

Dolutegravir (DTG, Tivicay, Tivicay PD)

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Formulations	
Tablets <ul style="list-style-type: none"> Dispersible tablets for oral suspension [Tivicay PD] 5 mg Film-coated tablets [Tivicay] 50 mg Fixed-Dose Combination (FDC) Tablets <ul style="list-style-type: none"> [Dovato] Dolutegravir 50 mg/lamivudine 300 mg [Juluca] Dolutegravir 50 mg/rilpivirine 25 mg [Triumeq] Abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg [Triumeq PD] Abacavir 60 mg/dolutegravir 5 mg/lamivudine 30 mg <p>When using FDC tablets, refer to other sections of Appendix A: Pediatric Antiretroviral Drug Information for information about the individual components of the FDC. See also Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents.</p> <p>For additional information, see Drugs@FDA or DailyMed.</p>	
Dosing Recommendations	Selected Adverse Events
<p>All formulations and FDCs of dolutegravir (DTG) are U.S. Food and Drug Administration (FDA)–approved for use in treatment-naïve or treatment-experienced pediatric, adolescent, and adult patients naïve to the integrase strand transfer inhibitor (INSTI) drug class. The Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV (the Panel) endorses the use of DTG as appropriate for some children with prior INSTI use (see Modifying Antiretroviral Regimens in Children With Sustained Virologic Suppression on Antiretroviral Therapy and Recognizing and Managing Antiretroviral Treatment Failure in Management of Children Receiving Antiretroviral Therapy).</p> <p>[Tivicay PD] DTG Dispersible Tablets</p> <p>Neonates (Gestational Age of ≥37 Weeks to Age of <4 Weeks and Weighing ≥2 kg)^a</p> <ul style="list-style-type: none"> Birth to age <14 days: DTG 5 mg orally every 48 hours Age ≥14 days to <4 weeks: DTG 5 mg orally once daily <p>Note: This dosing strategy is recommended by the Panel based on available pharmacokinetic (PK) modeling and simulation and clinical trial data. The above dosing strategy is not currently approved by the FDA. No dosing information is available in preterm neonates (gestational age <37 weeks) or infants weighing <2 kg.</p>	<ul style="list-style-type: none"> Insomnia Headache Neuropsychiatric symptoms (i.e., depression and/or suicidal thoughts or actions), especially in patients with a history of psychiatric illness Rare cases of hypersensitivity reactions (HSRs), including rash and DRESS (drug reaction [or rash] with eosinophilia and systemic symptoms), constitutional symptoms, and organ dysfunction (including liver injury)
	Special Instructions
	<ul style="list-style-type: none"> DTG may be taken with or without food. DTG should be taken 2 hours before or 6 hours after taking cation-containing antacids or laxatives, sucralfate, oral iron supplements, oral calcium supplements, or buffered medications.

Infant (Aged ≥4 Weeks and Weighing ≥2 kg), Child, and Adolescent Dose

Weight	Recommended Dose ^a of DTG Dispersible Tablets	Number of 5-mg Tablets	Volume of Water
2 kg to <3 kg ^b	5 mg once daily	1	5 mL
3 kg to <6 kg	5 mg once daily	1	5 mL
6 kg to <10 kg	15 mg once daily	3	5 mL
10 kg to <14 kg	20 mg once daily	4	10 mL
14 kg to <20 kg	25 mg once daily	5	10 mL
≥20 kg	30 mg once daily	6	10 mL

^a If certain drugs that induce uridine diphosphate glucuronyl transferase (UGT) 1A or cytochrome P450 (CYP) 3A are coadministered, administer DTG dispersible tablets twice daily (see the Drug Interactions section below).

^b This dosing is not currently approved by the FDA. DTG dispersible tablets have been approved only for those weighing ≥3 kg and aged ≥4 weeks. However, this dosing is recommended by the Panel based on available PK modeling and simulation and clinical trial data.

[Tivicay] DTG Film-Coated Tablets

Child and Adolescent (Weighing ≥14 kg) Dose

- DTG film-coated tablets and DTG dispersible tablets are not bioequivalent and are not interchangeable on a milligram-per-milligram basis. Each formulation has different doses.

Dosing of Film-Coated Tablets for Pediatric Patients Weighing ≥14 kg Who Can Swallow Tablets

Pediatric Body Weight	Recommended Dose ^a of DTG Film-Coated Tablets	Number of Tablets
14 kg to <20 kg	40 mg once daily	4 x 10 mg ^b
≥20 kg	50 mg once daily	1 x 50 mg

^a If certain drugs that induce UGT1A or CYP3A are coadministered, administer DTG tablets twice daily (see the Drug Interactions section below).

^b 10-mg tablets are no longer commercially available. Dosing from the package insert remains in the table above.

- For DTG dispersible tablets, fully disperse the dispersible tablets in 5 mL of drinking water (if using one or three tablets) or in 10 mL of drinking water (if using four, five, or six tablets) in the supplied cup; swirl the suspension so that no lumps remain. After full dispersion and within 30 minutes of mixing, administer the oral suspension. Rinse the dosing cup with a small amount of water (~2 mL) and give this additional water to the child to ensure the child takes the full dose and no medication remains in the dosing cup.

- DTG dispersible tablets may be swallowed whole. If more than one tablet is required, swallow one tablet at a time to reduce the risk of choking. DTG dispersible tablets should not be chewed or crushed.

- For ABC/DTG/3TC dispersible tablets, fully disperse the tablets in 5 mL of drinking water (if using one tablet), 15 mL of drinking water (if using three tablets) or 20 mL of drinking water (if using four to six tablets) in the supplied cup; swirl the suspension so that no lumps remain. After full dispersion and within 30 minutes of mixing, administer the oral suspension. Rinse the dosing cup with a small amount (~2 mL) of water and give this additional water to the child to ensure the child takes the full dose and no medication remains in the dosing cup.

- ABC/DTG/3TC dispersible tablets should not be swallowed whole, chewed, or crushed.
- No data exist regarding dispersion in breast milk or any vehicles other than water.
- In patients who have difficulty swallowing the film-coated tablets whole, 50-mg tablets may be either split into halves followed by immediate ingestion of **both halves** of the tablet or crushed and added to a small amount of semisolid food or liquid, all of which should be consumed **immediately**.¹

Some infants may have received raltegravir as presumptive HIV therapy prior to diagnosis. These infants and other infants and children with HIV who have received INSTIs are candidates to switch to once-daily DTG if they are virologically suppressed or have no mutations associated with resistance to INSTIs.

Adult Dose

- One 50-mg DTG film-coated tablet once daily
- If certain drugs that induce UGT1A or CYP3A are coadministered, administer DTG 50 mg twice daily (see the Drug Interactions section below).
- Adults who are INSTI-experienced with certain INSTI-associated resistance mutations or clinically suspected INSTI resistance should receive 50 mg DTG twice daily.

[Dovato] DTG/Lamivudine (3TC)

Adolescents Aged ≥12 Years and Weighing ≥25 kg and

Adult Dose

- One tablet once daily with or without food as a complete regimen in antiretroviral (ARV)-naïve adolescents with no known mutations associated with resistance to the individual components of Dovato

[Juluca] DTG/Rilpivirine

Adult Dose

- One tablet once daily with a meal as a complete regimen to replace the current ARV regimen in patients who have been virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen for at least 6 months, with no history of treatment failure, and no known mutations associated with resistance to the individual components of Juluca

[Triumeq PD] Abacavir (ABC)/DTG/3TC

Children Aged ≥4 Weeks and Weighing ≥3 kg to <25 kg

- Dispersible Triumeq PD tablets are FDA approved for children aged ≥3 months weighing ≥6 kg to <25 kg. They are not recommended for children weighing ≥25 kg.
- Population PK modeling and simulation supports the use of a single Triumeq PD tablet in infants weighing ≥3 kg to <6 kg and aged ≥4 weeks.
- Administer the appropriate number of tablets for a child's weight once daily. Tablets should be dispersed in appropriate volume of water (see Weight-Band Dosing table below and Special Instructions).

- The efficacy of DTG is reduced in patients with certain combinations of INSTI-resistance mutations. DTG dosing strategies in pediatric patients with first-generation INSTI mutations differ from those in adults (see [Table A](#) and the Resistance section below). Screen patients for hepatitis B virus (HBV) infection before using FDC tablets that contain 3TC. Severe acute exacerbations of HBV can occur after discontinuation of 3TC. Patients with HBV/HIV coinfection who receive Dovato will require additional treatment for chronic HBV infection.

- For any FDC tablets containing ABC, test patients for the HLA-B*5701 allele before starting therapy to predict the risk of HSRs. Patients who test positive for the HLA-B*5701 allele should not be given an ABC-containing FDC. Patients with no prior HLA-B*5701 testing who are tolerating an ABC-containing regimen do not need to be tested. See the [Abacavir](#) section.

Metabolism/Elimination

- Substrate for UGT1A1 and CYP3A. Also, a substrate of UGT1A3, UGT1A9, breast cancer resistance protein, and P-glycoprotein *in vitro*. Drugs that induce these enzymes and transporters may decrease plasma concentrations of DTG. Drugs that inhibit these enzymes or transporters may increase DTG plasma concentrations.

