Egyptian Drug Formulary

Central Administration of Pharmaceutical Care
General Administration of Drug Utilization and Pharmacy Practice

Egyptian National Antiretroviral Drugs Formulary 2026

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Contents

Preface

The Egyptian National Drug Formulary is published by the Egyptian Drug Authority, developed by the General Administration of Drug Utilization and Pharmacy Practice at the Central Administration of Pharmaceutical Care.

This formulary aims to provide pharmacists and other healthcare professionals with accessible and reliable information about the medications that are specified in the National HIV guidelines and provided through the National AIDS Program. The Egyptian Drug Formulary is a guide that should be interpreted in light of professional clinical knowledge. The working group ensures that the information is as accurate and up-to-date as possible at the date of publication, but knowledge and best practices change regularly. The work team assumes no responsibility for errors or omissions.

Egyptian National Drug Formulary Manual (Antiretroviral Drugs)

The Egyptian Drug Formulary (**Antiretroviral Drugs**) contains a list of medications that are specified in the National HIV guidelines and provided through the National AIDS Program. It is designed as drug monographs classified pharmacologically and arranged alphabetically.

The Egyptian National Drug Formulary (Antiretroviral Drugs) presents detailed practical information for healthcare providers about each medicine. Each monograph includes:

1. Generic name
2. Dosage form/strengths available in Egypt
3. Route of administration
4. Pharmacological category and ATC code
5. Indications: Labeled indications
6. Dosage regimens for adults and children
7. Dosage adjustments if needed
8. Contraindications
9. Adverse drug reaction
10. Monitoring parameters
11. Drug Interactions: that imply avoidance or considering modifications
12. Pregnancy and lactation
13. Administration
14. Warnings/Precautions
15. Storage conditions

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We are profoundly grateful to **Dr. Abeer ElBehairy, Head of the Central Administration of Pharmaceutical Care,** for her invaluable support, guidance, and continuous dedication throughout the development of this work. Her leadership has been instrumental in achieving the project's objectives and advancing pharmaceutical care services, while promoting the rational and safe use of medicines to enhance patient care and public health.

We also extend our sincere appreciation to the members of **the National Rational Antimicrobial Use Committee** for their expertise, commitment, and collaborative efforts in supporting this document. Their contributions have played a pivotal role in promoting antimicrobial stewardship, fostering the responsible use of antimicrobials, and strengthening national efforts to combat antimicrobial resistance.

Finally, we would like to acknowledge and thank all **Egyptian Drug Authority staff** and contributors whose hard work, professionalism, and dedication were essential to the successful completion of this project. Their collective efforts continue to support the EDA's mission of ensuring the quality, safety, efficacy, and rational use of medicines in Egypt.

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Abbreviations

3TC	Lamivudine
ABC	Abacavir
AM	ante meridiem
ART	Antiretroviral therapy
ATC	Anatomical Therapeutic Chemical
BCG	Bacillus Calmette–Guérin vaccine
BMI	Body Mass Index
BSA	Body Surface Area
°C	The degree Celsius
CART	Combination Antiretroviral Therapy
CBC	Complete Blood Count
CD4	Cluster of Differentiation 4
CMV	Cytomegalovirus
CNS	Central Nervous System
Crcl	Creatinine Clearance
CYP3A4	Cytochrome P450 3A4
DTG	Dolutegravir
DKA	Diabetic Ketoacidosis
EBR	Elbasvir
EDA	Egyptian Drug Authority
ENT	Ear, Nose, and Throat
EFV	Efavirenz

ETR	Etravirine
FTC	Emtricitabine
GZR	Grazoprevir
G/dl	Gram/ deciliter
HBV	Hepatitis B virus
HIV	Human Immunodeficiency Virus
IHD	Ischemic Heart Disease
Kg	Killogram
LFTs	Liver Function Tests
LPV/r	Lopinavir and Ritonavir
mg	Milligram
mg/ml	Milligram/milliliter
ml	Milliliter
mg/kg/hr	Milligram/Kilogram/Hour
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NVP	Nevirapine
PIL	Patient Information Leaflet
PMA	Postmenstrual Age
PM	post meridiem
PrEp	Pre-Exposure Prophylaxis
RAL	Raltegravir
RNA	Ribonucleic acid
SPC	Summary of Product Characteristics

TDF	Tenofovir Disoproxil Fumarate
USP	Unique Selling Proposition
ZDV	Zidovudine

a) Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

1. Abacavir (ABC)

<table>
<tr><th>Generic Name</th><th>Abacavir Sulphate</th></tr>
<tr><td>Dosage Form/Strengths</td><td>Tablets
Abacavir 300 mg
Abacavir + Lamivudine (120/60 mg)
Abacavir + Lamivudine (60/30mg)</td></tr>
<tr><td>Route of Administration</td><td>Oral</td></tr>
<tr><td>Pharmacologic Category</td><td>Nucleoside reverse transcriptase inhibitor (NRTI)
ATC: J05AF06</td></tr>
<tr><td>Indications</td><td>HIV-1 infection: Treatment of HIV-1 infection in combination with other antiretroviral agents (in adults, it is an alternative to the first-line regimen in special circumstances, in pediatrics, it is the preferred regimen).</td></tr>
<tr><td>Dosage Regimen</td><td>
<u>Adult</u>
Oral: 300 mg twice daily or 600 mg once daily in combination with other antiretroviral agents.
<u>Infants ≥ 4 weeks, Children, and Adolescents</u>

a) <u>Twice daily dose regimen</u>
For ABC 60 mg or 120 mg
<table>
<tr><th rowspan="2">Strength</th><th colspan="10">Number of tablets by weight band, morning and evening</th></tr>
<tr><th colspan="2">3 - < 6 kg</th><th colspan="2">6 - < 10 kg</th><th colspan="2">10 - < 14 kg</th><th colspan="2">14 - < 20kg</th><th colspan="2">20 - < 25 kg</th></tr>
<tr><th>AM</th><th>PM</th><th>AM</th><th>PM</th><th>AM</th><th>PM</th><th>AM</th><th>PM</th><th>AM</th><th>PM</th></tr>
<tr><td>Tablet 60 mg</td><td>1</td><td>1</td><td>1.5</td><td>1.5</td><td>2</td><td>2</td><td>2.5</td><td>2.5</td><td>3</td><td>3</td></tr>
<tr><td>120mg</td><td>0.5</td><td>0.5</td><td>0.5</td><td>1</td><td>1</td><td>1</td><td>1</td><td>1.5</td><td>1.5</td><td>1.5</td></tr>
</table>
For ABC 300 mg, if body weight ≥14 kg
Tablets (scored 300 mg tablets):
14 to <20 kg: 150 mg twice daily.
20 to <25 kg: 150 mg in the morning and 300 mg in the evening.
≥ 25 kg: 300 mg twice daily.
b) <u>Once daily dose regimen</u>
In clinically stable patients with undetectable viral load for more than 6 months (24 weeks) on abacavir twice daily, the daily dose can be changed from twice daily to once daily. Initiation with once-daily dosing is recommended for children who can be treated with tablet formulation.
For ABC 60 mg or 120 mg
<table>
<tr><th rowspan="2">Strength</th><th colspan="5">Number of tablets by weight band</th></tr>
<tr><th>3 - < 6 kg</th><th>6 - < 10 kg</th><th>10 - < 14 kg</th><th>14 - < 20kg</th><th>20 - < 25 kg</th></tr>
</table>
</td></tr>
</table>

	<table><tr><td><u>Tablet 60 mg</u></td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td></tr><tr><td><u>120mg</u></td><td>1</td><td>1.5</td><td>2</td><td>2.5</td><td>3</td></tr></table> • **For ABC 300 mg, if body weight ≥14 kg** **Tablets (scored 300 mg tablets), oral solution:** - 14 to <20 kg: 300 mg once daily - 20 to <25 kg: 450 mg once daily - ≥25 kg: 600 mg once daily
Dosage Adjustment	**Dosing: Renal Impairment** • There are no dosage adjustments. **Dosing: Hepatic Impairment Adults:** • Mild impairment (Child-Pugh class A): 200 mg twice daily (oral solution is recommended). • Moderate to severe impairment (Child-Pugh class B or C): Use is contraindicated **Dosing: Hepatic Impairment Pediatrics:** • Mild impairment: Dosing adjustment is required; however, pediatric-specific recommendations are not available. • Moderate to severe hepatic impairment (Child-Pugh class B or C): Use is contraindicated.
Contra-indications	• Hypersensitivity to abacavir or any component of the formulation. • Moderate to severe hepatic impairment. • Patients who are positive for the HLA-B*5701 allele.
Major Adverse Drug Reactions	**<u>>10%</u>** • **Central nervous system**: Headache (adults: ≤13%; infants, children, and adolescents: 1%), fatigue (≤12%), malaise (≤12%) • **Gastrointestinal**: Nausea (7% to 19%) **<u>1% to 10%</u>** • **Central nervous system**: Abnormal dreams (≤10%), sleep disorder (≤10%), chills (≤9%), migraine (≤7%), depression (6%), dizziness (6%), anxiety (5%) • **Dermatologic**: Skin rash (5% to 7%) • **Endocrine and metabolic**: Hypertriglyceridemia (grades 3/4: 2% to 6%) • **Gastrointestinal**: Nausea and vomiting (9% to 10%), diarrhea (7%), abdominal pain (≤6%), gastritis (≤6%), gastrointestinal signs and symptoms (≤6%), increased serum amylase (grades 3/4: 2% to 4%), vomiting (2%) • **Hematologic and oncologic**: Neutropenia (grades 3/4: 2% to 5%), thrombocytopenia (grades 3/4: 1%) • **Hepatic**: Increased serum alanine aminotransferase (grades 3/4: 6%), increased serum aspartate aminotransferase (grades 3/4: 6%) • **Hypersensitivity**: Drug-induced hypersensitivity (9%), hypersensitivity reaction (including anaphylaxis and multiorgan failure; 8%; excluding subjects carrying the HLA-B*5701 allele: 1%) • **Neuromuscular and skeletal**: Increased creatine phosphokinase (grades 3/4: 7% to 8%), musculoskeletal pain (5% to 6%) • **Respiratory**: ENT infection (5%), viral respiratory tract infection (5%), bronchitis (4%), pneumonia (infants, children, & adolescents: 4%) • **Miscellaneous**: Fever (≤9%)

