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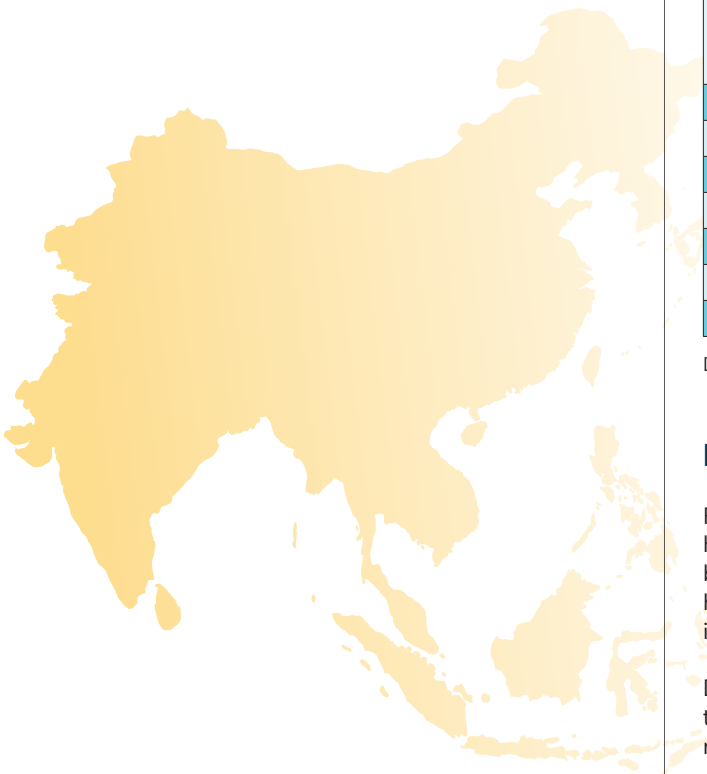
# Pediatric Dolutegravir: Securing Access to Dispersible Tablets for Children in the Asia-Pacific



## ONGOING CHALLENGES TO PREVENTING AND TREATING HIV IN INFANTS

In 2021, UNAIDS estimated that there were 130,000 children living with HIV in the Asia-Pacific region, with 14,000 new infections occurring through vertical transmission, which varied by country (Table 1). Malaysia, Maldives, Sri Lanka, and Thailand have met World Health Organization (WHO) criteria for elimination of mother-to-child transmission, but countries like Indonesia and the Philippines continue to have high rates of new infant infections due primarily to low rates of treatment for pregnant women living with HIV.

It is critically important to immediately diagnose and treat infants who acquire HIV with the most potent antiretroviral medicines available to prevent illness and death. However, due to the small numbers of infants and children with HIV in the region, countries have not prioritized procurement of pediatric antiretroviral formulations, leading to limited access for children and families.

**Table 1: 2021 vertical HIV transmission metrics in selected Asia-Pacific countries**

| Country | Treatment coverage of pregnant women living with HIV | Rate of vertical transmission | Number of children 0-14 years living with HIV |
|---|---|---|---|
| Cambodia | 80% | 14% | 2,300 |
| India | 64% | 24% | 70,000 |
| Indonesia | 15% | 31% | 19,000 |
| Malaysia | >98% | 2% | <700 |
| Philippines | 15% | 39% | <1,000 |
| Thailand | 97% | 2% | 2,000 |
| Vietnam | 75% | 18% | 4,900 |

Data: UNAIDS

## PEDIATRIC DOLUTEGRAVIR

Recent approvals of dispersible formulations of dolutegravir (DTG) for infants have created an opportunity to narrow these pediatric treatment gaps. DTG belongs to a class of antiretroviral medicines known as integrase inhibitors, and has been shown to successfully control HIV in infants, children, and adolescents in combination with other antiretrovirals.[1,2]

Dispersible formulations of DTG can be given to infants and children from 3 kg to 20 kg. Children and adolescents weighing more than 20 kg can take the 50 mg film-coated tablet formulation used in adults.

**Initial approval:** The U.S. Food and Drug Administration (US FDA) and European Medicines Agency (EMA) approved dispersible DTG in June and November 2020, respectively, for use in children from four weeks of age weighing at least 3 kg in combination with other antiretroviral medicines.

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**WHO recommendations:** In its 2019 recommendations on first- and second-line ART regimens, the WHO included the use of DTG for infants and children when appropriate formulations were available for their weight and age. With the regulatory approvals of dispersible formulations, this recommendation was further strengthened in the July 2021 *Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring.*

**Formulations and dosing:** The innovator version of dispersible DTG is 5 mg while the licensed generic companies manufacture 10 mg scored tablets. One bottle of the innovator version contains 60 tablets, and one bottle of the generic dispersible DTG contains 90 tablets. Dosing is according to the weight band of the child (Table 2). The number of tablets needed differs based on whether the innovator or licensed generic formulation is used.

