Abacavir + dolutegravir + lamivudine

Essential medicine status ✓

Section: 6. Anti-infective medicines > 6.4. Antiviral medicines > 6.4.2. Antiretrovirals > 6.4.2.5. Fixed-dose combinations of antiretrovirals

EMLc | ATC codes: J05AR13

Indication	Human immunodeficiency virus disease without mention of associated disease or condition, clinical stage unspecified ICD11 code: 1C62.Z
INN	Abacavir + dolutegravir + lamivudine
Medicine type	Chemical agent
List type	Core (EML) (EMLc)
Formulations	Oral > Solid > tablet: 60 mg (as sulfate) + 5 mg + 30 mg (dispersible, scored) (EMLc)
EML status history	First added in 2025 (TRS 1064)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Main patents have expired but secondary patents might remain active in some jurisdictions. For more information on specific patents and license status for developing countries visit www.MedsPal.org Read more about patents.
Wikipedia	Abacavir + dolutegravir + lamivudine
DrugBank	Abacavir, Dolutegravir, Lamivudine

Expert Committee recommendation

The Expert Committee recognized that age-appropriate, child-friendly formulations of antiretroviral medicines, when available and quality-assured, are essential public health interventions to meet the needs of paediatric patients with HIV. The Committee recalled the recommendations of previous Expert Committees to include the component medicines of the proposed fixed-dose combination in the EMLc based on favourable benefits and acceptable safety and public health need for paediatric patients. The Committee noted that new data from the IMPAACT 2019 trial indicated the achievement of pharmacokinetic targets of the proposed formulation across paediatric weight bands. The Committee also noted that a combination regimen of abacavir + dolutegravir + lamivudine was the preferred first-line treatment for infants and children recommended in WHO guidelines and considered that the availability of a dispersible tablet formulation supported the implementation of these guidelines by providing a simplified, age-appropriate treatment option. The Committee appreciated that the proposed formulation was the subject of licensing agreements with the Medicines Patent Pool, supporting affordable access in low- and middle-income countries, and that generic versions were already available and prequalified by WHO. Based on these considerations, the Expert Committee recommended the addition of abacavir + dolutegravir + lamivudine dispersible tablets to the core list of the EMLc for the treatment of paediatric patients with HIV, with use in accordance with recommendations in WHO guidelines.

Background

A triple fixed dose combination of abacavir + dolutegravir + lamivudine has not been previously considered for inclusion on the EMLc. Currently, the component medicines are all individually included on the EMLc as individual medicines (dolutegravir,

lamivudine) or dual fixed dose combinations (abacavir + lamivudine).

Public health relevance

According to the 2024 Global AIDS Update by UNAIDS, in 2023, nearly 40 million people were living with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) worldwide, with 1.3 million new HIV-1 infections reported (a decrease of 39% since 2010) and 630 000 HIV-related deaths. An estimated 1.4 million children aged 0–14 years were living with HIV, with 86% residing in sub-Saharan Africa. Despite a reduction in mother-to-child transmission of HIV in recent years, 120 000 new paediatric infections occurred in 2023 and 76 000 children died from AIDS-related causes (1). In the absence of antiretroviral treatment, over 50% of HIV-infected infants progress to AIDS or death by the age of 2 years (2). Despite recognition of the advantages of early treatment, paediatric treatment coverage still reached only 57% of children eligible for treatment in 2023 and only 48% of all children living with HIV have viral suppression, substantially fewer than the 78% of adults living with HIV (1). Non-nucleoside reverse transcriptase inhibitor (NNRTI)-based antiretroviral treatment has been widely used in paediatric patients for both prevention of transmission and treatment. A 2017 survey of newly diagnosed children in five sub-Saharan African countries indicated resistance to one or more NNRTIs in up to 53% of the cohort (3). These increasing rates of resistance to the previously recommended first-line treatments prompted WHO to recommend rapid transition to dolutegravir-based treatment in 2018 as child-friendly formulations become available.