Monitoring Parameters	• Blood count with differential, CD4 count, HIV RNA plasma levels, serum transaminases, fasting lipid panel; serum creatine kinase, serum amylase (as clinically indicated); HLA-B*5701 genotype status before initiation of therapy and before reinitiation of therapy in patients of unknown HLA-B*5701 status; signs and symptoms of hypersensitivity.
Drug Interactions	• **Risk X: Avoid combination** Atidarsagene Autotemcel, Betibeglogene Autotemcel, Cladribine, Elivaldogene Autotemcel, Lovotibeglogene Autotemcel
Pregnancy and Lactation	**Pregnancy** • Abacavir is a preferred (NRTI) for pregnant patients living with HIV who are antiretroviral naive, who have had ART therapy in the past but are restarting, or who require a new ART regimen (due to poor tolerance or poor virologic response of current regimen). Patients who become pregnant while taking abacavir may continue if viral suppression is effective and the regimen is well tolerated. **Lactation** • Abacavir is present in human milk. • There is no information on the effects of abacavir on the breastfed infant or the effects of the drug on milk production. • Because of the potential for (1) HIV-1 transmission (in HIV-negative infants), (2) developing viral resistance (in HIV-positive infants), and (3) adverse reactions in a breastfed infant, instruct mothers not to breastfeed if they are receiving abacavir
Administration	• **Oral**: May be administered without regard to food.
Warnings/ Precautions	• **Hypersensitivity reactions**: Serious and sometimes fatal hypersensitivity reactions have occurred. Patients who carry the HLA-B*5701 alleles are at a higher risk for a hypersensitivity reaction to abacavir • **Immune reconstitution syndrome**: Patients may develop immune reconstitution syndrome, resulting in the occurrence of an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves disease, polymyositis, Guillain-Barré syndrome) later in therapy; further evaluation and treatment may be required. • **Lactic acidosis/hepatomegaly** • **Coronary heart disease**: Use has been associated with an increased risk of MI in some cohort studies. Consider using with caution in patients with risks for coronary heart disease and minimizing modifiable risk factors (eg, hypertension, hyperlipidemia, diabetes mellitus, smoking) before use. • **Hepatic impairment**: Use with caution and adjust dosage in patients with mild hepatic impairment (contraindicated in moderate to severe impairment). • May cause mild **hyperglycemia**, more common in pediatric patients.
Storage	Store at 20°C to 25 °C. Oral solution may be refrigerated; do not freeze. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

2. Lamivudine (3TC)

<table>
<tr><th>Generic Name</th><th>Lamivudine</th></tr>
<tr><td>Dosage Form/Strengths</td><td>Tablets
Lamivudine 150 mg
Lamivudine/Zidovudine 150/300 mg
Abacavir + Lamivudine (120/60 mg)
Abacavir + Lamivudine (60/30 mg)</td></tr>
<tr><td>Route of Administration</td><td>Oral</td></tr>
<tr><td>Pharmacologic Category</td><td>Nucleoside reverse transcriptase inhibitor (NRTI)
ATC: J05AF05</td></tr>
<tr><td>Indications</td><td>HIV-1 infection, treatment: Treatment of HIV-1 in combination with other antiretroviral agents in adults and pediatrics (first line regimen, alternative to first line, second line, and alternative to second line)</td></tr>
<tr><td>Dosage Regimen</td><td><u>Dosing: Adult</u>
Oral (use in combination with other antiretroviral agents): 150 mg twice daily or 300 mg once daily
<u>Dosing: Infants ≥ 4 weeks, children, and adolescents</u>

a) <u>Twice-daily dosing</u>
<u>For 3TC 30 mg or 60 mg oral tablet</u>
<table>
<tr><th rowspan="2">Strength</th><th colspan="10">Number of tablets by weight band, morning and evening</th></tr>
<tr><th colspan="2">3 - < 6 kg</th><th colspan="2">6 - < 10 kg</th><th colspan="2">10 - < 14 kg</th><th colspan="2">14 - < 20kg</th><th colspan="2">20 - < 25 kg</th></tr>
<tr><th>AM</th><th>PM</th><th>AM</th><th>PM</th><th>AM</th><th>PM</th><th>AM</th><th>PM</th><th>AM</th><th>PM</th></tr>
<tr><td>30 mg</td><td>1</td><td>1</td><td>1.5</td><td>1.5</td><td>2</td><td>2</td><td>2.5</td><td>2.5</td><td>3</td><td>3</td></tr>
<tr><td>60mg</td><td>0.5</td><td>0.5</td><td>0.5</td><td>1</td><td>1</td><td>1</td><td>1</td><td>1.5</td><td>1.5</td><td>1.5</td></tr>
</table>
<u>For 3TC 150 mg oral tablet:</u> Weight-band dosing for patients ≥14 kg who can swallow tablets (scored 150 mg tablets)
<table>
<tr><th rowspan="2"></th><th colspan="6">Number of tablets by weight band, morning and evening</th></tr>
<tr><th colspan="2">14 to <20 kg</th><th colspan="2">20 to <25 kg</th><th colspan="2">≥25 kg</th></tr>
<tr><th>AM</th><th>PM</th><th>AM</th><th>PM</th><th>AM</th><th>PM</th></tr>
<tr><td>150 mg</td><td>0.5</td><td>0.5</td><td>0.5</td><td>1</td><td>1</td><td>1</td></tr>
</table>
b) <u>Once-daily dosing:</u> Oral: Note: Not recommended as initial therapy in children.
Patients can be transitioned to once-daily treatment after being stable on twice-daily treatment for ≥36 weeks with an undetectable viral load and stable CD4 count.
<u>For 3TC 30 mg or 60 mg oral tablet</u>
<table>
<tr><th rowspan="2">Strength</th><th colspan="5">Number of tablets by weight band</th></tr>
<tr><th>3 - < 6 kg</th><th>6 - < 10 kg</th><th>10 - < 14 kg</th><th>14 - < 20kg</th><th>20 - < 25 kg</th></tr>
<tr><td>30 mg</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td></tr>
<tr><td>60mg</td><td>1</td><td>1.5</td><td>2</td><td>2.5</td><td>3</td></tr>
</table>
For 3TC 150 mg oral tablet: Weight-band dosing for patients ≥14 kg</td></tr>
</table>

<table>
<tr><td></td><td>who can swallow tablets (scored 150 mg tablets)

<table><tr><th></th><th>14to <20 kg</th><th>20to <25 kg</th><th>≥25 kg</th></tr><tr><td><u>150 mg</u></td><td>1</td><td>1.5</td><td>2</td></tr></table></td></tr>
<tr><td>Dosage Adjustment</td><td>Renal Impairment: Adult
CrCl ≥ 50 mL/minute: No dosage adjustment necessary.
CrCl 30 to 49 mL/minute: Administer 150 mg once daily.
CrCl 15 to 29 mL/minute: Administer 150 mg first dose, then 100 mg once daily.
CrCl 5 to 14 mL/minute: Administer 150 mg first dose, then 50 mg once daily.
CrCl <5 mL/minute: Administer 50 mg first dose, then 25 mg once daily.
Hemodialysis or Peritoneal dialysis: Administer 50 mg first dose, then 25 mg once daily; dosing after hemodialysis is recommended. Supplemental dosing is not needed after Peritoneal dialysis
Renal Impairment: Pediatric
Infants, Children, and Adolescents <25 kg: Although there are insufficient data to recommend a specific dose adjustment of lamivudine tablets in pediatric patients with renal impairment, a reduction in the dose and/or an increase in the dosing interval should be considered.
Children and Adolescents ≥25 kg: the same as in adults.
Dosing: Hepatic Impairment
No dosage adjustment necessary. However, has not been studied in the setting of decompensated liver disease.</td></tr>
<tr><td>Contra-indications</td><td>Hypersensitivity to lamivudine or any component of the formulation</td></tr>
<tr><td>Adverse Drug Reactions</td><td><u>>10%:</u>
Dermatologic: Skin rash (infants, children, adolescents, adults: 9% to 12%)
Gastrointestinal: Diarrhea (infants, children, adolescents: 8%; adults: 14% to 18%), nausea (infants, children, adolescents, adults: ≤33%), vomiting (infants, children, adolescents, adults: ≤13%)
Hepatic: Hepatomegaly (infants, children, adolescents: 11%)
Nervous system: Fatigue (≤27%), headache (35%), malaise (≤27%), neuropathy (12%), sleep disturbance (11%; including insomnia)
Neuromuscular and skeletal: Musculoskeletal pain (12%)
Respiratory: Cough (infants, children, adolescents, adults: 15% to 18%), ENT infection (25%), nasal signs and symptoms (infants, children, adolescents: 8% [including rhinorrhea, nasal congestion]; adults: 20%), pharyngitis (13%)
Miscellaneous: Fever (infants, children, adolescents: 25%; adults: ≤10%)
<u>1% to 10%:</u>
Gastrointestinal: Abdominal cramps (6%), abdominal pain (9%), anorexia (≤10%), decreased appetite (≤10%), dyspepsia (5%), increased serum amylase (infants, children, adolescents, adults: grades 3/4: 2% to 4%), increased serum lipase (infants, children, adolescents: grades 3/4: 3%; adults: 10%), stomatitis (infants, children, adolescents: 6%)</td></tr>
</table>