DTG Dosing in Patients With Hepatic Impairment

- No dose adjustment is necessary in patients with mild or moderate hepatic impairment. Due to the lack of data, DTG is **not recommended** for use in patients with severe hepatic impairment.
- FDC tablets containing ABC or 3TC should not be used in patients with impaired hepatic function.

Weight-Band Dosing of Triumeq PD Tablets for Children Aged ≥ 4 Weeks and Weighing ≥ 3 kg

Weight	Recommended Daily Dose	Number of Triumeq PD Tablets	Volume of Water
3 kg to <6 kg ^a	ABC 60 mg, DTG 5 mg, 3TC 30 mg once daily	1	5 mL
6 kg to <10 kg	ABC 180 mg, DTG 15 mg, 3TC 90 mg once daily	3	15 mL
10 kg to <14 kg	ABC 240 mg, DTG 20 mg, 3TC 120 mg once daily	4	20 mL
14 kg to <20 kg	ABC 300 mg, DTG 25 mg, 3TC 150 mg once daily	5	20 mL
20 kg to <25 kg	ABC 360 mg, DTG 30 mg, 3TC 180 mg once daily	6	20 mL
≥ 25 kg	Use Triumeq. See below.		

^a This dosing is not currently approved by the FDA. ABC/DTG/3TC dispersible tablet dosing has been approved only for those weighing ≥ 6 kg and aged ≥ 3 months. However, this dosing is recommended by the Panel based on available PK modeling and simulation data.

- For use in patients who are ARV naive or ARV experienced (but INSTI naive) and who are not being treated with UGT1A1 or CYP3A inducers
- See the [Abacavir](#) section for special instructions about testing for ABC hypersensitivity.

[Triumeq] ABC/DTG/3TC

Child and Adolescent (Weighing ≥ 25 kg) and Adult Dose

- One tablet once daily with or without food
- For use in patients who are ARV naive or ARV experienced (but INSTI naive) and who are not being treated with UGT1A1 or CYP3A inducers
- See the [Abacavir](#) section for special instructions about testing for ABC hypersensitivity.

DTG Dosing in Patients With Renal Impairment

- DTG decreases tubular secretion of creatinine and increases measured serum creatinine without affecting glomerular filtration.
- No dose adjustment is required in INSTI-naïve patients with mild, moderate, or severe renal impairment, or in INSTI-experienced patients with mild or moderate renal impairment.
- Use DTG with caution in INSTI-experienced patients with severe renal impairment (creatinine clearance [CrCl] <30 mL/min), because DTG concentrations will be decreased. The cause of this decrease is unknown.
- FDC tablets containing 3TC (Dovato, Triumeq PD, and Triumeq) should not be used in patients who have CrCl <30 mL/min or patients who are on dialysis because the doses of 3TC cannot be adjusted. Data about the FDC DTG/3TC (Dovato) suggest that patients with a sustained creatinine clearance 30–49 mL/min may experience a higher 3TC exposure and should be monitored for hematologic toxicities and potential FDC discontinuation and subsequent adjustment of the treatment regimen. See package inserts for additional information.

Drug Interactions

Additional information about drug interactions is available in the [Liverpool HIV Drug Interaction Checker](#).

- *Metabolism:* Dolutegravir (DTG) is a uridine diphosphate glucuronosyltransferase (UGT) 1A and cytochrome P450 (CYP) 3A substrate and may require dose adjustments when administered with UGT1A-modulating or CYP3A-modulating medications. DTG dosing should be adjusted to twice daily (i.e., twice the usual dose) when coadministered with drugs such as efavirenz and rifampin.²⁻⁴ Because etravirine (ETR) significantly reduces plasma DTG concentrations, DTG **should not be administered** with ETR without coadministration of atazanavir/ritonavir, darunavir/ritonavir (DRV/r), or lopinavir/ritonavir, which counteract this effect on DTG concentrations. DTG **should not be administered** with nevirapine because of insufficient data on interactions between these drugs. See the product label for a full listing of significant drug–drug interactions.
- Atazanavir (ATV) is an inhibitor of UGT1A1. In a pharmacologic survey of adult patients who were receiving DTG, patients who also received ATV had plasma concentrations of DTG that were twofold to fourfold higher than those of patients who received other antiretroviral (ARV) drugs.⁵
- Before administering DTG, clinicians should carefully review a patient's medication profile for potential drug interactions.

Major Toxicities

- *More common:* Insomnia and headache. Excessive weight gain and increased body mass index (BMI) have been reported in adults who received DTG in clinical trials and in some pediatric and adolescent cohorts (see [Table 17h. Lipodystrophies and Weight Gain](#)),⁶⁻⁹ whereas other cohort studies have not identified an association with excessive weight gain.¹⁰
- *Less common (more severe):* Hypersensitivity reactions characterized by rash, constitutional symptoms, and sometimes organ dysfunction; neuropsychiatric symptoms, especially in patients with a history of psychiatric illness. Multiple postmarketing reports note that neuropsychiatric adverse events (AEs) have occurred following the initiation of DTG-based therapy in adults.^{11,12}
- *Immune reconstitution inflammatory syndrome (IRIS):* In retrospective observational studies, severe cases of IRIS that required hospitalization appeared to be more frequent in patients who presented with advanced HIV disease and who initiated treatment with integrase strand transfer inhibitors (INSTIs), particularly DTG.^{13,14} This phenomenon is presumed to be linked to the rapid decline in HIV RNA observed in patients receiving INSTI-based therapy.
- *Rare:* Hepatotoxicity has been reported; two cases of liver injury were presumed to be related to the use of DTG. One of these cases required liver transplantation.^{15,16}
- *Rare:* A single case of drug reaction (or rash) with eosinophilia and systemic symptoms (or DRESS) has been reported.¹⁷

Resistance

The International Antiviral Society–USA maintains a [list of updated resistance mutations](#), and the [Stanford University HIV Drug Resistance Database](#) offers a discussion of each mutation. For additional considerations on the impact of nucleoside reverse transcriptase inhibitor (NRTI) resistance and the use of DTG-containing fixed-dose combinations (FDCs), see [Recognizing and Managing Antiretroviral Treatment Failure](#).

The efficacy of DTG is reduced in patients with the INSTI-resistance Q148 substitution plus two or more additional INSTI-resistance mutations, and this reduced efficacy cannot be completely overcome with increased DTG dosing.^{18,19}

For INSTI-experienced adults with certain INSTI-resistance mutations or clinically suspected INSTI resistance, the [Tivicay package insert](#) recommends giving the standard 50-mg dose twice daily rather than once daily. However, modeling and simulation of this potential strategy with the dispersible tablet formulation of DTG in children suggested elevated maximum plasma concentrations (C_{max}) in comparison to historical data in adults, adolescents, and children would result. Thus, a different dosing strategy was needed for children with certain or clinically suspected INSTI-resistance mutations. The proposed dosing schedule in [Table A](#) below was based on simulations with the goal of achieving geometric mean concentration at 12 hours postdose $>1.97 \mu\text{g/mL}$ and area under the curve (AUC) through 12 hours postdose $>32.2 \mu\text{g}\cdot\text{h/mL}$ while avoiding elevated C_{max} values.²⁰ Additionally, the coformulated dispersible tablet containing abacavir (ABC)/DTG/lamivudine (3TC) cannot be used in combination with a separate dose of single-agent dispersible release DTG because the dosing of the separate formulation is not double the regular dose and the modified dosing strategy would result in underdosing the ABC and 3TC components.

Table A. Weight-Band Dosing of Dolutegravir Dispersible Tablets for Pediatric Patients Weighing ≥ 3 kg and Aged ≥ 3 Months With First-Generation Integrase Strand Transfer Inhibitors—Resistance Mutations

Weight	Recommended Twice-Daily Dose	Number of Tablets per Dose
3 kg to <6 kg	5 mg	1
6 kg to <10 kg	10 mg	2
10 kg to <14 kg	15 mg	3
14 kg to <20 kg	15 mg	3
20 kg to <30 kg	20 mg	4
30 kg to <40 kg	20 mg	4

Pediatric Use

Approval

DTG is approved by the U.S. Food and Drug Administration (FDA) for use, in combination with other ARV drugs, in pediatric patients aged ≥ 4 weeks and weighing ≥ 3 kg who are treatment naive or treatment experienced but INSTI naive (see [Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents](#)). DTG dispersible tablets and film-coated tablets in either the single-entity or FDC form can be administered with or without food.^{21,22} Pediatric patients weighing ≥ 20 kg may take the DTG 50-mg film-coated tablets if they are able to swallow tablets.

The combination tablet ABC/DTG/3TC (Triumeq) is approved by the FDA for use in children and adolescents weighing ≥ 25 kg. Dispersible ABC/DTG/3TC tablets (Triumeq PD) are FDA approved for use in children weighing ≥ 6 kg to <25 kg.

The combination tablet DTG/3TC (Dovato) is approved by the FDA for adolescents weighing ≥ 25 kg and aged ≥ 12 years but is not approved for use in children aged < 12 years.