**Table 2: Dosing of dispersible DTG tablets**

| Weight band | Dosing | Number of tablets per day | |
|---|---|---|---|
| | | Innovator | Generic |
| 3 to <6 kg | 5 mg once daily | 1 | ½ |
| 6 to <10 kg | 15 mg once daily | 3 | 1½ |
| 10 to <14 kg | 20 mg once daily | 4 | 2 |
| 14 to <20 kg | 25 mg once daily | 5 | 2½ |

**Access scenario:** All low- and middle-income countries in the Asia-Pacific region are included in the voluntary license between the Medicines Patent Pool (MPP) and ViiV Healthcare that allows for purchasing and distribution of adult and pediatric formulations of generic DTG. As of September 2022, 13 companies have received sub-licenses from the MPP to manufacture and market DTG.

**Table 3: Status of registration, approval, and inclusion in national guidelines of dispersible 10 mg DTG tablets in selected Asia-Pacific countries**

| Country | Applied for registration | Approved | Included in national guidelines |
|---|---|---|---|
| Cambodia | Yes | Yes | Yes |
| India | Yes | Yes | Yes |
| Indonesia | No | No | No |
| Malaysia | No | No | No |
| Philippines | No | No | No |
| Thailand | Yes | No | No |
| Vietnam | Yes | No | No |

Data: Medicines Patent Pool; NCHADS, Cambodia; TREAT Asia/amfAR

To date, two generic companies manufacture the dispersible 10 mg formulation; one has both US FDA tentative approval and WHO pre-qualification, and the other has WHO pre-qualification. Approvals through these external quality assurance processes allow national programs to purchase dispersible DTG using funding from global donors (e.g., U.S. PEPFAR Program; Global Fund to Fight AIDS, TB and Malaria).

The WHO's Collaborative Procedure for Accelerated Registration of WHO-prequalified medicines can be utilized to enable fast-track approval of dispersible DTG. National governments that choose to use this procedure are able to finalize decisions on whether to approve a WHO pre-qualified medicine within 90 days. Bangladesh, Bhutan, Laos, Malaysia, Nepal, Philippines, Sri Lanka, and Thailand are part of this WHO Collaborative Procedure, which can be used to obtain dispersible 10 mg DTG.

**Pricing:** One bottle of generic dispersible 10 mg DTG is 4.50 USD (September 2022). The monthly or annual cost depends on a child's weight. The generic, film-coated 50 mg tablet used in adolescents and adults is priced at 27 USD per person per year (September 2022). In comparison, the dispersible 10 mg tablet at the highest weight band is 45 USD per child per year.

**Table 4: Prices of generic dispersible 10 mg DTG tablets**

| Weight band | Dosing | Number of bottles per child per year | Annual cost |
|---|---|---|---|
| 3 to <6 kg | 5 mg once daily | 2 bottles | 9 USD |
| 6 to <10 kg | 15 mg once daily | 6 bottles | 27 USD |
| 10 to <14 kg | 20 mg once daily | 8 bottles | 36 USD |
| 14 to <20 kg | 25 mg once daily | 10 bottles | 45 USD |

Data: Global Fund pooled procurement mechanism, June 2022

**Securing access to dispersible DTG:** The procurement needs for dispersible 10 mg DTG vary by country and are primarily dependent on the local rate of vertical transmission and total numbers of infants and young children living with HIV. At this time, within the region, only Cambodia and India have both approved the formulation and included it in their national HIV program guidelines—leaving large access gaps.

Potential ways forward to enable availability and access to the dispersible 10 mg DTG formulation include the following:

i) Generate reliable real-time estimates of the numbers of infants and children who will need this formulation to inform procurement negotiations between national programs and generic manufacturers.

ii) Support advocacy by local civil society and physician groups to:

   a. Work with ministries of health and other agencies to obtain registration dossiers from generic companies to facilitate applications for drug registration.

   b. Secure expedited regulatory approvals after applications for registration have been filed with national regulators. Where appropriate, utilize the WHO Collaborative Procedure for this process.

   c. Ensure dispersible DTG is included in national HIV programs and paid for under health benefits packages of children living with HIV.

[1] Amuge P, et al. Once-daily dolutegravir-based antiretroviral therapy in infants and children living with HIV from age 4 weeks: results from the below 14 kg cohort in the randomized ODYSSEY trial. *Lancet HIV*. 2022 Sep; 9(9):e638-e648.

[2] Turkova A, et al. Dolutegravir as first- or second-line treatment for HIV-1 infection in children. *N Engl J Med*. 2021 Dec 30;385(27):2531-2543.