	• **Hematologic and oncologic**: Decrease in absolute neutrophil count (infants, children, adolescents, adults: grades 3/4: 7% to 8%), lymphadenopathy (infants, children, adolescents: 9%), thrombocytopenia (infants, children, adolescents: grades 3/4: 1%; adults: 4%, grades 3/4: <1%) • **Hepatic**: Increased serum alanine aminotransferase (infants, children, adolescents: grades 3/4: 1%; adults: grades 3/4: 4%), increased serum aspartate aminotransferase (infants, children, adolescents, adults: grades 3/4: 2% to 4%) • **Immunologic**: Splenomegaly (infants, children, adolescents: 5%) • **Nervous system**: Chills (≤10%), depression (9%), dizziness (10%) • **Neuromuscular and skeletal**: Arthralgia (5%), increased creatine phosphokinase in blood specimen (9%), myalgia (8%) • **Respiratory**: Abnormal breath sounds (infants, children, adolescents: ≤7%), wheezing (infants, children, adolescents: ≤7%)
Monitoring Parameters	• Hepatic function, signs/symptoms of lactic acidosis; signs/symptoms of pancreatitis, coinfection with HBV (before therapy); HIV viral load and CD4 count; immune reconstitution syndrome.
Drug Interactions	• **Risk X: Avoid combination** Atidarsagene Autotemcel, Betibeglogene Autotemcel, Cladribine, Elivaldogene Autotemcel, and Lovotibeglogene Autotemcel. • **Risk D: Consider therapy modification** Fexinidazole, Risdiplam, Sorbitol, Tafenoquine, Vimseltinib.
Pregnancy and Lactation	• **Pregnancy** Lamivudine has a high level of transfer across the human placenta. No increased risk of overall teratogenic effects has been observed following the first trimester. • **Breastfeeding** Lamivudine is present in breast milk. Lamivudine is a recommended component of an initial regimen for early (acute/recent) HIV infection in postpartum patients. Interrupt breastfeeding immediately if seroconversion is suspected, and do not continue if infection is diagnosed. Breast milk may be expressed and stored while waiting for test results.
Administration	• May be administered without regard to meals. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**
Warnings/ Precautions	***Concerns related to adverse effects:*** • **Immune reconstitution syndrome**: Patients may develop immune reconstitution syndrome, resulting in the occurrence of an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves disease, polymyositis, Guillain-Barré syndrome) later in therapy; further evaluation and treatment may be required. • **Lactic acidosis/hepatomegaly**: Lactic acidosis and severe hepatomegaly with steatosis have been reported with nucleoside analogues, including fatal cases; suspend treatment in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity. Use with caution in patients with risk factors for liver disease (risk may be increased with female gender or obesity) and discontinue in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatotoxicity. Transaminase elevation may/may not accompany hepatomegaly and steatosis.

	• **Pancreatitis**: Has been reported, particularly in HIV-infected pediatric patients with a history of nucleoside use. Discontinue treatment if signs or symptoms of pancreatitis occur. ***Disease-related concerns:*** **Resistance** • **HIV**: Lamivudine-resistant HIV-1 can develop rapidly and limit treatment options if used in unrecognized or untreated HIV-1 infection or if a patient becomes coinfected during HBV treatment. Lamivudine dosing for hepatitis B is also subtherapeutic if used for HIV-1/HBV coinfection treatment. If lamivudine is chosen as part of a HIV-1 treatment regimen in coinfected patients, the higher lamivudine dosage indicated for HIV-1 therapy should be used, with other drugs, in an appropriate combination regimen. • **HBV**: Emergence of lamivudine-resistant HBV variants has also been reported in HIV-1/HBV coinfected patients who have received lamivudine-containing antiretroviral regimens. ***Other warnings/precautions:*** Appropriate use: • **HIV**: Do not use as monotherapy in the treatment of HIV. Treatment of HIV in patients with unrecognized/untreated HBV may lead to rapid HBV resistance; patients with HIV should be screened for hepatitis B before starting lamivudine HIV therapy. Lamivudine combined with emtricitabine is not recommended as a dual-nucleoside reverse transcriptase inhibitor (NRTI) combination due to similar resistance patterns and negligible additive antiviral activity
Storage	• Store at 20° to 25°C; excursions permitted to 15° to 30°C. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

3. Tenofovir Disoproxil Fumarate (TDF)

Generic Name	Tenofovir Disoproxil Fumarate
Dosage Form/Strengths	Tablets: • Emtricitabine/Tenofovir disoproxil fumarate 200/300 mg
Route of Administration	• Oral
Pharmacological Category	• Reverse Transcriptase Inhibitor; Antiretroviral, Nucleotide (Anti-HIV) • ATC: J05AF07
Indications	• Treatment of HIV-1 infection in adults and pediatrics ≥2 years of age weighing ≥10 kg, in combination with other antiretroviral agents (first line regimen, alternative to first line, and alternative to the second line regimen).
Dosage Regimen	**Dosing: Adult** • Oral: 300 mg once daily (in combination with other antiretrovirals). **Dosing: Pediatric** **HIV-1 infection, treatment** • ***Weight-directed dosing****: Children ≥2 years weighing ≥10 kg and Adolescents: 8 mg/kg/dose once daily; maximum daily dose:* **300 mg/day** • ***Dosage form specific fixed dosing****:* Children ≥2 years weighing ≥17 kg and Adolescents: - 17 to <22 kg: 150 mg once daily - 22 to <28 kg: 200 mg once daily - 28 to <35 kg: 250 mg once daily - ≥35 kg: 300 mg once daily **HIV-1 nonoccupational postexposure prophylaxis (nPEP)** • **Children ≥ 2 years**: Age- and weight-appropriate dosing (see HIV-1 infection, treatment above) for 28 days in combination with other antiretroviral agents. Initiate therapy within 72 hours of exposure. • **Adolescents**: The combination product is recommended.
Dosage Adjustment	**Dosing: Renal Impairment: Adult** • **CrCl ≥50 mL/minute**: No dosage adjustment necessary. • **CrCl 30 to 49 mL/minute**: 300 mg every 48 hours • **CrCl 10 to 29 mL/minute**: 300 mg every 72 to 96 hours (twice weekly) • **CrCl <10 mL/minute**: has not been studied, avoid use.

	• If no alternative therapy is available, then one may consider 300 mg every 7 days; use with caution and close monitoring. • **Hemodialysis**: 300 mg following dialysis every 7 days or after a total of ~12 hours of dialysis. **Dosing: Hepatic Impairment: Adult** • No dosage adjustment necessary. **Dosing: Renal Impairment: Pediatric** • Not recommended for use in pediatrics with renal impairment. **Dosing: Hepatic Impairment: Pediatric** • Children ≥2 years and Adolescents: No dosage adjustment required.
Contra-indications	• Hypersensitivity to tenofovir or any component of the formulation
Adverse Drug Reactions	**>10%** • **Endocrine and metabolic**: Increased serum triglycerides (11%) • **Gastrointestinal:** Diarrhea (11% to 16%), nausea (8% to 11%) • **Nervous system**: Asthenia (7% to 11%), pain (12%) • **Neuromuscular and skeletal**: Increased creatine phosphokinase in blood specimen (grades 3/4: 2% to 12%) **1% to 10%** • **Cardiovascular**: Chest pain (3%) • **Dermatologic**: Diaphoresis (3%), skin rash (5% to 7%, including maculopapular rash, pruritus, pustular rash, urticaria, vesiculobullous dermatitis) • **Endocrine and metabolic**: Increased serum glucose (grades 3/4: 3%), weight loss (2% to 4%) • **Gastrointestinal**: Abdominal pain (4% to 7%), anorexia (3% to 4%), dyspepsia (3% to 4%), flatulence (3% to 4%), increased serum amylase (grades 3/4: 4% to 7%), vomiting (4% to 7%) • **Genitourinary**: Glycosuria (grades 3/4: 3%) • **Hematologic and oncologic**: Increased serum neutrophils (grades 3/4: 2%) • **Hepatic**: Increased serum alanine aminotransferase (grades 3/4: 10%), increased serum aspartate aminotransferase (grades 3/4: 4%) • **Nervous system**: Depression (4% to 8%), dizziness (3%), fatigue (≥5%), headache (8%), insomnia (3% to 4%), peripheral neuropathy (5%) • **Neuromuscular and skeletal**: Back pain (4%), myalgia (4%) • **Respiratory**: Nasopharyngitis (≥5%), pneumonia (2% to 3%) • **Miscellaneous**: Fever (4%)
Monitoring Parameters	• Serum phosphorus (baseline and as clinically indicated in patients with chronic kidney disease); serum creatinine, urine glucose, urine protein (baseline and as clinically indicated during therapy); hepatic

	function tests; bone density (patients with a history of bone fracture or who have risk factors for bone loss); weight (children). • CBC with differential, reticulocyte count, creatine kinase, CD4 count, HIV RNA plasma levels, and testing for HBV before the initiation of antiretroviral therapy.
Drug Interactions	• **Risk X: Avoid combination** Adefovir, Atidarsagene Autotemcel, Betibeglogene Autotemcel, Cladribine, Elivaldogene Autotemcel, Leniolisib, Lovotibeglogene Autotemcel, Sparsentan, Taurursodiol • **Risk D: Consider therapy modification** Atazanavir, Belumosudil, Ledipasvir, Nonsteroidal Anti-Inflammatory Agents, Vimseltinib.
Pregnancy and Lactation	**Pregnancy Category** • Tenofovir has a high level of transfer across the human placenta following maternal use of tenofovir disoproxil fumarate. • No increased risk of overall teratogenic effects has been observed following first-trimester exposure according to data collected by the antiretroviral pregnancy registry. Maternal antiretroviral therapy (ART) may be associated with adverse pregnancy outcomes, including preterm birth, low birth weight, and small for gestational age infants. High viral loads are also associated with adverse outcomes, including preterm birth and pregnancy loss. **Lactation**: • Tenofovir disoproxil fumarate is a recommended component of a regimen when acute HIV infection is detected in patients who are breastfeeding. **Because of the potential for:** (1) HIV transmission (in HIV-negative infants) (2) developing viral resistance (in HIV-positive infants) (3) adverse reactions in a breastfed infant similar to those seen in adults, instruct mothers not to breastfeed if they are taking tenofovir disoproxil fumarate for the treatment of HIV
Administration	**Administration: Oral** • Tablets may be administered without regard to meals. • Do not crush oral tablets • Consider calcium and vitamin D supplementation. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**
Warnings/ Precautions	***Concerns related to adverse effects*** • Decreased bone mineral density • **Immune reconstitution syndrome**: Patients may develop immune reconstitution syndrome, resulting in the occurrence of an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves' disease, polymyositis, Guillain-Barré

	syndrome) later in therapy; further evaluation and treatment may be required. • Lactic acidosis/hepatomegaly • **Osteomalacia and renal dysfunction**: May cause osteomalacia with proximal renal tubulopathy. Bone pain, extremity pain, fractures, arthralgias, weakness, and muscle pain have been reported. In patients at risk for renal dysfunction, persistent or worsening bone or muscle symptoms should be evaluated for hypophosphatemia and osteomalacia. • Renal toxicity ***Disease-related concerns*** • **Hepatic impairment**: Use with caution in patients with hepatic impairment. • Limited data supporting treatment of chronic hepatitis B in patients with decompensated liver disease; observe for increased adverse reactions, including kidney dysfunction. ***Concurrent drug therapy issues*** • Concomitant therapy: Do not use in combination with other tenofovir disoproxil fumarate or tenofovir alafenamide products, or with adefovir. ***Other warnings/precautions*** • Appropriate use: Hepatitis B coinfection: In patients coinfected with HIV and HBV, an appropriate antiretroviral combination should be selected due to HIV resistance potential; these patients should receive tenofovir dosed for HIV therapy.
Storage	• Store at 25°C, dispense only in the original container to protect from light and moisture. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