The combination tablet DTG/rilpivirine (RPV) (Juluca) is not approved by the FDA for use in children or adolescents. However, the doses of the component drugs that make up this FDC tablet are approved for use in adolescents, and the Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV (the Panel) generally endorses the use of adult formulations for drugs that have been approved for use in children and adolescents. The FDC tablet may be appropriate for use in certain adolescents. See [Modifying Antiretroviral Regimens in Children With Sustained Virologic Suppression on Antiretroviral Therapy](#) for additional considerations on the use of this combination.

Formulation Differences: Film-Coated Tablet Compared to Dispersible Tablet

DTG is currently available as either film-coated tablets or dispersible tablets (tablets for oral suspension). The dispersible tablet has 60% to 80% greater bioavailability in adults than the film-coated tablet,²³ so recommended doses using the dispersible tablet cannot be directly compared to those using the film-coated tablets. The drug exposure provided by the 50-mg film-coated tablet is approximately equal to that of DTG 30 mg administered as dispersible tablets.

Efficacy and Pharmacokinetics

Pediatric Patients Aged < 4 Weeks

DTG is primarily metabolized by UGT1A1 (90%) and to a minor extent by CYP3A4 (10%). Because UGT enzyme activity is low at birth, DTG elimination is prolonged in neonates, and thus further assessments are needed to evaluate potential dosing strategies accounting for enzyme maturation in this population. Dosing of dispersible release DTG in full-term neonates (≥ 37 weeks' gestation) aged < 4 weeks was evaluated in two separate studies: PETITE-DTG and IMPAACT 2023.

PETITE-DTG was a Phase I/II, open-label, two-stage study in South Africa that evaluated the pharmacokinetic (PK) and safety of DTG in full-term neonates (≥ 37 weeks gestational age) weighing ≥ 2 kg and born to individuals receiving a DTG-containing therapy during pregnancy.²⁴ In Stage 1, single doses of DTG 5 mg were administered to eight neonates aged < 14 days and eight neonates aged ≥ 14 to < 28 days. These data were incorporated into population PK modeling to identify a dosing regimen to be used in Stage 2 that achieved the protocol-defined PK targets of a geometric mean concentration at the end of the dosing interval (C_{tau}) ≥ 0.67 mcg/mL and maximum plasma concentration (C_{max}) < 17.0 mcg/mL. During Stage 2, DTG 5 mg was administered every 48 hours for the first 2 weeks of life, followed by once daily administration through 4 weeks of life. A total of 41 infants were enrolled, with DTG administered either as half of a scored dispersible 10-mg tablet (51%) or one 5-mg dispersible film (49%).²⁵ The scored 10-mg dispersible tablet is a generic formulation available in South Africa and other resource-limited settings, but the film is still an investigational product. Both formulations achieved the protocol-defined PK targets and achieved comparable exposures to each other. No AEs related to DTG occurred, and all 39 infants who completed follow-up were HIV seronegative at the time of study exit.

IMPAACT 2023 was a Phase 1 open-label, noncomparative dose-finding study of the safety, tolerability, and PK of DTG in full-term neonates (≥ 37 weeks gestational age) perinatally exposed to HIV-1 and weighing ≥ 2 kg. The study enrolled infants with and without *in utero* DTG exposure and was conducted in two sequential cohorts. In Cohort 1, 18 neonates received single doses of DTG using either a weight-based liquid formulation or a 5-mg dispersible tablet formulation within 5 days of birth, with a repeat single dose 7 to 10 days after the initial dose. Population PK modeling was

performed to characterize neonatal DTG disposition and to inform the selection of an appropriate multidose regimen for evaluation in Cohort 2 that achieved protocol-defined PK targets of $C_{\text{trough}} > 0.697$ mcg/mL, $AUC_{0-\text{tau}} > 37$ mcg·h/mL, and $C_{\text{max}} < 18.35$ mcg/mL). In Cohort 2, 18 neonates initiated the dispersible tablet formulation of DTG within 5 days of birth and received 5 mg every 48 hours during the first 2 weeks of life, followed by 5 mg once daily through 4 to 6 weeks of age.²⁶ Available PK data demonstrate that this regimen achieves exposures within acceptable target ranges, regardless of whether the mother received a DTG-containing regimen, with variability consistent with maturation of drug-metabolizing pathways (UGT1A1 and CYP3A4) during the neonatal period. No serious AEs were attributed to DTG, and the regimen was generally well tolerated. The study has since been fully enrolled, and ongoing analyses of the data support the Panel's neonatal dosing recommendations for full-term infants weighing ≥ 2 kg.

Pediatric Patients Aged 4 Weeks to <18 Years

Single-Entity Dolutegravir

[IMPAACT P1093](#) was a multinational, open-label trial of DTG in children with HIV. Data from IMPAACT P1093 Cohort 1 (aged 12 years to <18 years) and Cohort 2 (aged 6 years to <12 years) provided support for use of DTG film-coated tablets in pediatric patients weighing ≥ 14 kg; Cohort 3 (aged 2 years to <6 years), Cohort 4 (aged 6 months to <2 years), and Cohort 5 (aged 4 weeks to <6 months) provided evidence supporting the use of DTG 5-mg dispersible tablets. Dosing recommendations that previously included the 25-mg film-coated tablets have been replaced with other formulations.

Results of PK, safety, and efficacy assessments have been reported sequentially for different age and weight cohorts as data became available; similarly, dosing recommendations have been revised sequentially.²⁷⁻²⁹ A total of 181 participants were enrolled across these cohorts, of whom 96 received dispersible DTG tablets and 85 received nondispersible formulations.²⁹ Seventy-five participants received the recommended doses of the film-coated or dispersible tablets based on their weight and age, of whom 80% were treatment experienced and all were INSTI naive.³⁰ At Week 48, of the 42 participants with available data, 69% achieved HIV RNA <50 copies/mL and 79% achieved HIV RNA <400 copies/mL. The effectiveness observed in the trial was comparable to that of treatment-experienced adult participants.³⁰ The median CD4 T lymphocyte cell (CD4) count (percent) increased from baseline to Week 48 by 141 cells/mm³ (7%). Overall, the safety profile in P1093 participants was comparable to that observed in adults, and both formulations were well tolerated.³⁰ Follow-up data among 16 adolescents in Cohort 1 through 144 weeks showed 43% and 35% of participants achieving and maintaining HIV RNA levels <400 copies/mL and <50 copies/mL, respectively.³¹ Genotypic testing was available at the time of treatment failure for 6 of the 13 participants; one of these adolescents developed DTG resistance.^{29,31}

The Once-daily DTG-based ART in Young people vS Standard thErapY (ODYSSEY) trial, conducted by the Pediatric European Network for the Treatment of AIDS (PENTA), enrolled both treatment-naïve and treatment-experienced pediatric patients from the European Union, Thailand, and several African countries; this trial initially evaluated doses approved by the European Medicines Agency at the time the trial started. A total of 707 children aged <18 years were enrolled; 311 children started DTG as first-line therapy, and 396 started DTG as second-line therapy.³² DTG-based antiretroviral therapy (ART) as both first-line therapy and second-line therapy in children was superior to standard care through 96 weeks of treatment.³³ Results from the younger ODYSSEY cohort of children weighing between 3 kg and 14 kg showed superiority of DTG-based ART compared with other regimens, of which over 70% were protease inhibitor (PI)-based regimens.³³⁻³⁵ Follow-up data through 192 weeks continued to demonstrate the superiority of DTG-containing ART for virologic suppression compared with first- and second-line ART.³⁶ **Secondary analyses have also shown that DTG resulted in faster virologic suppression versus those on standard of care (SOC), which**

consisted primarily of PIs, and that those on DTG with a backbone containing ABC or tenofovir were at lower risk of virologic failure than those on zidovudine (ZDV).³⁷

Nested PK substudies within ODYSSEY also evaluated simplified pediatric dosing that aligned with World Health Organization (WHO)–recommended weight bands. PK data are available from a cohort of children weighing >25 kg who switched to the DTG 50-mg film-coated tablet, 20 kg to <25 kg who received either the DTG 50-mg film-coated tablet or DTG 30 mg administered as six 5-mg dispersible tablets,^{38,39} 14 kg to <20 kg who received 25 mg, 3 kg to <6 kg and younger than 6 months who received 5 mg DTG, 3 kg to <6 kg and older than 6 months who received 10 mg, 6 kg to <10 kg who received 15 mg, and 10 kg to <14 kg who received 20 mg.³⁹ A total of 19 children weighing <20 kg experienced Grade 3 or higher AEs, including two deaths (one kwashiorkor and one accidental trauma) assessed as unrelated to the study drug. Eleven participants experienced serious AEs, 69% of which were due to infectious diseases.

Combined PK data from P1093 and ODYSSEY across all age/weight cohorts form the basis for the current FDA dose recommendations and are summarized in [Table B](#) below. Generally speaking, the AUC and C_{max} values were comparable to or higher than adult values, whereas troughs were slightly lower and more variable, but exposures still fell within acceptable exposure ranges across weight bands. These data support the administration of either DTG 30 mg as dispersible tablets or DTG 50 mg as a film-coated tablet in patients weighing ≥20 kg. In addition, modeling and simulations that included UGT1A1 maturation in infants were used to support the dose of DTG in infants ≥4 weeks of age and weighing ≥3 kg. Dosing in neonates is under investigation.

