir, equivalent to a maximum of one patient per year in Wales.
- Assuming a single patient is treated each year in line with the company's assumptions about uptake, the budget impact is estimated to be £1,123 per year. Assuming all 12 eligible patients are treated the estimated budget impact is £13,476 per year. Cost estimates are based on the medicine acquisition costs only.
- The budget impact is based on there being no use of a comparator medicine such as nevirapine in children eligible for lopinavir/ritonavir. The displacement of nevirapine by lopinavir/ritonavir could reduce the budget impact or result in net medicine acquisition cost savings. It is unclear what the company's estimate of uptake is based on.

Additional information

- AWTTC is of the opinion that, if recommended, lopinavir/ritonavir is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipate that lopinavir/ritonavir may be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 27 October 2017.
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. Lopinavir/ritonavir (Kaletra®) 80 mg/20 mg oral solution. Reference number: 3557. January 2018.