4. Zidovudine (ZDV)

<table>
<tr><th>Generic Name</th><th>Zidovudine</th></tr>
<tr><td>Dosage Form/Strengths</td><td>Tablets: Lamivudine/zidovudine 150/300 mg
Syrup: 10 mg/ml</td></tr>
<tr><td>Route of Administration</td><td>Oral</td></tr>
<tr><td>Pharmacologic Category</td><td>Antiretroviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HIV)
ATC: J05AF01</td></tr>
<tr><td>Indications</td><td>• Treatment of Human Immunodeficiency Virus (HIV-1) infection in combination with other antiretroviral agents (second-line regimen if failed TDF regimen in combination with 3TC + DTG or LPV/r)
• Prevention of maternal-fetal HIV-1 transmission.</td></tr>
<tr><td>Dosage Regimen</td><td>Adults
<u>HIV-1 infection, treatment</u>
• 300 mg twice daily in combination with other antiretroviral agents
<u>Prevention of maternal-fetal HIV-1 transmission.</u>
• Maternal dosing pregnant women (greater than 14 weeks of pregnancy): 100 mg orally 5 times per day until the start of labor. During labor and delivery, intravenous zidovudine should be administered at 2 mg per kg (total body weight) over 1 hour, followed by a continuous intravenous infusion of 1 mg per kg per hour (total body weight) until clamping of the umbilical cord.

Pediatrics: (syrup 10 mg/ml)
<u>Prevention of maternal-fetal HIV-1 transmission.</u>
Neonatal Dosing: Start neonatal dosing within 12 hours after birth and continue through 6 weeks of age.
a) Dosage according to the gestational age and body weight
≥ 35 Weeks Gestation at Birth
Birth to Age ≤6 Weeks
• ZDV 4 mg/kg per dose orally twice daily
≥30 Weeks to <35 Weeks of Gestation at Birth
Birth to Age 2 Weeks
• ZDV 2 mg/kg per dose orally twice daily
Age 2 Weeks to ≤6 Weeks
• ZDV 3 mg/kg per dose orally twice daily
<30 Weeks of Gestation at Birth
Birth to Age 4 Weeks
• ZDV 2 mg/kg per dose orally twice daily
Age 4 Weeks to ≤6 Weeks
• ZDV 3 mg/kg per dose orally twice daily
b) Dosage according to body weight

<table><tr><th>Body Weight (kg)</th><th>Dosage Regimen</th></tr><tr><td>4 to < 9</td><td>12 mg/kg/12 hr</td></tr><tr><td>>- 9 to < 30</td><td>9 mg /kg/12 hr</td></tr><tr><td>>- 30</td><td>300 mg/12 hr</td></tr></table></td></tr>
<tr><td>Dosage Adjustment</td><td>Renal impairment</td></tr>
</table>

	• In patients maintained on hemodialysis or peritoneal dialysis or with creatinine clearance (CrCl) by Cockcroft-Gault less than 15 mL per min, the recommended oral dosage is 100 mg every 6 to 8 hours. **Hepatic impairment** • There are insufficient data to recommend dose adjustment of zidovudine in patients with impaired hepatic function or liver cirrhosis. Frequent monitoring of hematologic toxicities is advised.
Contra-indications	• Potentially life-threatening hypersensitivity to zidovudine or any component of the formulation. • Neutrophil count < 750/mm^3 or hemoglobin <7.5 g/dL.
Adverse Drug Reactions	**>10%** • Gastrointestinal: Anorexia (20%), nausea (51%), vomiting (17%) • Hematologic and oncologic: Anemia (neonates: 22%; adults: grades 3/4: 1%) • Nervous system: Headache (63%), malaise (53%)
Monitoring Parameters	• CBC with differential (more frequent monitoring required in patients with poor bone marrow reserve); LFTs; serum creatinine; HIV viral load and CD4 count.
Drug Interactions	• ***Risk X: Avoid combination*** Atidarsagene Autotemcel, BCG (Intravesical), Betibeglogene Autotemcel, Chloramphenicol (Systemic), Cladribine, Elivaldogene Autotemcel, Fexinidazole, Lovotibeglogene Autotemcel, Stavudine. • ***Risk D: Consider therapy modification*** Amodiaquine, Clarithromycin, Deferiprone, Doxorubicin (Conventional), Doxorubicin (Liposomal), Ribavirin (Oral Inhalation), Ribavirin (Systemic), Ropeginterferon Alfa-2b.
Pregnancy and Lactation	***Pregnancy*** • No increased risk of overall teratogenic effects has been observed following first-trimester exposure. ***Lactation*** • Zidovudine is present in breast milk. • Concentrations of zidovudine in breast milk may be similar to those in the maternal serum. Zidovudine has not been detected in the serum of breastfeeding infants exposed only via breast milk.
Administration	May be administered without regard to meals. **Refer to the manufacturer's PIL if there are specific considerations**
Warnings/ Precautions	• **Hematologic toxicity (neutropenia and severe anemia):** Hematologic toxicity, including neutropenia and severe anemia, has been reported with use, especially with advanced HIV-1 disease.

	Toxicity may be related to duration of use and prior bone marrow reserve. Hemoglobin reduction may occur as early as 2 to 4 weeks; neutropenia usually occurs after 6 to 8 weeks. Pancytopenia has been reported (usually reversible). Use with caution in patients with bone marrow compromise (granulocytes <1,000 cells/mm^3 or hemoglobin <9.5 g/dL). Dose interruption may be required in patients who develop anemia or neutropenia. • Immune reconstitution syndrome, Lactic acidosis/hepatomegaly, lipoatrophy, myopathy.
Storage	Store at 15°C to 25 °C. Protect capsules from moisture. **N.B. Refer to the manufacturer's PIL if there are specific considerations**

b) Non-nucleoside Reverse Transcriptase Inhibitors

5. Efavirenz

<table>
<tr><th>Generic Name</th><th>Efavirenz</th></tr>
<tr><td>Dosage Form/Strengths</td><td>* Efavirenz (EFV) 200, 600 mg as a film-coated tablet</td></tr>
<tr><td>Route of Administration</td><td>Oral</td></tr>
<tr><td>Pharmacologic Category</td><td>• Pharmacologic category: Antiretroviral, Reverse Transcriptase Inhibitor, Non-nucleoside (Anti-HIV) (NNRTIs)
• ATC Classification: J05AG03</td></tr>
<tr><td>Indications</td><td>• Efavirenz is indicated in antiviral combination treatment of human immunodeficiency virus-1 (HIV-1) infected adults, adolescents, and children 3 months of age and older who weigh at least 3.5 kg.</td></tr>
<tr><td>Dosage Regimen</td><td><u>Adults and adolescents (weighing at least 40kg) Dosing</u>:
• The recommended dose of efavirenz in combination with nucleoside analogue reverse transcriptase inhibitors (NRTIs) with or without a PI (protease inhibitor) is 600 mg orally, once daily.
<u>Pediatric dose over 3 years, weighing at least 13 kg, who can reliably swallow tablets.</u>
<table>
<tr><th>Kg</th><th>Dose (mg) (once daily)</th></tr>
<tr><td>13 to 15</td><td>200</td></tr>
<tr><td>15 to 20</td><td>250</td></tr>
<tr><td>20 to 25</td><td>300</td></tr>
<tr><td>25 to 32.5</td><td>350</td></tr>
<tr><td>32.5 to <40</td><td>400</td></tr>
<tr><td>≥ 40</td><td>600</td></tr>
</table></td></tr>
<tr><td>Dosage Adjustment</td><td>Dosing Renal Impairment
• No dose adjustment required with close safety monitoring for severe renal failure.
Dosing Hepatic Impairment
• Mild impairment (Child-Pugh class A): No dosage adjustment necessary; use with caution.
• Moderate-to-severe impairment (Child-Pugh class B or C): Use is not recommended</td></tr>
<tr><td>Contra-indications</td><td>• Hypersensitivity to the active substance or to any of the excipients.
• Patients with severe hepatic impairment (Child Pugh Grade C).
• Co-administration with terfenadine, astemizole, cisapride, midazolam, triazolam, pimozide, bepridil, or ergot alkaloids (for example, ergotamine, dihydroergotamine, ergonovine, and methylergonovine) because competition for CYP3A4 by efavirenz could result in inhibition of metabolism and create the potential for serious and/or life-threatening adverse reactions (for example, cardiac arrhythmias, prolonged sedation or respiratory depression).
• Co-administration with elbasvir (EBR) and grazoprevir (GZR) due to the potential for significant decreases in plasma concentrations of EBR and GZR.
• Herbal preparations containing St. John’s wort (Hypericum</td></tr>
</table>