Table B. Summary of Pharmacokinetic Parameters in Pediatric Participants With HIV-1 (Pooled Analyses for IMPAACT P1093 and ODYSSEY Trials)

Weight Band ^a	Dose ^b of DTG FCT or DTG DT	n	Pharmacokinetic Parameter Geometric Mean (% CV)		
			C _{max} (mcg/mL)	AUC _{0-24h} (mcg·h/mL)	C _{24h} (ng/mL)
3 kg to <6 kg	DTG DT 5 mg once daily	8	3.80 (34)	49.37 (49)	962 (98)
6 kg to <10 kg	DTG DT 15 mg once daily	17	5.27 (50)	57.17 (76)	706 (177)
10 kg to <14 kg	DTG DT 20 mg once daily	13	5.99 (33)	68.75 (48)	977 (100)
14 kg to <20 kg	DTG DT 25 mg once daily	19	5.97 (42)	58.97 (44)	725 (75)
20 kg to <25 kg	DTG DT 30 mg once daily	9	7.16 (26)	71.53 (26)	759 (73)
≥20 kg	DTG FCT 50 mg once daily	49	4.92 (40)	54.98 (43)	778 (62)
Adults ^c	DTG FCT 50 mg once daily	N/A	3.67 (20)	53.6 (27)	1,110 (46)

Table B: Summary of Pharmacokinetic Parameters in Pediatric Participants With HIV-1 (Pooled Analyses for IMPAACT P1093 and ODYSSEY Trials)

Weight Band ^a	Dose ^b of DTG FCT or DTG DT	n	Pharmacokinetic Parameter Geometric Mean (% CV)		
			C _{max} (mcg/mL)	AUC _{0-24h} (mcg·h/mL)	C _{24h} (ng/mL)
Adults ^c	DTG FCT 50 mg twice daily	N/A	4.15 (29)	75.1 (35)	2,120 (47)

^a Data are from two weight-band-based pharmacokinetic substudies in the ODYSSEY trial.

^b The bioavailability of DTG tablets for oral suspension is approximately 1.6-fold that of DTG film-coated tablets.

^c Adult pharmacokinetic data are based on population pharmacokinetic analyses from clinical trials.³⁰

Key: AUC_{0-24h} = 24-hour area under the curve; C_{24h} = concentration at 24 hours postdose; C_{max} = maximum plasma concentration; CV = coefficient of variation; DT = dispersible tablets; DTG = dolutegravir; FCT = film-coated tablets

Separate PK studies and population PK models have continued to support adequate DTG exposures among children and adolescents at the currently recommended doses.^{21,40-45} One of these analyses identified that tenofovir alafenamide fumarate/emtricitabine may reduce DTG bioavailability by approximately 20% in comparison to those on backbones of ABC or ZDV, but DTG AUC and C_{trough} were still adequate.⁴⁵ Separate assessments of metabolic ratios of DTG glucuronide (a major DTG metabolite) to DTG in infants and children with HIV did not identify any difference in metabolic ratios by age, weight, NRTI backbone, or kidney function.⁴⁶ The only factor that altered these ratios was rifampicin subsequent to its known induction of metabolism. Exploratory investigations also have identified that genetic variants in adenosine triphosphate-binding cassette subfamily G member 2 (ABCG2), nuclear receptor subfamily 1 group I member 2, and UGT1A1 may affect DTG PK in infants and children, which may explain some of the additional variability observed in this population.⁴⁷ Genetic variants in ABCG2 and UGT1A1 that were associated with higher DTG exposures showed a trend toward sustained virologic suppression.

Dolutegravir/Abacavir/Lamivudine

The PK, safety, tolerability, and efficacy of dispersible and immediate-release ABC/DTG/3TC FDC tablet formulations were investigated in the IMPAACT 2019 study.^{48,49} A total of 57 children weighing 6 kg to <40 kg and aged <12 years were enrolled and dosed across five weight bands in alignment with the WHO ARV dosing recommendations for each component. Children weighing 6 kg to <25 kg received dispersible FDC tablets containing ABC 60 mg/DTG 5 mg/3TC 30 mg (Triumeq PD), and those weighing 25 kg to <40 kg received the immediate-release FDC tablet containing ABC 600 mg/DTG 50 mg/3TC 300 mg (Triumeq). Drug exposures for all three components were comparable to previous studies in children and adults with HIV, including DTG exposures from IMPAACT P1093 and ODYSSEY.⁴⁸ Dosing was confirmed based on PK and safety criteria across all weight bands. At Week 24, 54 of 57 (95%) participants were suppressed to HIV-1 RNA <200 copies/mL, 52 of 57 (91%) were suppressed to HIV-1 RNA <50 copies/mL, and all treatment-experienced patients who switched to ABC/DTG/3TC maintained suppression. At Week 48, a total of 54 participants remained on treatment, of whom all achieved HIV-1 RNA <200 copies/mL, and 45 (83%) achieved HIV-1 RNA <50 copies/mL.⁴⁹ A single participant discontinued treatment due to drug-induced liver injury that occurred at Week 36. This event was attributed to ABC and DTG. CD4 counts were stable throughout the 48 weeks of treatment. Both formulations were otherwise safe and well tolerated, with 10 of 11 participants in the highest weight band able to swallow the larger immediate-release tablet whole and intact (see [Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for](#)

[Use in Children and Adolescents](#)).^{48,49} This finding contrasted a separate cohort of 12 adolescents in Spain, where half needed to crush or split the immediate-release tablet because of its size.⁵⁰

Population PK modeling of IMPAACT 2019 data through 48 weeks further demonstrated alignment of PK data collected within this study with existing population PK models for the individual components, further supporting dose confirmation of the dispersible FDC.⁴⁴ These models were then modified with maturation functions specific to each component to evaluate whether a single ABC 60 mg/DTG 5 mg/3TC 30 mg tablet in infants weighing ≥ 3 kg to < 6 kg (aged ≥ 4 weeks) could achieve comparable drug exposures observed in older children and adults based on dosing simulations, and thus provide comparable safety and efficacy observed in older children and adults.⁵¹ These models used data from young children across weight bands from IMPAACT 2019 (≥ 6 kg), P1093 (≥ 3 kg), ODYSSEY (≥ 3 kg) clinical trials for DTG, and the PETITE clinical trial for ABC and 3TC.^{29,39,44,48,52,53} Review of the ABC/3TC data from the PETITE study in neonates^{52,53} and available ABC, 3TC, and DTG safety data in infants aged < 3 months (see below under Pediatric Postmarketing Safety Studies) were used to interpolate safety for infants aged ≥ 4 weeks to < 3 months and suggested no safety concerns for coadministration of ABC/3TC/DTG in young infants. Notably, the doses in the safety evaluation were mostly in alignment with the WHO weight-band dose recommendations of fixed-dose formulations of ABC 120 mg/3TC 60 mg, which were higher than those under evaluation in this modeling and simulation. Based on these findings, the Panel supports the use of the single ABC/3TC/DTG FDC dispersible tablet as an alternative to the separate formulations of ABC, 3TC, and DTG in infants weighing ≥ 3 kg to < 6 kg and aged ≥ 4 weeks to facilitate treatment adherence.

Retrospective & Prospective Cohort Studies

The efficacy and safety of DTG-based regimens have been evaluated in a few randomized controlled trials and multiple observational cohort studies.⁵⁴⁻⁵⁹

Observational cohort studies have included a variety of populations, including children, adolescents, and young adults who were ART experienced but INSTI naive and either virologically suppressed or viremic at baseline. Virologic suppression rates between about 80% to 93% have been reported following at least 6 months to 24 months of DTG-containing therapy.^{55-58,60,61} Discontinuation rates due to toxicity have generally been low ($< 1\%$).⁵⁵ Factors associated with a higher likelihood of virologic suppression following the switch included suppressed viral loads at baseline,^{54-56,58,60} use of once-daily tenofovir disoproxil fumarate (TDF)/3TC/DTG as a single-tablet regimen (compared with ABC/3TC/DTG or ZDV/3TC/DTG),⁵⁵ and good medication adherence. Factors associated with lower odds of virologic suppression included age increases and poorer adherence.^{55,57,58} Given the retrospective nature of these analyses, many of which were performed following national rollout programs, direct comparisons among participants who were not suppressed and did not switch to a DTG-containing regimen could not always be performed.⁵⁵

Although observational studies have shown high virologic suppression rates, emerging INSTI mutations specific to DTG have been reported among children being monitored in national treatment programs.⁶¹ Thus, continued assessments of sustained long-term virologic suppression (i.e., > 24 months) and the development of resistance will be important.^{62,63} Additionally, one study noted⁶⁰ more than one-third of children experienced at least two regimen changes during the follow-up period from 2019 to 2021, some of which involved switching from DTG to either a PI or non-nucleoside reverse transcriptase inhibitor (NNRTI). These changes were attributable, in part, to drug shortage, illustrating the importance of continued access to and supply of DTG to support rollout initiatives.⁵⁰

Pediatric Postmarketing Safety Studies

Several studies continue to investigate longer-term safety outcomes in pediatric populations with the expanded use of DTG. Notable outcomes of interest include neuropsychiatric outcomes and growth, weight gain, and metabolic effects over time based on findings in adults.