Benefits

In 2017, the Paediatric Antiviral Drug Optimization-3 working group meeting, convened by WHO, reviewed available data and recommended the development of a triple fixed-dose combination of abacavir + dolutegravir + lamivudine in a dispersible tablet formulation (4). Paediatric data used to inform this recommendation came from the IMPAACT P1093 and ODYSSEY clinical trials. IMPAACT P1093 was a phase I/II single-arm, open-label trial to assess the pharmacokinetics safety and efficacy of dolutegravir plus an optimized background regimen in HIV-infected children and adolescents (5–7). Data from the P1093 trial included: cohorts 1 (aged 12 to < 18 years) and 2 (6 to < 12 years), which provided evidence supporting the use of dolutegravir 50 mg film-coated tablets in paediatric patients weighing more than 14 kg; and cohorts 3 (2 to < 6 years), 4 (6 months to < 2 years) and 5 (4 weeks to < 6 months), which provided evidence supporting the use of dolutegravir 25 mg dispersible tablets. Seventy-five study participants ranging in age from 1 month to 18 years received the currently approved dose (determined by weight and age) of dolutegravir film-coated tablets or dispersible tablets. Eighty percent of participants were treatment-experienced, but none had received integrase strand transfer inhibitor. Among the 75 participants, 42 received dolutegravir for at least 48 weeks. At week 48, 69% of participants achieved HIV RNA < 50 copies/mL and 79% achieved HIV RNA < 400 copies/mL. The median CD4 count (per cent) increase from baseline to week 48 was 141 cells/mm3 (7%). The effectiveness observed in the trial was comparable to that of treatment-experienced adult subjects. ODYSSEY was an open-label, randomized, non-inferiority trial that compared the efficacy and safety of dolutegravir-based antiretroviral treatment with standard care in 707 children and adolescents aged < 18 years and weighing at least 14 kg starting first- or second-line treatment (8). Participants were randomly assigned to receive dolutegravir-based antiretroviral treatment (n = 350 of whom 154 started dolutegravir as first-line therapy and 196 as second-line therapy or the local standard treatment (n = 357). Of the first-line treatment participants, 92% received efavirenz and of the second-line treatment participants, 98% received a boosted protease inhibitor. Across all arms, 65% of participants received abacavir + lamivudine as the nucleoside reverse transcriptase inhibitor backbone. The primary endpoint was the proportion of participants with virological or clinical treatment failure by 96 weeks. By 96 weeks, 47 participants in the dolutegravir group and 75 in the standard-care group experienced treatment failure (adjusted hazard ratio (HR) 0.60, 95% confidence interval (CI) 0.42 to 0.86). Treatment effects were similar between first- and second-line cohorts. Of the participants in whom first-line dolutegravir therapy failed, none had a major dolutegravir-related resistance mutation, whereas 29 participants in whom the standard care failed developed non-nucleoside reverse transcriptase inhibitor and/or nucleoside reverse transcriptase inhibitor resistance mutations. The study concluded that dolutegravir-based antiretroviral therapy was superior to standard care in children and adolescents with HIV-1 infection starting first- or second-line treatment. IMPAACT 2019 was a phase I/II, open-label, single-arm dose-confirmation study that evaluated the pharmacokinetics, safety and tolerability of a fixed-dose combination formulations (immediate-release or dispersible tablets) of abacavir + dolutegravir + lamivudine (9). Fifty-seven infants and children younger than 12 years and weighing 6 kg to < 40 kg were enrolled, 54 of whom were treatment-experienced. Participants weighing < 25 kg received the dispersible tablet formulation (60 mg + 5 mg + 30 mg) and participants weighing 25 kg to < 40 kg received the immediate-release tablet formulation (600 mg + 50 mg + 300 mg). The primary pharmacokinetic outcome measures were the geometric mean area

under the concentration time curve over the 24-hour dosing interval, maximum concentration and concentration at 24 hours post-dose for dolutegravir, abacavir, and lamivudine for each of five weight-bands. Overall, pharmacokinetic targets were achieved in all weight bands confirming the selected doses through 24 weeks of dosing. After 24 weeks, all treatment-experienced participants and 2/3 treatment-naïve participants had virological suppression. The study concluded that dosing of abacavir, dolutegravir and lamivudine was confirmed in children weighing 6 kg < 40 kg, and both formulations were safe, well tolerated and efficacious through 24 weeks of treatment.

Harms

In the IMPAACT 2019 study, the safety profile was comparable to that observed in adults and both formulations were well tolerated by paediatric patients In the ODYSSEY trial, similar rates of grade 3 or 4 adverse events and serious adverse events occurred in participants receiving either dolutegravir or standard care. Participants receiving dolutegravir-based treatment were observed to have slightly increased weight, height and body mass index for age compared with those receiving standard care, which was attributed to improvement in normal growth as weight and height both increased. Overall adherence, acceptability and palatability were considered favourable. Both formulations were well tolerated and there were no grade 3 or higher adverse events related to abacavir + dolutegravir + lamivudine and no discontinuation of treatment due to adverse events (9).

Cost / cost effectiveness

No cost–effectiveness studies for abacavir + lamivudine + dolutegravir dispersible tablets were identified in the application. The Clinton Health Access Initiative and Unitaid have negotiated ceiling prices with Aurobindo and Mylan/Viatris of 15 United States dollars (US$) ex-works per 180-count pack of abacavir + dolutegravir + lamivudine dispersible tablets. These prices are available to all public-sector procurers buying for countries included in the relevant Medicines Patent Pool licenses. In almost all low- and middle-income settings where abacavir + dolutegravir + lamivudine dispersible tablets would be accessed, governments and donors pay for antiretroviral treatments in public facilities so there are no costs to patients. The estimated per person per year costs of abacavir + dolutegravir + lamivudine dispersible tablets and comparator regimens are presented in Table 7 (refer to TRS 1064). Although abacavir + dolutegravir + lamivudine dispersible tablets represents a slight increase in per person per year costs compared with separate abacavir + lamivudine and dolutegravir dispersible tablets, it is anticipated that the price of abacavir + dolutegravir + lamivudine dispersible tablets will decrease as volumes increase. Additionally, abacavir + dolutegravir + lamivudine dispersible tablets are expected to bring cost savings from warehousing and freight efficiencies due to fewer bottles required per patient, reducing transportation and storage costs.