	perforatum) due to the risk of decreased plasma concentrations and reduced clinical effects of efavirenz. • Patients with: - a family history of sudden death or of congenital prolongation of the QTc interval on electrocardiograms, or with any other clinical condition known to prolong the QTc interval. - a history of symptomatic cardiac arrhythmias or with clinically relevant bradycardia or with congestive cardiac failure accompanied by reduced left ventricular ejection fraction. - severe disturbances of electrolyte balance, e.g., hypokalemia or hypomagnesemia. - Patients taking drugs that are known to prolong the QTc interval (proarrhythmic), e.g., antiarrhythmics of classes IA and III. neuroleptics, antidepressant agents. certain antibiotics, including some agents of the following classes: macrolides, fluoroquinolones, imidazole and triazole antifungal agents, certain non-sedating antihistamines (terfenadine, astemizole), cisapride, flecainide, certain antimalarials, and methadone. **N.B Refer to the manufacturer's PIL if there are specific considerations**
Adverse Drug Reactions	>10% • **Dermatologic**: Skin rash (5% to 32%) • **Endocrine and metabolic**: Hypercholesterolemia (20% to 40%), increased HDL cholesterol (25% to 35%), increased serum triglycerides (≥751 mg/dL: 6% to 11%) • **Gastrointestinal**: Diarrhea (3% to 14%) • **Nervous system**: Central nervous system toxicity (53%), dizziness (2% to 28%), depression (3% to 19%), insomnia (7% to 16%), anxiety (2% to 13%), pain (1% to 13%) 1% to 10% • **Dermatologic**: Pruritus (≤9%), erythema multiforme (≤2%) • **Endocrine and metabolic**: Increased gamma-glutamyl transferase (grades 3/4: 5% to 8%), increased amylase (grades 3/4: grades 3/4: 4% to 6%), hyperglycemia (>250 mg/dL: 2% to 5%) • **Gastrointestinal**: Nausea (2% to 10%), vomiting (3% to 6%), dyspepsia (4%), abdominal pain (2% to 3%), anorexia (≤2%) • **Hematologic and oncologic**: Neutropenia (grades 3/4: 2% to 10%) • **Hepatic**: Increased serum aspartate aminotransferase (grades 3/4: 5% to 8%; incidence higher with hepatitis B and/or C coinfection), increased serum alanine aminotransferase (grades 3/4: 2% to 8%; incidence higher with hepatitis B and/or C coinfection). • **Nervous system**: Lack of concentration (3% to 8%), fatigue (2% to 8%), headache (2% to 8%), drowsiness (2% to 7%), nervousness (2% to 7%), abnormal dreams (1% to 6%), severe depression (2%), hallucination (1%).
Monitoring Parameters	• Cholesterol and triglycerides • Monitor liver function • Glucose level • Signs and symptoms of infection; psychiatric effects
Drug Interactions	**Category X: Avoid combination** • Abemaciclib, Acoramidis, Amodiaquine, Antihepaciviral Combination Products, Atidarsagene Autotemcel, Atrasentan, Avacopan,

	Avapritinib, Bedaquiline, Betibeglogene Autotemcel, Cabotegravir, Capivasertib, Capmatinib, CarBAMazepine, Cobimetinib, Daridorexant, Dasabuvir, Defactinib, Deflazacort, Dordaviprone, DOXOrubicin (Conventional), Elacestrant Elbasvir and Grazoprevir, Elinzanetant, Elivaldogene Autotemcel, Ensartinib, Entrectinib, Ergonovine, Etuvetidigene Autotemcel, Fedratinib, Fexinidazole, Finerenone, Ibrexafungerp, Ivabradine, Lazertinib, Lemborexant, Leniolisib, Letermovir, Levoketoconazole, Lonafarnib, Lovotibeglogene Autotemcel, Lumateperone, Mavacamten, Methoxyflurane, Mobocertinib, Nerandomilast, Neratinib, Nirogacestat, Nisoldipine, Olaparib, Olutasidenib, Omaveloxolone, Palovarotene, Pemigatinib, Pimavanserin, Posaconazole, Pretomanid, Quizartinib, Ranolazine, Remibrutinib, Repotrectinib, Reverse Transcriptase Inhibitors (Non-Nucleoside), Revumenib, Rilzabrutinib, Rimegepant, Sacituzumab Govitecan, Sebetralstat, Selpercatinib, Selumetinib, Sevabertinib, Simeprevir, Sonidegib, Suzetrigine, Taletrectinib, Tazemetostat, Ulipristal, Vanzacaftor, Tezacaftor, and Deutivacaftor, Velpatasvir, Venetoclax, Voclosporin, Vonoprazan, Vorapaxar, Voxilaprevir, Ziftomenib, Zoliflodacin, Zuranolone. **Category D: Consider therapy modification** • Aficamten, Alfentanil, Atazanavir, Atogepant, Atovaquone, Avanafil, Axitinib, Brigatinib, Cabozantinib, Cariprazine, Caspofungin, Clarithromycin, Crinecerfont, Daclatasvir, Deferasirox, Darunavir, Dolutegravir, Duvelisib, Erdafitinib, Erlotinib, Flibanserin, Fosamprenavir, Fruquintinib, Ganaxolone, Gepotidacin, Glasdegib, Glecaprevir and Pibrentasvir, GuanFACINE, Hormonal Contraceptives, Itraconazole, Ketoconazole (Systemic), Larotrectinib, Lefamulin (Intravenous), Lefamulin, Lenacapavir, Lopinavir, Lorlatinib, Lurasidone, Maraviroc, Maribavir, MiFEPRIStone, Mitapivat, Mitapivat, Paltusotine, Perampanel, Pirtobrutinib, Pralsetinib, Praziquantel, Rifabutin, Ripretinib, Sunvozertinib, Ubrogepant, Valoctocogene Roxaparvovec, Voriconazole, Zanubrutinib.
Pregnancy and Lactation	**Pregnancy:** • Because of the potential risk of neural tube defects, EFV should not be used in the first trimester of pregnancy. Efavirenz should not be used during pregnancy, unless the patient's clinical condition requires such treatment. • Females of reproductive potential should undergo pregnancy testing before initiation, use of adequate contraceptive measures and continue for 12 weeks after discontinuation of efavirenz is recommended. **Lactation:** • Efavirenz is present in breast milk. • Breastfeeding should be discontinued during treatment with efavirenz. • It is recommended that women living with HIV not breastfeed their infants to avoid transmission of HIV.
Administration	**Administration** • Should be taken on an empty stomach, preferably at bedtime (may improve tolerability of CNS symptoms). **N.B. Refer to the manufacturer's PIL if there are specific considerations**.

Warnings/ Precautions	• Efavirenz must not be used as a single agent to treat HIV or added on as a monotherapy agent to a failing regimen. • The administration of Efavirenz with food may increase Efavirenz exposure and may lead to an increase in the frequency of adverse reactions • Co-administration with the fixed combination tablet containing efavirenz, emtricitabine, and tenofovir disoproxil is not recommended unless needed for dose adjustment • **Rash:** mild to moderate rash has been reported in clinical studies, and usually resolves. • With continued therapy, efavirenz must be discontinued in patients developing severe rash associated with blistering, desquamation, mucosal involvement, or fever. • **CNS effects:** There are reported cases where efavirenz has caused insomnia, abnormal dreams, and hallucinations; symptoms usually start during the first 1 to 2 days of treatment and generally resolve after 2 to 4 weeks; administration at bedtime may improve the tolerability of CNS symptoms. - CNS depression also may happen (e.g., impaired concentration, dizziness, or drowsiness); avoid driving or operating machinery. - Treatment with EFV was associated with an increase in the occurrence of these selected psychiatric symptoms (Severe depression (2.4%, 0.9%), suicidal ideation (0.7%, 0.3%), nonfatal suicide attempts (0.5%, 0), aggressive behavior (0.4%, 0.5%), paranoid reactions (0.4%, 0.3%), and manic reactions (0.2%, 0.3%) - Patients with serious psychiatric adverse experiences should seek immediate medical evaluation to assess the possibility that the symptoms may be related to the use of EFV, and if so, to determine whether the risks of continued therapy outweigh the benefits. • **Embryo-Fetal Toxicity:** - Encourage reproductive-age women receiving EFV to avoid getting pregnant, as it may cause fetal harm when administered during the first trimester. • **Fat redistribution** - Combination of antiretrovirals may cause redistribution/accumulation of body fat (eg, central obesity, dorsocervical fat enlargement [buffalo hump], peripheral wasting, facial wasting, breast enlargement, cushingoid appearance). • **Hepatotoxicity** - Reported cases in patients treated with efavirenz acquire hepatitis, including fulminant hepatitis, sometimes fatal or progressing to liver failure requiring transplantation. Consider discontinuing treatment in patients with persistent serum transaminase elevations >5 times or if serum transaminase elevations are accompanied by signs/symptoms of hepatitis or hepatic decompensation. • **Hypercholesterolemia:** Increases in total cholesterol and triglycerides have been reported with efavirenz. • **Immune reconstitution syndrome** - Occurrence with combination antiretroviral therapy as an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves' disease, polymyositis, Guillain-Barré

	syndrome, autoimmune hepatitis) later in therapy. • **QT prolongation** - Consider alternative therapy in patients at risk of torsade de pointes or when administered with medications with known risk of torsade de pointes. • **Convulsions** - Caution should be taken in any patient with a history of seizures. - Patients who are receiving concomitant anticonvulsant medications primarily metabolized by the liver, such as phenytoin and phenobarbital, may require periodic monitoring of plasma levels. • Efavirenz has not been evaluated in children below 3 months of age or who weigh less than 3.5 kg. **N.B. Refer to the manufacturer's PIL if there are specific considerations**.
Storage	Store in a dry place, at a temperature no exceeding 30 °C. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

6. Etravirine (ETR)

Generic Name	Etravirine
Dosage Form/Strengths	Tablets 100 mg or 200 mg
Route of Administration	Oral
Pharmacologic Category	• Antiretroviral, Reverse Transcriptase Inhibitor, Non-nucleoside (Anti-HIV) (NNRTI) • **ATC**: J05AG04
Indications	• Treatment of Human Immunodeficiency Virus (HIV-1) infection in combination with other antiretroviral medicinal products, in treatment-experienced adult patients and paediatric patients from 2 years of age with viral strains resistant to an NNRTI and other antiretroviral agents (third-line regimen).
Dosage Regimen	**Adult** Two tablets 100 mg (or one tablet 200 mg) taken orally twice daily following a meal. **Paediatrics** (for paediatric patients 2 years to less than 18 years of age) • Body weight ≥ 10 to < 20 kg---------- 100 mg twice daily. • Body weight ≥ 20 to < 25 kg---------- 125 mg twice daily. • Body weight ≥ 25 to < 30 kg ---------- 150 mg twice daily. • Body weight ≥ 30 kg---------- 200 mg twice daily **Missed dose** • If the patient misses a dose of etravirine within 6 hours of the time it is usually taken, the patient should take it following a meal as soon as possible and then take the next dose at the regularly scheduled time. • If a patient misses a dose by more than 6 hours from the time it is usually taken, the patient should not take the missed dose and simply resume the usual dosing schedule. • If a patient vomits within 4 hours of taking the medicine, another dose of etravirine should be taken following a meal as soon as possible. • If a patient vomits more than 4 hours after taking the medicine, the patient does not need to take another dose until the next regularly scheduled time.
Dosage adjustment	**Dosing: Renal Impairment in Adults** • No dose adjustment is required in patients with renal impairment • As etravirine is highly bound to plasma proteins, it is unlikely that it will be significantly removed by haemodialysis or peritoneal dialysis. **Dosing: Hepatic Impairment Adults** • No dose adjustment is suggested in patients with mild or moderate hepatic impairment (Child-Pugh Class A or B) • Etravirine should be used with caution in patients with moderate hepatic impairment. • It is not recommended in patients with severe hepatic impairment. **Dosing: Renal Impairment: Pediatric**