ODYSSEY reported a small number of neuropsychiatric AEs among 707 children and adolescents randomized to DTG, which was not significantly different from those reported in study participants receiving standard care. However, participants receiving DTG were more likely to have suicidal ideation than those receiving SOC; however, these symptoms were described as transient and did not lead to changes in ART.³⁴ In IMPAACT 2019, 6 of 57 (10.5%) participants reported at least one central nervous system disorder event, but all were Grade 1 severity.⁴⁹ Sleep and mood questionnaires revealed one participant had expressed thoughts that life was not worth living at Week 4 only, and an increase in frequency of nightmares was also reported at Weeks 4 and 24 in comparison to study entry. A separate systematic review of INSTI use in 3,448 children with perinatal HIV infection identified rates of neuropsychiatric effects from 1% to 16% among those receiving DTG.⁶⁴

Reports of weight gain among adults enrolled in clinical trials prompted similar studies to investigate the metabolic effects of DTG in adolescents. Some studies have identified increases in weight-for-age z-score and BMI-for-age z-score,^{7,9,35,49} as well as trunk fat and trunk/total body fat ratios.⁶ However, others have not identified significant changes^{8,10,65} or lower rates of change among those with baseline BMI $\geq$ 50th percentile.⁶⁶ Lipid changes also have been evaluated, with one study detailing decreases in total cholesterol and low-density lipoproteins, while serum triglycerides decreased early in the study and subsequently increased.⁶ In another study, adolescents who switched to DTG (n = 30) demonstrated reduced hepatic steatosis and lower total cholesterol and triglycerides compared to those who remained on their initial ART regimens (84% PI-based).⁶⁵ Based on these collective data, weight gain may be observed in adolescents receiving DTG, as observed in adults; the long-term clinical significance of these changes is unclear, and further studies are needed in adolescents and children receiving DTG. See the [What to Start](#) section for additional considerations.

Simplification of Treatment

Dolutegravir With Rilpivirine

Two trials in adults (Regimen Switch to DTG + Rilpivirine from Current Antiretroviral Regimen in Human Immunodeficiency Virus Type 1 Infected and Virologically Suppressed Adults [SWORD-1 and SWORD-2]) supported the approval of a DTG 50-mg/RPV 25-mg FDC tablet as a complete regimen for treatment simplification or maintenance therapy in selected patients. The two identical SWORD trials enrolled 1,024 virologically suppressed patients who had been on stable ART for at least 6 months and who had no history of treatment failure or evidence of resistance mutations. The participants were randomized either to receive DTG/RPV or to continue their suppressive ARV regimen. After 48 weeks of treatment, 95% of patients in both arms maintained HIV RNA levels <50 copies/mL.⁶⁷ After 52 weeks, the participants who had been randomized to continue their suppressive ARV regimen were switched to DTG/RPV. At 148 weeks, 84% of the early-switch patients and 90% of the late-switch patients remained virologically suppressed, and only 11 patients receiving dual therapy met virologic failure criteria. No INSTI resistance was identified.⁶⁸ During the comparative randomized phase of the study, more AEs were reported and led to discontinuation in the DTG/RPV arm. In a subgroup of the SWORD study, small but statistically significant increases in hip and spine bone mineral density and bone turnover markers were observed in patients whose original ARV regimen contained TDF.⁶⁹

Although Juluca is not approved by the FDA for use in adolescents, the doses of the component drugs that make up this FDC tablet are approved for use in adolescents. The Panel generally endorses the use of adult formulations for drugs that have been approved for use in children and adolescents, and these products may be appropriate for use in certain adolescents. The use of DTG/RPV regimens could be useful in patients in whom there is concern for toxicity from NRTIs. However, the Panel notes that adolescents may have difficulties adhering to therapy and suggests considering close monitoring with viral load testing (see the Treatment Simplification section of [Management of Children Receiving Antiretroviral Therapy](#)).

Dolutegravir With Lamivudine

The approval of DTG 50 mg/3TC 300 mg as a complete regimen in adults was supported by data from two randomized, double-blind, controlled trials (Efficacy, Safety, and Tolerability Study Comparing DTG Plus Lamivudine With DTG Plus Tenofovir/Emtricitabine in Treatment naive HIV Infected Subjects [GEMINI-1 and GEMINI-2]). GEMINI-1 and GEMINI-2 were identical 148-week trials that enrolled a total of 1,433 adults with HIV who had plasma HIV RNA levels between 1,000 copies/mL and $\leq 500,000$ copies/mL at screening and no evidence of major resistance mutations or hepatitis B virus infection. Participants were randomized to receive either DTG plus 3TC or DTG plus 3TC/TDF. During 96 weeks of treatment, 86% of patients who received DTG plus 3TC and 89.5% of patients who received DTG plus 3TC/TDF achieved HIV RNA levels < 50 copies/mL. Patients who received DTG plus 3TC had a lower rate of adverse drug reactions (19.6%) than those who received DTG plus 3TC/TDF (25%).⁷⁰

The combination of DTG/3TC was evaluated as initial ART in adolescents weighing ≥ 25 kg and aged ≥ 12 years to < 18 years with baseline HIV-1 RNA between 1,000 copies/mL and $\leq 500,000$ copies/mL through the DANCE study. A total of 32 participants were enrolled, of whom 81% and 69% achieved HIV RNA levels < 50 copies/mL at Weeks 48 and 96, respectively.^{71,72} These results included individuals with missing data due to site closures; thus, sensitivity analyses were performed with the participants excluded. Virologic suppression rates in the sensitivity analyses were 87% (26 of 30) at Week 48 and 88% (22 of 25) at Week 96. Drug exposures for both components were also comparable to historical data in adults, and the combination was overall safe and well tolerated.

Both film-coated tablet and dispersible tablet formulations of DTG/3TC are also under active investigation in children aged 2 years to < 15 years of age and weighing 6 kg to < 40 kg through the D3/Penta21 study.⁷³ The doses under evaluation include DTG 15 mg/3TC 90 mg for 6 kg to < 10 kg, DTG 20 mg/3TC 120 mg for 10 kg to < 14 kg, DTG 25 mg/3TC 150 mg for 14 kg to < 20 kg, DTG 30 mg/3TC 180 mg or DTG 50 mg/3TC 300 mg film-coated tablet for 20 kg to < 25 kg, and DTG 50 mg/3TC 300 mg for ≥ 25 kg, with DTG 50 mg/3TC 300 mg as the only film-coated formulation. These doses were largely aligned with the WHO weight-band dosing recommendations, except for the DTG 50 mg/3TC 300 mg film-coated tablet option in those weighing 20 kg to < 25 kg, which is 1.3 times higher than the currently recommended dose from that weight band. PK data from nested substudies in 72 children weighing 10 kg to < 40 kg demonstrated that all participants achieved DTG C_{trough} above the *in vitro* protein-adjusted 90% maximal inhibitory concentration (IC_{90}) of 0.064 mg/L and 69 of 72 children exceeded the 90% effective concentration of 0.32 mg/L.⁷⁴ Exposures for DTG and 3TC were generally comparable to historical data from ODYSSEY and IMPAACT 2019, respectively.

Dolutegravir With Darunavir/Ritonavir

The combination of once-daily DRV/r with an INSTI is being investigated in a randomized non-inferiority trial among virologically suppressed children aged 6 years to < 18 years through the SMILE Penta-17-ANRS 152 clinical trial.⁷⁵ Participants were randomized to either once-daily DRV/r with an INSTI or continuing their SOC regimen consisting of a boosted PI or NNRTI with a NRTI backbone.

A total of 318 participants were enrolled between 2016 and 2019, of whom 158 were randomized to DRV/r with an INSTI (97% DTG, 3% elvitegravir). DRV/r with an INSTI was non-inferior to SOC at Week 48 (HIV viral load ≥ 50 copies/mL in 5% for DRV/r with an INSTI vs. 7.6% in the SOC arm; difference -2.5% [95% confidence interval (CI), -7.6% and 2.5%]). Secondary analyses comparing DRV/r with an INSTI versus SOC revealed decreases in CD4 counts (-48.3 cells/mm³ [95% CI, -93.4 and -3.2; $P = 0.036$]) and mean high-density lipoprotein change from baseline (-4.1 mg/dL [95% CI, -6.7 and -1.4; $P = 0.003$]), and increases in weight and BMI (+1.97 kg [95% CI, 1.1 and 2.9; $P < 0.001$]) and +0.66 kg/m² [95% CI, 0.3 and 1.0; $P < 0.001$], respectively). A nested PK substudy in 153 adolescents aged ≥ 12 years to < 18 years from SMILE also demonstrated that total and unbound DTG concentrations were adequate and well above the protein-adjusted IC₉₀ for DTG.⁷⁶ DTG C_{trough} were also comparable to those measured in adults receiving 50 mg once daily. Apparent clearance of the unbound DTG was influenced by total bilirubin concentrations, Asian ethnicity and unbound darunavir concentrations, but the impacts on DTG concentrations were deemed not clinically relevant.⁷⁷

Crushing Film-Coated Tablets for Administration

Dispersible tablets are now considered the preferred formulation for pediatric patients weighing < 20 kg, and film-coated tablets should not be used in children weighing < 14 kg. In children weighing > 14 kg who have difficulty swallowing whole tablets, when the preferred dispersible tablets are not available, the 50-mg tablets either may be split into halves followed by immediate ingestion of **both halves** of the tablet or crushed and added to a small amount of semisolid food or liquid, all of which must be consumed **immediately**.¹ In healthy adults, the use of crushed tablets resulted in slightly higher exposures than the use of whole tablets.⁷⁸ No information exists on the impact of splitting or crushing film-coated tablets on palatability. Some case reports describe DTG-containing film-coated tablets being crushed and successfully administered via orogastric tube⁷⁹ or nasogastric tube.⁸⁰ If DTG is administered via enteral tube, care should be taken to disperse the tablets completely and flush the tube to avoid clogging.