WHO guidelines

The 2021 WHO consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring recommend a regimen of dolutegravir in combination with an nucleoside reverse transcriptase inhibitor backbone of abacavir and lamivudine as the preferred first-line treatment for infants and children with HIV older than 4 weeks and weighing at least 3 kg (conditional recommendation, low-certainty evidence) (10).

Availability

The innovator product, TRIUMEQ PD (ViiV Healthcare), has received regulatory approval for the treatment of HIV in children at least 3 months of age and weighing at least 6 kg in several major markets, including Chile, European Union, Switzerland, United Kingdom of Great Britain and Northern Ireland, and the United States. Generic versions are available from at least three generic manufacturers, two of which are currently prequalified by WHO. Generic versions are being procured and introduced in low- and middle-income countries through licensing agreements between ViiV Healthcare and the Medicines Patent Pool. These agreements facilitate access to affordable generic versions of abacavir + dolutegravir + lamivudine dispersible tablets in 120 countries included in the licence. Additionally, there are nine more countries outside the licenced territory where no patents have been found, potentially allowing Medicines Patent Pool sublicencees to supply these markets.

Other considerations

Based on the WHO paediatric quality product profile assessment tool, this formulation was determined to be appropriate for the

ages and weights indicated (older than 4 weeks and weighing more than 6 kg). The dispersible tablet formulation is particularly beneficial for young children who may have difficulty swallowing solid dosage forms. This age-appropriate formulation supports adherence and effective treatment outcomes in paediatric populations.

1. The urgency of now: AIDS at a crossroads. Geneva: Joint United Nations Programme on HIV/AIDS; 2024. (https://www.unaids.org/en/resources/documents/2024/global-aids-update-2024). Licence: CC BY-NC-SA 3.0 IGO.
2. Newell M-L, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. Lancet. 2004;364(9441):1236–43 (https://doi.org/https://doi.org/10.1016/S0140-6736(04)17140-7).
3. Jordan MR, Penazzato M, Cournil A, Vubil A, Jani I, Hunt G et al. Human immunodeficiency virus (HIV) drug resistance in African infants and young children newly diagnosed with HIV: a multicountry analysis. Clin Infect Dis. 2017;65(12):2018–25 (https://doi.org/10.1093/cid/cix698).
4. Paediatric ARV drug optimization 3 review: summary report. Geneva: World Health Organization; 2018 (https://iris.who.int/handle/10665/272292). Licence: CC BY-NC-SA 3.0 IGO.
5. Viani RM, Alvero C, Fenton T, Acosta EP, Hazra R, Townley E et al. Safety, pharmacokinetics and efficacy of dolutegravir in treatment-experienced HIV-1 infected adolescents: forty-eight-week results from IMPAACT P1093. Pediatr Infect Dis J. 2015;34(11):1207–13 (https://doi.org/10.1097/inf.0000000000000848).
6. Wiznia A, Alvero C, Fenton T, George K, Townley E, Hazra R et al. IMPAACT 1093: dolutegravir in 6- to 12-year-old HIV-infected children: 48-week results. a [CROI abstract 816]. In: Abstracts from the 2016 Conference on Retroviruses and Opportunistic Infections. Top Antivir Med. 2016;24(e-1):343.
7. Ruel T, Acosta EP, Singh R, Alvero C, Fenton T, George K et al. Pharmacokinetic and 4-week safety/efficacy of dolutegravir (S/GSKI 349572) dispersible tablets in HIV-infected children aged 4 weeks to <6 years: results from IMPAACT [Poster Number: LBPEB023]. Presented at the XXII International AIDS Conference, Amsterdam, Netherlands, 25 July 2018.
8. Turkova A, White E, Mujuru HA, Kekitiinwa AR, Kityo CM, Violari A et al. Dolutegravir as first- or second-line treatment for HIV-1 infection in children. N Engl J Med. 2021;385(27):2531–43 (https://doi.org/10.1056/NEJMoa2108793).
9. Brooks KM, Kiser JJ, Ziemba L, Ward S, Rani Y, Cressey TR et al. Pharmacokinetics, safety, and tolerability of dispersible and immediate-release abacavir, dolutegravir, and lamivudine tablets in children with HIV (IMPAACT 2019): week 24 results of an open-label, multicentre, phase 1–2 dose-confirmation study. Lancet HIV. 2023;10(8):e506–e17 (https://doi.org/https://doi.org/10.1016/S2352-3018(23)00107-8).
10. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, 2021 update. Geneva: World Health Organization; 2021. (https://apps.who.int/iris/handle/10665/342899). Licence: CC BY-NC-SA 3.0 IGO.