	• Children ≥2 years and Adolescents: No dosage adjustments required. Due to extensive protein binding, significant removal by hemodialysis or peritoneal dialysis is unlikely. **Dosing: Altered Liver Function: Pediatric** Children ≥2 years weighing at least 10 kg and Adolescents: • Mild to moderate impairment: No dosage adjustments required. • Severe impairment: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).
Contra-indications	• Hypersensitivity to etravirine or any component of the formulation • Concomitant use with the hepatitis C combination regimen of ombitasvir, paritaprevir, ritonavir, and with drugs containing dasabuvir or elbasvir/grazoprevir.
Adverse Drug Reactions	>10%: • Dermatologic: Skin rash (adults 10 %; children 15%). • Endocrine & metabolic: Hypercholesterolemia (grades 2 to 3: 8% to 20%), increased LDL cholesterol (grade 2: 13%), increased serum glucose (grades 2 to 3: 4% to 15%). • Gastrointestinal: Diarrhea (children and adolescents: all grades: ≥2%).
Monitoring Parameters	• Viral load, CD4 count, cholesterol, triglycerides, hepatic transaminases (if signs or symptoms of hypersensitivity develop); signs of skin rash, signs and symptoms of infection.
Drug Interactions	• **Risk X: Avoid combination** Abemaciclib, Antihepaciviral Combination Products, Atidarsagene Autotemcel, Atrasentan, Avacopan, Avanafil, Avapritinib, Bedaquiline, Betibeglogene Autotemcel, Capivasertib, Capmatinib, Cariprazine, Cobimetinib, CYP3A4 Inducers (Strong), Daclatasvir, Daridorexant, Dasabuvir, Defactinib, Deflazacort, DOXOrubicin (Conventional), Elacestrant, Elbasvir and Grazoprevir, Elivaldogene Autotemcel, Ensartinib, Entrectinib, Ergonovine, Fedratinib, Fexinidazole, Finerenone, Flibanserin, Fosamprenavir, Ibrexafungerp, Ivabradine, Lazertinib, Lemborexant, Leniolisib, Letermovir, Lonafarnib, Lovotibeglogene Autotemcel, Lumateperone, Mavacamten , Mobocertinib, Neratinib , Nirogacestat, Nisoldipine, Olaparib, Olutasidenib, Omaveloxolone, Palovarotene, Pemigatinib, Phenobarbital-Primidone, Pimavanserin, Pretomanid, Quizartinib, Ranolazine, Repotrectinib, Reverse Transcriptase Inhibitors (Non-Nucleoside), Revumenib, Rifabutin, Rifapentine, Rimegepant, Selpercatinib, Selumetinib, Simeprevir, St John's Wort, Suzetrigine, Sonidegib, Taletrectinib, Tazemetostat, Tipranavir, Ulipristal, Vanzacaftor, Velpatasvir, Venetoclax, Voclosporin, Vonoprazan, Vorapaxar, Voxilaprevir, Zuranolone • **Risk D: Consider therapy modification** Alfentanil, Atazanavir, Atogepant, Axitinib, Brigatinib, Cabozantinib, Clarithromycin, Clopidogrel, Crinecerfont, Darunavir, Dolutegravir, Duvelisib, Erdafitinib, Erlotinib, Fruquintinib, Ganaxolone, Glasdegib,

	Guanfacine, Indinavir, Larotrectinib, Lefamulin, Lenacapavir, Lorlatinib, Lurasidone, Maraviroc, MiFEPRIStone, Mitapivat, Perampanel, Pirtobrutinib, Pralsetinib, Praziquantel, Ripretinib, Ritonavir, Ubrogepant, Voxelotor, Zanubrutinib
Pregnancy	**Pregnancy** Given the increased etravirine exposure during pregnancy, caution should be applied for pregnant patients who require concomitant medicinal products or have comorbidities that may further increase etravirine exposure.
Administration	• Administer after meals. • Tablets should be swallowed whole. • If unable to swallow whole tablets, may disperse tablets in water (5 mL [at least enough to cover tablets]); stir well (until water looks milky), then add ~15 mL of water, milk, or orange juice, and drink immediately. Tablets should not be placed in orange juice or milk without first adding water. Rinse glass several times (with water, milk, or orange juice) and swallow the entire contents with each rinse to ensure administration of the dose. Do not use carbonated beverages or warm (>40°C) water. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**
Warnings/ Precautions	**Concerns related to adverse effects** • Fat redistribution: May cause redistribution of fat (eg, buffalo hump, peripheral wasting with increased abdominal girth, cushingoid appearance). • Immune reconstitution syndrome: Patients may develop immune reconstitution syndrome, resulting in the occurrence of an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (eg, Graves disease, polymyositis, Guillain-Barré syndrome, autoimmune hepatitis) later in therapy; further evaluation and treatment may be required. • Skin reactions/hypersensitivity: Severe and possibly life-threatening skin reactions (including Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme) and hypersensitivity reactions ranging from rash (including grades 3/4 rash and drug rash with eosinophilia and systemic symptoms) and/or constitutional symptoms to occasional organ dysfunction (including hepatic failure) have been reported. Rash occurs most commonly in the first 6 weeks of therapy and is more frequent in females. Discontinue immediately with signs or symptoms of severe skin reaction or hypersensitivity. **Special populations** • Appropriate use: Not for use in treatment-naive patients, or experienced patients without evidence of viral mutations conferring resistance to nonnucleoside reverse transcriptase inhibitors and protease inhibitors. **Warnings: Additional pediatric considerations** • Rash is more common and severe in pediatric patients (2 years to <18 years) than in adults, particularly those <6 years of age and females; usually described as mild to moderate, pruritic, maculopapular skin eruptions (incidence: Children 2 to <6 years: 50%; pediatric patients ≥6 years: 15%, adults: 10%). In pediatric patients, rash usually appeared in the second week of therapy and generally resolved within a week. Discontinue etravirine if severe rash (involving blistering, desquamation, mucosal

	involvement, ulceration, or fever) occurs. **Overdosage** • There is no specific antidote for overdose with etravirine. • The highest dose studied in healthy volunteers was 400 mg once daily. • Treatment of overdose with it consists of general supportive measures, including monitoring of vital signs and observation of the clinical status of the patient. • Because etravirine is highly protein-bound, dialysis is unlikely to result in significant removal of the active substance.
Storage	• Store at room temperature of 25°C; excursions permitted to 15°C to 30°C. Protect from moisture. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

7. Nevirapine (NVP)

<table>
<tr><th>Generic Name</th><th>Nevirapine</th></tr>
<tr><td>Dosage Form/Strengths</td><td>Suspension: 50mg/5ml</td></tr>
<tr><td>Route of Administration</td><td>Oral</td></tr>
<tr><td>Pharmacologic Category</td><td>Antiretroviral, Reverse Transcriptase Inhibitor, Non-nucleoside (Anti-HIV)
ATC: J05AG01</td></tr>
<tr><td>Indications</td><td>• Nevirapine (NVP) often is used as part of newborn antiretroviral regimens to prevent perinatal transmission of HIV.</td></tr>
<tr><td>Dosage Regimen</td><td><u>Pediatrics</u>
Nevirapine may be dosed in paediatric patients either by body surface area (BSA) or by body weight as follows:
• By BSA: the recommended oral dose for paediatric patients of all ages is 150 mg/m2 once daily for two weeks, followed by 150 mg/m2 twice daily thereafter.
• By weight: the recommended oral dose for paediatric patients up to 8 years of age is 4 mg/kg once daily for two weeks, followed by 7 mg/kg twice daily thereafter. For patients 8 years and older, the recommended dose is 4 mg/kg once daily for two weeks, followed by 4 mg/kg twice daily thereafter.
<table>
<tr><th rowspan="2"><u>Strength</u></th><th colspan="10"><u>Simplified age-based Nevirapine dosing for administering enhanced and prolonged postnatal prophylaxis</u></th></tr>
<tr><th colspan="2">0-6 weeks</th><th colspan="2">6-12 weeks</th><th colspan="2">12 weeks – 6 months</th><th colspan="2">6-9 months</th><th colspan="2">9- 24 months</th></tr>
<tr><th><u>AM</u></th><th><u>PM</u></th><th><u>AM</u></th><th><u>PM</u></th><th><u>AM</u></th><th><u>PM</u></th><th><u>AM</u></th><th><u>PM</u></th><th><u>AM</u></th><th><u>PM</u></th></tr>
<tr><td><u>Syrup 10 mg/ml</u></td><td>1.5 ml</td><td>-</td><td>2 ml</td><td>-</td><td>2 ml</td><td>-</td><td>3 ml</td><td>-</td><td>4 ml</td><td>-</td></tr>
</table></td></tr>
<tr><td>Dosage Adjustment</td><td>Renal impairment
• CrCl <20 mL/minute: There are no dosage adjustments (has not been studied).
• Hemodialysis: An additional 200 mg dose is recommended following a dialysis session.
Hepatic impairment
• Permanently discontinue if symptomatic hepatic events occur.
• Mild impairment (Child-Pugh class A): There are no dosage adjustments; use with caution.
• Moderate to severe impairment (Child-Pugh class B or C): Use is contraindicated</td></tr>
<tr><td>Contra-indications</td><td>• Moderate to severe hepatic impairment (Child-Pugh class B or C)
• Use in occupational or nonoccupational postexposure prophylaxis (PEP) regimens
• Hypersensitivity to nevirapine or any component of the formulation</td></tr>
<tr><td>Adverse Drug Reactions</td><td><u>>10%</u>
• Endocrine & metabolic: Decreased serum phosphate (≤38%),</td></tr>
</table>