References

1. Duggan JM, Akpanudo B, Shukla V, et al. Alternative antiretroviral therapy formulations for patients unable to swallow solid oral dosage forms. *Am J Health Syst Pharm*. 2015;72(18):1555-1565. Available at: <https://pubmed.ncbi.nlm.nih.gov/26346211>.
2. Jacobs TG, Mumbiro V, Cassia U, et al. Twice-daily dosing of dolutegravir in infants on rifampicin treatment: a pharmacokinetic substudy of the EMPIRICAL trial. *Clin Infect Dis*. 2024;78(3):702-710. Available at: <https://pubmed.ncbi.nlm.nih.gov/37882611>.
3. Naidoo A, Waalewijn H, Naidoo K, et al. Pharmacokinetics and safety of dolutegravir in children receiving rifampicin tuberculosis treatment in South Africa (ORCHID): a prospective cohort study. *Lancet HIV*. 2025;12(4):e273-e282. Available at: <https://pubmed.ncbi.nlm.nih.gov/40023169>.
4. Turkova A, Waalewijn H, Chan MK, et al. Dolutegravir twice-daily dosing in children with HIV-associated tuberculosis: a pharmacokinetic and safety study within the open-label, multicentre, randomised, non-inferiority ODYSSEY trial. *Lancet HIV*. 2022;9(9):e627-e637. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/35868341>.
5. Cattaneo D, Minisci D, Cozzi V, et al. Dolutegravir plasma concentrations according to companion antiretroviral drug: unwanted drug interaction or desirable boosting effect? *Antivir Ther*. 2017;22(4):353-356. Available at: <https://pubmed.ncbi.nlm.nih.gov/28008867>.
6. Giacommet V, Lazzarin S, Manzo A, et al. Body fat distribution and metabolic changes in a cohort of adolescents living with HIV switched to an antiretroviral regimen containing dolutegravir. *Pediatr Infect Dis J*. 2021;40(5):457-459. Available at: <https://pubmed.ncbi.nlm.nih.gov/33847293>.
7. Thivalapill N, Simelane T, Mthethwa N, et al. Transition to dolutegravir is associated with an increase in the rate of body mass index change in a cohort of virally suppressed adolescents. *Clin Infect Dis*. 2021;73(3):e580-e586. Available at: <https://pubmed.ncbi.nlm.nih.gov/33119739>.
8. Yeoh DK, Campbell AJ, Bowen AC. Increase in body mass index in children with HIV, switched to tenofovir alafenamide fumarate or dolutegravir containing antiretroviral regimens. *Pediatr Infect Dis J*. 2021;40(5):e215-e216. Available at: <https://pubmed.ncbi.nlm.nih.gov/33847305>.
9. Koay WLA, Dirajlal-Fargo S, Levy ME, et al. Integrase strand transfer inhibitors and weight gain in children and youth with perinatal human immunodeficiency virus in the DC Cohort. *Open Forum Infect Dis*. 2021;8(7):ofab308. Available at: <https://pubmed.ncbi.nlm.nih.gov/34295943>.
10. Belfrage E, Soeria-Atmadja S, Naver L. Growth, weight gain and BMI in virally suppressed children on antiretroviral therapy with specific reference to dolutegravir. *BMC Pediatr*. 2023;23(1):339. Available at: <https://pubmed.ncbi.nlm.nih.gov/37403042>.
11. Elzi L, Erb S, Furrer H, et al. Adverse events of raltegravir and dolutegravir. *AIDS*. 2017;31(13):1853-1858. Available at: <https://pubmed.ncbi.nlm.nih.gov/28692533>.
12. Fettiplace A, Stainsby C, Winston A, et al. Psychiatric symptoms in patients receiving dolutegravir. *J Acquir Immune Defic Syndr*. 2017;74(4):423-431. Available at: <https://pubmed.ncbi.nlm.nih.gov/27984559>.

13. Dutertre M, Cuzin L, Demonchy E, et al. Initiation of antiretroviral therapy containing integrase inhibitors increases the risk of IRIS requiring hospitalization. *J Acquir Immune Defic Syndr*. 2017;76(1):e23-e26. Available at: <https://pubmed.ncbi.nlm.nih.gov/28418992>.
14. Wijting IEA, Wit F, Rokx C, et al. Immune reconstitution inflammatory syndrome in HIV infected late presenters starting integrase inhibitor containing antiretroviral therapy. *EClinicalMedicine*. 2019;17:100210. Available at: <https://pubmed.ncbi.nlm.nih.gov/31891143>.
15. Wang B, Abbott L, Childs K, et al. Dolutegravir-induced liver injury leading to sub-acute liver failure requiring transplantation: a case report and review of literature. *Int J STD AIDS*. 2018;29(4):414-417. Available at: <https://pubmed.ncbi.nlm.nih.gov/29059031>.
16. Christensen ES, Jain R, Roxby AC. Abacavir/dolutegravir/lamivudine (trumeq)-induced liver toxicity in a human immunodeficiency virus-infected patient. *Open Forum Infect Dis*. 2017;4(3):ofx122. Available at: <https://pubmed.ncbi.nlm.nih.gov/28748198>.
17. Martin C, Payen MC, De Wit S. Dolutegravir as a trigger for DRESS syndrome? *Int J STD AIDS*. 2018;29(10):1036-1038. Available at: <https://pubmed.ncbi.nlm.nih.gov/29621952>.
18. Rhee SY, Grant PM, Tzou PL, et al. A systematic review of the genetic mechanisms of dolutegravir resistance. *J Antimicrob Chemother*. 2019;74(11):3135-3149. Available at: <https://pubmed.ncbi.nlm.nih.gov/31280314>.
19. Santoro MM, Fornabaio C, Malena M, et al. Susceptibility to HIV-1 integrase strand transfer inhibitors (INSTIs) in highly treatment-experienced patients who failed an INSTI-based regimen. *Int J Antimicrob Agents*. 2020;56(1):106027. Available at: <https://pubmed.ncbi.nlm.nih.gov/32450199>.
20. Chandasana H, Buchanan AM, Henegar CA, et al. Model-informed dolutegravir dose selection in pediatrics with first-generation INSTI resistance. *Pediatr Infect Dis J*. 2026. Available at: <https://pubmed.ncbi.nlm.nih.gov/41634915>.
21. Bevers LAH, Waalewijn H, Szubert AJ, et al. Pharmacokinetic data of dolutegravir in second-line treatment of children with human immunodeficiency virus: results from the CHAPAS4 trial. *Clin Infect Dis*. 2023;77(9):1312-1317. Available at: <https://pubmed.ncbi.nlm.nih.gov/37280040>.
22. Chandasana H, Marnoch R, McKenna M, et al. Effect of food on the pediatric dispersible tablet formulations of TRIUMEQ and DOVATO in healthy adult participants. *Pharmaceutics*. 2023;15(5):1470. Available at: <https://pubmed.ncbi.nlm.nih.gov/37242711>.
23. Parasrampur R, Adkison K, Wolstenholme A, et al. Comparison of relative bioavailability of TIVICAY Immediate release and dispersible pediatric tablets to immediate release TIVICAY adult tablets. Presented at: 19th International Workshop on Clinical Pharmacology of Antiviral Therapy. 2018. Baltimore, MD. Available at: https://www.natap.org/2018/Pharm/Pharm_19.htm.
24. Cressey TR, Salvadori N, Rabie H, et al. Single doses of pediatric dolutegravir dispersible tablets in neonates support multidosing: PETITE-Dolutegravir study. *J Acquir Immune Defic Syndr*. 2025;99(2):195-201. Available at: <https://pubmed.ncbi.nlm.nih.gov/39972540>.
25. Bekker A, Salvadori N, Rabie H, et al. Safety and pharmacokinetics of dolutegravir dispersible tablets and oral films in term neonates exposed to HIV in South Africa (PETITE-DTG study): an open-label, randomised, phase 1/2 trial. *Lancet HIV*. 2025;12(11):e753-e762. Available at: <https://pubmed.ncbi.nlm.nih.gov/41075812>.