	hypercholesterolemia (3% to 19%), increased LDL cholesterol (5% to 15%). • Hepatic: Hepatic impairment (≤11%, including cholestatic hepatitis, fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis, hepatotoxicity, hyperbilirubinemia, increased gamma-glutamyl transferase, jaundice), increased serum alanine aminotransferase (2% to 14%).
Monitoring Parameters	• Monitor CBC and viral load. • Intensive monitoring is required during the initial 18 weeks of therapy to detect potentially life-threatening hepatic, dermatologic, and hypersensitivity reactions. • Liver function tests, at baseline, before dose escalation, and 2 weeks post-escalation. • Assess/evaluate AST/ALT immediately in any patients with a rash
Drug Interactions	• **Risk X: Avoid combination** Atazanavir, Atidarsagene Autotemcel, Carbamazepine, Daclatasvir, Ergonovine, Itraconazole, Lenacapavir, Letermovir, Levoketoconazole, Methoxyflurane, Nelfinavir, Reverse Transcriptase Inhibitors (Non-Nucleoside), Rifampin, Saquinavir, Simeprevir, St John's Wort, Velpatasvir. • **Risk D: Consider therapy modification** Atogepant, Caspofungin, Clarithromycin, CYP3A4 Inducers (Strong), Darunavir, Dolutegravir, Fosamprenavir, Indinavir, Ketoconazole (Systemic), Lopinavir, Ubrogepant.
Pregnancy and Lactation	***Pregnancy*** • Currently available data on pregnant women indicate no malformative or foeto/ neonatal toxicity. To date, no other relevant epidemiological data are available. No observable teratogenicity was detected in reproductive studies performed in pregnant rats and rabbits. There are no adequate and well-controlled studies in pregnant women. • Caution should be exercised when prescribing nevirapine to pregnant women. ***Lactation*** • It is recommended that women living with HIV not breastfeed their infants to avoid transmission of HIV.
Administration	• May be administered with or without food. • Shake suspension gently before administration; the use of an oral dosing syringe is recommended, especially if the dose is ≤5 mL; if using a dosing cup, after administration, rinse cup with water and also administer rinse **N.B. Refer to the manufacturer's PIL if there are specific considerations.**
Warnings/ Precautions	Fat redistribution, hepatotoxicity, Severe, life-threatening skin reactions, Immune reconstitution syndrome, and rhabdomyolysis.
Storage	Store at 20°C to 25°C; excursion permitted to 15°C to 30°C. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

c) Protease inhibitors

8. Lopinavir and Ritonavir (LPV/r)

Generic Name	Lopinavir/Ritonavir
Dosage Form/Strengths	• Tablets: 200/50 mg, 100/25 mg • Pellets or granules: 40/10 mg
Route of Administration	Oral
Pharmacologic Category	• Antiretroviral, Protease Inhibitor (Anti-HIV) • **ATC**: J05AR10
Indications	• Treatment of HIV-1 infection in adults and pediatric patients 14 days of age and older in combination with other antiretroviral agents (adults: It is used as a component of a second-line regimen if a failed TDF or AZT regimen, pediatrics: it is the preferred regimen).
Dosage Regimen	**Adults** • **Patients receiving concomitant antiretroviral therapy without efavirenz, nelfinavir, or nevirapine:** Twice-daily dosing: Lopinavir 400 mg/ritonavir 100 mg twice daily. Once-daily dosing: Therapy-naive or experienced patients with <3 Lopinavir resistance-associated substitutions: Lopinavir 800 mg/ritonavir 200 mg once daily. • **Dosage adjustment for combination therapy with efavirenz, nelfinavir, or nevirapine:** Tablet: Lopinavir 500 mg/ritonavir 125 mg twice daily. (Once daily dosing is not recommended). • In the presence of rifampicin, adjusted dose of LPV/r (double-dose LPV 800 mg + ritonavir 200 mg twice daily or super boosted with LPV 400 mg/ + ritonavir 100 mg twice daily plus additional doses of ritonavir 300 mg twice daily), with close monitoring. In the presence of rifabutin, no dose adjustment is required. Rifapentine should not be used. • **Pregnant women**: tablet, oral: Lopinavir 400 mg/ritonavir 100 mg twice, may increase dose of lopinavir 600 mg/ritonavir 150 mg twice daily, or lopinavir 500 mg/ritonavir 125 mg twice daily, during the second and third trimesters of pregnancy, avoid use once daily or solution form. **Pediatrics** • Use of tablets in patients <15 kg or <0.6 m2 is not recommended, oral solution preferable. Once-daily dosing is not recommended in children <18 years of age. **(Infants (≥42 weeks PMA)** • Patients not receiving concomitant efavirenz, nelfinavir, or nevirapine: Lopinavir 16 mg/kg/dose or 300 mg/ m2/dose, twice daily.

Simplified dosing of lopinavir/ritonavir for twice daily dosing for infants and children 4 weeks of age and older.

Strength	Number of tablets by weight band, morning and evening									
	3 - < 6 kg		6 - < 10 kg		10 - < 14 kg		14 - < 20 kg		20 - < 25 kg	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
Tablet 100/25 mg	-	-	-	-	2	1	2	2	2	2
Pellets 40/10 mg	2	2	3	3	4	4	5	5	6	6

Simplified dosing of lopinavir/ritonavir for twice daily dosing for infants younger than 4 weeks of age.

	3 - < 5 kg	
Granules (sachets) 40/10 mg	2	2

- Patients with concomitant efavirenz, nelfinavir, or nevirapine: lopinavir/ritonavir is not recommended in infants who are receiving these agents.

Children and adolescents

- **Patients not receiving concomitant efavirenz, nelfinavir, or nevirapine:**
  <15 kg: Lopinavir 12 mg/kg/dose twice daily.
  15 to 40 kg: Lopinavir 10 mg/kg/dose twice daily.
  >40 kg: Lopinavir 400 mg twice daily.
- **Antiretroviral-experienced or suspected decreased sensitivity to lopinavir**: **Note**: This dose is also used by some clinicians for initial therapy in all patients:
  Weight-directed dosing:
  <15 kg: Lopinavir 13 mg/kg/dose twice daily.
  15 to 45 kg: Lopinavir 11 mg/kg/dose twice daily.
  >45 kg: Lopinavir 400 mg twice daily.
  Weight-band dosing for children and adolescents weighing ≥15 kg and able to swallow tablets:
  15 to 20 kg: 200 mg twice daily.
  >20 to 30 kg: 300 mg twice daily.
  >30 kg: 400 mg twice daily.

Patients with concomitant efavirenz, nelfinavir, or nevirapine *(or treatment-experienced patients not receiving these agents who have suspected decreased susceptibility to lopinavir):*

<15 kg: Lopinavir 13 mg/kg/dose twice daily.
≥15 to 45 kg: Lopinavir 11 mg/kg/dose twice daily.
>45 kg: Oral solution: Lopinavir 520 mg twice daily.
Tablets: Lopinavir 500 mg twice daily.

Dosage Adjustment

Renal impairment

- No dosage adjustments provided
- Hemodialysis: Avoid once-daily dosing

Hepatic impairment

	• Mild to moderate impairment: There are no dosage adjustments; use with caution. • Severe impairment: There are no dosage adjustments (has not been studied); use with caution
Contra-indications	Hypersensitivity (e.g., toxic epidermal necrolysis, Stevens-Johnson syndrome) to lopinavir, ritonavir, or any component of the formulation.
Adverse Drug Reactions	**>10%** • **Endocrine and metabolic**: Increased gamma-glutamyl transferase (grade 3/4: 10% to 29%). • **Gastrointestinal:** Diarrhea (children and adults: 12% to 20%; greater with once-daily dosing), dysgeusia (children: 22%), vomiting (children: 21%; adults: 7%). • **Hepatic:** Increased serum alanine aminotransferase (grade 3/4: children and adults: 1% to 11%). • **Respiratory:** Upper respiratory tract infection (14%).
Monitoring Parameters	• Before therapy, consider genotypic or phenotypic testing for lopinavir resistance-associated substitutions. • Triglycerides and cholesterol (before initiation, then periodically thereafter), LFTs, electrolytes, glucose, basic HIV monitoring, viral load, and CD4 count.
Drug Interactions	• **Risk X: Avoid combination** Acalabrutinib, Acoramidis, Alfuzosin, ALPRAZolam, Amiodarone, Antihepaciviral Combination Products, Apalutamide, Aprepitant, Atazanavir, Atidarsagene Autotemcel, Atrasentan, Avanafil, Avapritinib, Barnidipine, Betibeglogene Autotemcel, Bilastine, Blonanserin, Bosutinib, Budesonide (Topical), Bulevirtide, Cabotegravir, Cisapride, Clobetasone, Cobicistat, Cobimetinib, Conivaptan, CYP3A4 Inducers (Strong) Dapoxetine, Daridorexant, Darunavir, Defactinib, Disulfiram, Domperidone, DOXOrubicin (Conventional), Dronedarone, Elacestrant, Elagolix, Estradiol, and Norethindronem Elbasvir and Grazoprevir, Eletriptan, Elivaldogene Autotemcel, Ensartinib, Eplerenone, Ergot Derivatives (Vasoconstrictive CYP3A4 Substrates), Everolimus, Finerenone, Flecainide, Flibanserin, Fluticasone (Nasal), Fosamprenavir, Fosaprepitant, Futibatinibm, Garlic, Gepirone, Glecaprevir and Pibrentasvir, Ibrutinib, Isavuconazonium Sulfate, Ivabradine, Lefamulin, Lemborexant, Leniolisib, Lercanidipine, Letermovir, Levoketoconazole, Lomitapide, Lonafarnib, Lovastatin, Lovotibeglogene Autotemcel, Lurasidone, Macitentan, Meptazinol, Methotrimeprazine, Methoxyflurane, MetroNIDAZOLE (Systemic), Midazolam, Mitapivat, Mobocertinib, Naloxegol, Neratinib, NIFEdipine (Topical), NiMODipine, Nirogacestat, Nisoldipine, Pacritinib, Palovarotene, PAZOPanib, Pimozide, Propafenone, QuiNIDine, QuiNINE, Radotinib, Ranolazine, Red Yeast Rice, Regorafenib, Repotrectinib, Resmetirom, Revefenacin, RifAMPin, Rimegepant, Rivaroxaban, Rupatadine, Ruxolitinib (Topical), Sacituzumab Govitecan, Salmeterol, Sebetralstat , Secnidazole,Sertindole, Silodosin, Simeprevir, Simvastatin, Sirolimus (Protein Bound) Sonidegib, Sparsentan, St John's Wort, Suvorexant: Suzetrigine, Taletrectinib, Tamsulosin, Taurursodiol, Tazemetostat, Ticagrelor, Tipranavir, Tolvaptan, Topotecan, Trabectedin, Triazolam, Ubrogepant, Udenafil, Vincristine, Vinflunine, Voclosporin, Vorapaxar,