26. Momper J, Chandasana H, Wang J, et al. Pharmacokinetics and safety of chronic dolutegravir administration in neonates exposed to HIV-1 (IMPAACT 2023). Presented at: Conference on Retroviruses and Opportunistic Infections. 2025. Available at: <https://www.croiconference.org/abstract/3628-2025>.
27. Viani RM, Alvero C, Fenton T, et al. Safety, pharmacokinetics and efficacy of dolutegravir in treatment-experienced HIV-1 infected adolescents: 48-week results from IMPAACT P1093. *Pediatr Infect Dis J*. 2015;34(11):1207-1213. Available at: <https://pubmed.ncbi.nlm.nih.gov/26244832>.
28. Wiznia A, Alvero C, Fenton T, et al. IMPAACT 1093: dolutegravir in 6- to 12-year-old HIV-infected children: 48-week results. Presented at: Conference on Retroviruses and Opportunistic Infections. 2016. Boston, MA.
29. Ruel TD, Acosta EP, Liu JP, et al. Pharmacokinetics, safety, tolerability, and antiviral activity of dolutegravir dispersible tablets in infants and children with HIV-1 (IMPAACT P1093): results of an open-label, Phase 1-2 trial. *Lancet HIV*. 2022;9(5):e332-e340. Available at: <https://pubmed.ncbi.nlm.nih.gov/35489377>.
30. Dolutegravir (Tivicay and Tivicay PD) [package insert]. Food and Drug Administration. 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/204790s033lbl.pdf.
31. Viani RM, Ruel T, Alvero C, et al. Long-term safety and efficacy of dolutegravir in treatment-experienced adolescents with human immunodeficiency virus infection: results of the IMPAACT P1093 study. *J Pediatric Infect Dis Soc*. 2020;9(2):159-165. Available at: <https://pubmed.ncbi.nlm.nih.gov/30951600>.
32. Moore CL, Turkova A, Mujuru H, et al. ODYSSEY clinical trial design: a randomised global study to evaluate the efficacy and safety of dolutegravir-based antiretroviral therapy in HIV-positive children, with nested pharmacokinetic sub-studies to evaluate pragmatic WHO-weight-band based dolutegravir dosing. *BMC Infect Dis*. 2021;21(1):5. Available at: <https://pubmed.ncbi.nlm.nih.gov/33446115>.
33. Amuge P, Lugemwa A, Wynne B, 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 randomised ODYSSEY trial. *Lancet HIV*. 2022;9(9):e638-e648. Available at: <https://pubmed.ncbi.nlm.nih.gov/36055295>.
34. Turkova A, White E, Kekitiinwa AR, et al. Neuropsychiatric manifestations and sleep disturbances with dolutegravir-based antiretroviral therapy versus standard of care in children and adolescents: a secondary analysis of the ODYSSEY trial. *Lancet Child Adolesc Health*. 2023;7(10):718-727. Available at: <https://pubmed.ncbi.nlm.nih.gov/37562418>.
35. Turkova A, Kityo C, Mujuru HA, et al. Weight gain in children and adolescents on dolutegravir vs standard of care in the ODYSSEY trial. Abstract PEB202. Presented at: 11th International AIDS Society Conference on HIV Science. 2021. Virtual Conference. Available at: <https://theprogramme.ias2021.org/Abstract/Abstract/1311>.
36. Mujuru A, White EM, Kekitiinwa A, et al. ODYSSEY 192-week follow-up evidences superior efficacy of DTG for children on first/second-line ART. Presented at: Conference on Retroviruses and Opportunistic Infections. 2024. Denver, CO. Available at: <https://www.croiconference.org/abstract/odyssey-192-week-follow-up-evidences-superior-efficacy-of-dtg-for-children-on-first-second-line-art>.

37. White E, Kityo C, Spyer MJ, et al. Virological outcomes and genotypic resistance on dolutegravir-based antiretroviral therapy versus standard of care in children and adolescents: a secondary analysis of the ODYSSEY trial. *Lancet HIV*. 2025;12(3):e201-e213. Available at: <https://pubmed.ncbi.nlm.nih.gov/39978387>.
38. Bollen PDJ, Moore CL, Mujuru HA, et al. Simplified dolutegravir dosing for children with HIV weighing 20 kg or more: pharmacokinetic and safety substudies of the multicentre, randomised ODYSSEY trial. *Lancet HIV*. 2020;7(8):e533-e544. Available at: <https://pubmed.ncbi.nlm.nih.gov/32763217>.
39. Waalewijn H, Chan MK, Bollen PDJ, et al. Dolutegravir dosing for children with HIV weighing less than 20 kg: pharmacokinetic and safety substudies nested in the open-label, multicentre, randomised, non-inferiority ODYSSEY trial. *Lancet HIV*. 2022;9(5):e341-e352. Available at: <https://pubmed.ncbi.nlm.nih.gov/35189082>.
40. Waalewijn H, Stol K, van der Knaap L, et al. Adequate exposure of 50 mg dolutegravir in children weighing 20 to 40 kg outside of sub-Saharan Africa. *AIDS*. 2022;36(14):2077-2079. Available at: <https://pubmed.ncbi.nlm.nih.gov/36111542>.
41. Martyn-Dickens C, Ojewale O, Sly-Moore E, et al. Pharmacokinetics and pharmacodynamics of adult dolutegravir tablets in treatment-experienced children with HIV weighing at least 20 kg. *AIDS*. 2023;37(9):1409-1417. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/37070558>.
42. Rungsapphaiboon A, Wacharachaisurapol N, Anugulruengkitt S, et al. Pharmacokinetics of generic pediatric dolutegravir dispersible tablet in Thai young children living with HIV weighing below twenty kilograms. *Pediatr Infect Dis J*. 2024;43(8):789-794. Available at: <https://pubmed.ncbi.nlm.nih.gov/39018516>.
43. Chandasana H, Thapar M, Hayes S, et al. Population pharmacokinetic modeling of dolutegravir to optimize pediatric dosing in HIV-1-infected infants, children, and adolescents. *Clin Pharmacokinet*. 2023;62(10):1445-1459. Available at: <https://pubmed.ncbi.nlm.nih.gov/37603217>.
44. Chandasana H, van Dijkman SC, Mehta R, et al. Population pharmacokinetic modeling of abacavir/dolutegravir/lamivudine to support a fixed-dose combination in children with HIV-1. *Infect Dis Ther*. 2024;13(8):1877-1891. Available at: <https://pubmed.ncbi.nlm.nih.gov/38961048>.
45. Waalewijn H, Wasmann RE, Bamford A, et al. Population pharmacokinetics of dolutegravir in African children: results from the CHAPAS-4 trial. *J Pediatric Infect Dis Soc*. 2024;13(9):496-500. Available at: <https://pubmed.ncbi.nlm.nih.gov/39066509>.
46. Jacobs TG, Waalewijn H, Houlden L, et al. Influence of age and co-medication on dolutegravir glucuronidation in paediatric patients. *Br J Clin Pharmacol*. 2024;90(11):2947-2952. Available at: <https://pubmed.ncbi.nlm.nih.gov/39228168>.
47. Spector SA, Brummel SS, Chang A, et al. Impact of genetic variants in ABCG2, NR112, and UGT1A1 on the pharmacokinetics of dolutegravir in children. *J Acquir Immune Defic Syndr*. 2024;95(3):297-303. Available at: <https://pubmed.ncbi.nlm.nih.gov/38180896>.

48. Brooks KM, Kiser JJ, Ziemba L, 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-e517. Available at: <https://pubmed.ncbi.nlm.nih.gov/37541705>.
49. Rabie H, Yin DE, Ward S, et al. Efficacy, safety and tolerability of dispersible and immediate release abacavir/dolutegravir/lamivudine tablets in children with HIV: IMPAACT 2019 week 48 Results. *Pediatr Infect Dis J*. 2025;44(8):777-784. Available at: <https://pubmed.ncbi.nlm.nih.gov/40440679>.
50. Bossacoma Busquets F, Noguera-Julian A, Sanchez E, Fortuny C. Dolutegravir plus abacavir/lamivudine works in adolescents, but size matters. *J Antimicrob Chemother*. 2017;72(10):2958-2960. Available at: <https://pubmed.ncbi.nlm.nih.gov/29091219>.
51. Chandasana H, Brooks KM, Buchanan A, et al. A single once daily ABC/DTG/3TC tablet predicts safe and effective exposures in children 3 to <6kg. Presented at: Conference of Retroviruses and Opportunistic Infections. 2023. Denver, CO. Available at: <https://www.croiconference.org/abstract/a-single-once-daily-abc-dtg-3tc-tablet-predicts-safe-and-effective-exposures-in-children-3-to>.
52. Bekker A, Capparelli EV, Violari A, et al. Abacavir dosing in neonates from birth to 3 months of life: a population pharmacokinetic modelling and simulation study. *Lancet HIV*. 2022;9(1):e24-e31. Available at: <https://pubmed.ncbi.nlm.nih.gov/34883066>.
53. Bekker A, Salvadori N, Rabie H, et al. Paediatric abacavir-lamivudine fixed-dose dispersible tablets and ritonavir-boosted lopinavir granules in neonates exposed to HIV (PETITE study): an open-label, two-stage, single-arm, phase 1/2, pharmacokinetic and safety trial. *Lancet HIV*. 2024;11(2):e86-e95. Available at: <https://pubmed.ncbi.nlm.nih.gov/38296364>.
54. Frange P, Blanche S, Veber F, Avettand-Fenoel V. Dolutegravir in the long term in children and adolescents: frequent virological failure but rare acquired genotypic resistance. *HIV Med*. 2021;22(10):958-964. Available at: <https://pubmed.ncbi.nlm.nih.gov/34369051>.
55. Bacha JM, Dlamini S, Anabwani F, et al. Realizing the promise of dolutegravir in effectively treating children and adolescents living with HIV in real-world settings in 6 countries in eastern and southern Africa. *Pediatr Infect Dis J*. 2023;42(7):576-581. Available at: <https://pubmed.ncbi.nlm.nih.gov/36795586>.
56. Devendra A, Kohler M, Letsika M, et al. HIV viral suppression in children and adolescents 2 years after transition to dolutegravir: a multicentre cohort study. *AIDS*. 2024;38(7):1013-1023. Available at: <https://pubmed.ncbi.nlm.nih.gov/38381717>.
57. Ezenwosu IL, Onu JU, Chukwuma UV, et al. Effect of dolutegravir-based drug combinations on the level of medication adherence and viral load among adolescents living with HIV in resource-limited setting: a pre-post design. *Int J Adolesc Med Health*. 2023;35(6):457-465. Available at: <https://pubmed.ncbi.nlm.nih.gov/38059505>.
58. Makonokaya L, Maida A, Kalitera LU, et al. Early effects of scaling up dolutegravir-based ARV regimens among children living with HIV in Malawi. *AIDS Behav*. 2024;28(6):2148-2155. Available at: <https://pubmed.ncbi.nlm.nih.gov/38615099>.
59. Musiime V, Bwakura-Dangarembizi M, Szubert AJ, et al. Second-line antiretroviral therapy for children living with HIV in Africa. *N Engl J Med*. 2025;392(19):1917-1932. Available at: <https://pubmed.ncbi.nlm.nih.gov/40367375>.

60. Gill MM, Herrera N, Guilaze R, et al. Virologic outcomes and ARV switch profiles 2 years after national rollout of dolutegravir to children less than 15 years in southern Mozambique. *Pediatr Infect Dis J*. 2023;42(10):893-898. Available at: <https://pubmed.ncbi.nlm.nih.gov/37409808>.
61. Konu YR, Takassi E, Peytavin G, et al. Pharmaco-virological outcomes and genotypic resistance profiles among children and adolescents receiving a DTG-based regimen in Togo. *Clin Infect Dis*. 2025;80(1):144-152. Available at: <https://pubmed.ncbi.nlm.nih.gov/38748464>.
62. Kamori D, Barabona G, Rugemalila J, et al. Emerging integrase strand transfer inhibitor drug resistance mutations among children and adults on ART in Tanzania: findings from a national representative HIV drug resistance survey. *J Antimicrob Chemother*. 2023;78(3):779-787. Available at: <https://pubmed.ncbi.nlm.nih.gov/36680436>.
63. Malinga S, Khan A, Archary M. Breaking the unbreakable: a paediatric case of dolutegravir resistance from KwaZulu-Natal. *South Afr J HIV Med*. 2023;24(1):1458. Available at: <https://pubmed.ncbi.nlm.nih.gov/37293603>.
64. Failla M, Pasquali E, Galli L, Chiappini E. Integrase strand transfer inhibitor use in children with perinatal HIV-1 infection: a narrative review. *AIDS Res Hum Retroviruses*. 2023;39(6):263-284. Available at: <https://pubmed.ncbi.nlm.nih.gov/36352827>.
65. Rose PC, De la Rey Nel E, Cotton MF, et al. Decreased hepatic steatosis in South African adolescents with perinatal HIV switching to dolutegravir-containing regimens. *Pediatr Infect Dis J*. 2023;42(7):564-572. Available at: <https://pubmed.ncbi.nlm.nih.gov/36917035>.
66. Frange P, Avettand-Fenoel V, Veber F, Blanche S. No overall impact on body mass index for age change after dolutegravir initiation in a French paediatric cohort. *HIV Med*. 2022;23(9):1019-1024. Available at: <https://pubmed.ncbi.nlm.nih.gov/35306718>.
67. Llibre JM, Hung CC, Brinson C, et al. Phase III SWORD 1&2: switch to DTG+RPV maintains virologic suppression through 48 wks. Presented at: Conference on Retroviruses and Opportunistic Infections. 2017. Seattle, WA. Available at: https://www.natap.org/2017/CROI/croi_11.htm.
68. van Wyk J, Orkin C, Rubio R, et al. Brief report: durable suppression and low rate of virologic failure 3 years after switch to dolutegravir + rilpivirine 2-drug regimen: 148-week results from the SWORD-1 and -2 randomized clinical trials. *J Acquir Immune Defic Syndr*. 2020;85(3):325-330. Available at: <https://pubmed.ncbi.nlm.nih.gov/32675772>.
69. McComsey GA, Lupo S, Parks D, et al. Switch from tenofovir disoproxil fumarate combination to dolutegravir with rilpivirine improves parameters of bone health. *AIDS*. 2018;32(4):477-485. Available at: <https://pubmed.ncbi.nlm.nih.gov/29239893>.
70. Cahn P, Madero JS, Arribas JR, et al. Durable efficacy of dolutegravir plus lamivudine in antiretroviral treatment-naïve adults with HIV-1 infection: 96-week results from the GEMINI-1 and GEMINI-2 randomized clinical trials. *J Acquir Immune Defic Syndr*. 2020;83(3):310-318. Available at: <https://pubmed.ncbi.nlm.nih.gov/31834000>.
71. Puthanakit T, Aurpibul L, Lopez M, et al. Efficacy and safety of the two-drug regimen dolutegravir-lamivudine in adolescents living with HIV-1 naïve to antiretroviral therapy at 48 weeks (DANCE): a single-arm, open-label, phase 3b trial. *J Acquir Immune Defic Syndr*. 2025;99(2):202-210. Available at: <https://pubmed.ncbi.nlm.nih.gov/39988749>.

72. Puthanakit T, Aupibul L, Lopez M, et al. Efficacy and safety of dolutegravir/lamivudine (DTG/3TC) in antiretroviral therapy (ART)- naive adolescents living with HIV-1: DANCE study week 96 results. Presented at: International AIDS Society. July 23–26, 2023. Brisbane, Australia. Available at: https://medinfo.gsk.com/5f95dbd7-245e-4e65-9f36-1a99e28e5bba/450b1aad-cf09-4084-b484-0c909235ec90/450b1aad-cf09-4084-b484-0c909235ec90_viewable_rendition_v.pdf?medcommid=REF--ALL-005098&product=Dolutegravir%2BLamivudine.
73. Turkova A, Chan MK, Kityo C, et al. D3/Penta 21 clinical trial design: a randomised non-inferiority trial with nested drug licensing substudy to assess dolutegravir and lamivudine fixed dose formulations for the maintenance of virological suppression in children with HIV-1 infection, aged 2 to 15 years. *Contemp Clin Trials*. 2024;142:107540. Available at: <https://pubmed.ncbi.nlm.nih.gov/38636725>.
74. Bevers LAH, Toledo G, Kisekka M, et al. Once-daily dolutegravir/lamivudine fixed-dose formulations in children living with HIV: a pharmacokinetic and safety sub-study nested in the open-label, multicentre, randomised, non-inferiority D3/PENTA 21 trial. *EBioMedicine*. 2025;120:105929. Available at: <https://pubmed.ncbi.nlm.nih.gov/41014973>.
75. Compagnucci A, Chan MK, Saiidi Y, et al. Nucleoside/nucleotide reverse transcriptase inhibitor sparing regimen with once daily integrase inhibitor plus boosted darunavir is non-inferior to standard of care in virologically-suppressed children and adolescents living with HIV-week 48 results of the DA SMILE Penta-17-ANRS 152 clinical trial. *EClinicalMedicine*. 2023;60:102025. Available at: <https://pubmed.ncbi.nlm.nih.gov/37304494>.
76. Abdalla S, Compagnucci A, Zheng Y, et al. Population pharmacokinetics of unbound and total dolutegravir concentrations in children aged 12 years and older: a PK substudy of the SMILE trial. *J Antimicrob Chemother*. 2023;78(4):1041-1049. Available at: <https://pubmed.ncbi.nlm.nih.gov/36869720>.
77. Abdalla S, Compagnucci A, Bamford A, et al. Assessment of the steady-state drug-drug interactions between dolutegravir and ritonavir-boosted darunavir in adolescents. *AIDS*. 2025;39(10):1385-1391. Available at: <https://pubmed.ncbi.nlm.nih.gov/40327672>.
78. Roskam-Kwint M, Bollen P, Colbers A, et al. Crushing of dolutegravir fixed-dose combination tablets increases dolutegravir exposure. *J Antimicrob Chemother*. 2018;73(9):2430-2434. Available at: <https://pubmed.ncbi.nlm.nih.gov/29796595>.
79. Turley SL, Fulco PP. Enteral administration of twice-daily dolutegravir and rilpivirine as a part of a triple-therapy regimen in a critically ill patient with HIV. *J Int Assoc Provid AIDS Care*. 2017;16(2):117-119. Available at: <https://pubmed.ncbi.nlm.nih.gov/28198203>.
80. Chrdle A, Jerhotová Z, Vacik M, et al. Crushed dolutegravir/abacavir/lamivudine given via nasogastric tube in gastric outlet obstruction caused by cancer resulted in rapid viral load suppression. *Int J STD AIDS*. 2019;30(1):94-98. Available at: <https://pubmed.ncbi.nlm.nih.gov/30231834>.