	Voxilaprevir, Zavegepant (Nasal) • **Risk D: Consider therapy modification** Abemaciclib, Adagrasib, Ado-Trastuzumab Emtansine, Afatinib, Alfentanil, Alitretinoin (Systemic), Almotriptan, Alpelisib, Apixaban, ARIPiprazole, Atogepant, Atorvastatin, Avacopan, Axitinib, Bedaquiline, Bosentan, Brexpiprazole, Brigatinib, Brincidofovir, Bromocriptine, Budesonide (Oral Inhalation, systemic), BusPIRone, Cabazitaxel, Cabozantinib, Canagliflozin, Capivasertib, CarBAMazepine, Cariprazine, Ceritinib, Cilostazol, Cladribine, Clarithromycin, Clopidogrel, Colchicine, Copanlisib, Crizotinib, CycloSPORINE (Systemic), Dabrafenib, Daclatasvir, Darifenacin, Dasatinib, Deferasirox Deflazacort, Delamanid, DexAMETHasone (Systemic), Digoxin, DOCEtaxel, Duvelisib, Efavirenz, Elexacaftor, Tezacaftor, and Ivacaftor, Eliglustat, Eluxadoline, Entrectinib, Erdafitinib, Erlotinib, Erythromycin (Systemic), Eszopiclone, Etravirine, Fedratinib, Felodipine, FentaNYL, Fesoterodine, Fexinidazole, Fluticasone (Oral Inhalation), Fosphenytoin, Fusidic Acid (Systemic), Gepotidacin, Gilteritinib, Glasdegib, GuanFACINE, Halofantrine, Hormonal Contraceptives, Ibrexafungerp, Idelalisib, Iloperidone, Indinavir, Irinotecan Products, Istradefylline, Itraconazole, Ivacaftor, Ivosidenib, Ixabepilone, Ketoconazole (Systemic), LamoTRIgine, Lapatinib, Larotrectinib, Levomilnacipran, Lorlatinib, Lumateperone, Lurbinectedin, Manidipine, Maraviroc, Mavacamten, Mavorixafor, Midostaurin, MiFEPRIStone, Mirodenafil, Nelfinavir, Nevirapine, NIFEdipine (Systemic), Nilotinib, Olaparib, Omaveloxolone, Osilodrostat, Palbociclib, Panobinostat, Pemigatinib, Pexidartinib, PHENobarbital, Phenytoin, Pimavanserin, Pirtobrutinib, PONATinib, Pralsetinib, Primidone, QUEtiapine, Quizartinib, Relugolix, Estradiol, and Norethindrone, Revumenib, Ribociclib, Rifabutin, Riociguat, Rosuvastatin, Ruxolitinib (Systemic), SAXagliptin, Selpercatinib, Selumetinib, Sildenafil, Sirolimus (Conventional), Solifenacin, SUFentanil, SUNItinib, Sunvozertinib, Tacrolimus (Systemic), Tadalafil, Temsirolimus, Tezacaftor and Ivacaftor, Thioridazine, Thiotepa, Tofacitinib, Tolterodine, Toremifene, TraZODone, Tretinoin (Systemic), Triamcinolone (Systemic), Upadacitinib, Valbenazine, Vamorolone, Vanzacaftor, Tezacaftor, and Deutivacaftor, Vardenafil, Vemurafenib, Venetoclax, Vilazodone, Voriconazole, Zanubrutinib, Zopiclone, Zuranolone.
Pregnancy and Lactation	• No dose adjustment is required for lopinavir/ritonavir during pregnancy and postpartum. • Once daily administration of lopinavir/ritonavir is not recommended for pregnant women due to the lack of pharmacokinetic and clinical data. • Studies in rats revealed that lopinavir is excreted in the milk. It is not known whether this medicinal product is excreted in human milk. As a general rule, it is recommended that women living with HIV not breastfeed their babies to avoid transmission of HIV.
Administration	• **Solution**: Must be administered with food • **Tablet**: May be taken with or without food. Swallow whole, do not break, crush, or chew. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**
Warnings/	• Cardiovascular concerns: Possible higher risk of myocardial infarction

Precautions	associated with the cumulative use of lopinavir/ritonavir; consider avoiding lopinavir/ritonavir-based regimens in patients with high cardiac risk. • May alter cardiac conduction and prolong the QTc and/or PR interval. • Fat redistribution. • Hepatotoxicity, use with caution in patients with Hepatitis B or C and cirrhosis. • Immune reconstitution syndrome. • Increased cholesterol. • Changes in glucose tolerance, hyperglycemia, exacerbation of diabetes, DKA, • Use with caution in patients with hemophilia A or B • Hepatic impairment: Use with caution; lopinavir concentrations may be increased. • Pancreatitis: Use with caution in patients with increased triglycerides
Storage	• Oral solution: Store at 2°C to 8°C. Avoid exposure to excessive heat. If stored at 25°C, use within 2 months. • Tablet: Store at 20 °C to 25 °C; excursions permitted to 15°C to 30°C. Exposure to high humidity outside of the original container or USP equivalent tight container for >2 weeks is not recommended. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

d) Integrase Inhibitors

9. Cabotegravir

Generic Name	Cabotegravir
Dosage Form/Strengths	• **Intramuscular Injection:** Apretude: 600 mg/3 mL (3 mL) • **Tablet, Oral:** Apretude: 30 mg**,** Vocabria: 30 mg
Route of Administration	*Oral/injection*
Pharmacologic Category	• Antiretroviral, Integrase Inhibitor (Anti-HIV). • **ATC classification**: J05AJ04.
Indications	**Cabotegravir** is indicated, in combination with safer sex practices or in combination with rilpivirine tablets as appropriate, for short-term use in adults and adolescents (at least 12 years of age and weighing at least 35 kg) for: • **Pre-exposure prophylaxis (PrEP)** to reduce the risk of sexually acquired HIV-1 infection in individuals at high risk. • **Treatment of HIV-1 infection** in virologically suppressed individuals (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen, with no present or past evidence of viral resistance to integrase strand transfer inhibitors (INSTIs) or non-nucleoside reverse transcriptase inhibitors (NNRTIs), and no prior virological failure with agents of these classes. Cabotegravir tablets may be used as an **oral lead-in** to assess tolerability prior to initiation of long-acting injectable therapy, or as **oral therapy** for individuals who will miss planned dosing with cabotegravir injection.
Dosage Regimen	**HIV infection, preexposure prophylaxis:** **Oral lead-in therapy:** **Oral:** 30 mg once daily for 1 month (at least 28 days). In case of missed doses, the individual should take the missed dose as soon as possible, providing the next dose is not due within 12 hours. If the next dose is due within 12 hours, the individual should **not** take the missed dose and simply resume the usual dosing schedule. **then** Administer IM initiation injection on the last day of oral lead-in, or within 3 days after. **Initiation injections:** **IM:** 600 mg once monthly for **2 doses**; then, **Continuation injections:** **IM:** 600 mg once **every 2 months**, starting 2 months after the last initiation injection **Note:** injection may be administered up to 7 days before or after the date the individual is scheduled to receive the injection. **Missed doses:** **Planned missed injections:** • If an injection is delayed by more than **7 days**, it is considered a missed dose. • **Oral cabotegravir 30 mg once daily** may be used for **up to 2 months** to replace one missed injection. • Oral therapy should start about **2 months (±7 days)** after the last injection.

<table>
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Injections should be resumed on the day oral dosing ends or within 3 days thereafter, as recommended in the following Table.
If oral cabotegravir is continued for >2 months, an alternative oral PrEP regimen is recommended.

Unplanned missed injections:
<table>
<tr><th colspan="2">Missed Doses</th></tr>
<tr><th>Time since last injection</th><th>Recommendation</th></tr>
<tr><td colspan="2">If the second injection is missed and the time since the first injection is:</td></tr>
<tr><td>≤2 months</td><td>Administer one 600 mg injection as soon as possible and continue with every 2-month injection dosing schedule.</td></tr>
<tr><td>> 2 months</td><td>Restart the individual on one 600 mg initiation injection, followed by a second 600 mg initiation injection one month later. Then follow every two-month injection dosing schedule.</td></tr>
<tr><td colspan="2">If the third or subsequent injection is missed and the time since the prior injection is:</td></tr>
<tr><td>≤3 months</td><td>Administer one 600 mg injection as soon as possible and continue with every 2-month injection dosing schedule.</td></tr>
<tr><td>> 3 months</td><td>Restart the individual on one 600 mg initiation injection, followed by a second 600 mg initiation injection one month later. Then follow every two-month injection dosing</td></tr>
</table>
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</tr>
<tr>
<td>Dosage Adjustment</td>
<td>
Hepatic impairment

Mild or moderate (Child-Pugh score A or B): No dose adjustment
Severe (Child-Pugh score C): Use with caution.

Renal impairment

No dose adjustment is required in mild, moderate, and severe renal impairment.
In an individual on renal replacement therapy: Use with caution

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</tr>
<tr>
<td>Contra-indications</td>
<td>

Hypersensitivity to the active substance or to any of the excipients
Individuals with an unknown or positive HIV-1 status (if taken for prophylaxis)
Concomitant use with rifampicin, rifapentine, carbamazepine, oxcarbazepine, phenytoin, or phenobarbital.

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<tr>
<td>Adverse Drug Reactions</td>
<td>
<u>>10%</u>

Local: Induration at injection site, injection-site nodule, injection-site reaction, pain at injection site, swelling at injection site, tenderness at injection site
Nervous system: Headache.
Neuromuscular and skeletal: Increased creatine phosphokinase in the blood specimen.

<u>1% to 10%</u>

Dermatologic: Skin rash

</td>
</tr>
</table>

	• Gastrointestinal: Abdominal distress, abdominal pain, decreased appetite, diarrhea, flatulence, increased serum lipase, nausea, vomiting • Hepatic: Increased serum alanine aminotransferase, increased serum aspartate aminotransferase • Local: Abscess at injection site, bruising at injection site, erythema at injection site, injection-site numbness, injection-site pruritus, skin discoloration at injection site, warm sensation at injection site • Nervous system: Anxiety, asthenia, dizziness, drowsiness, fatigue, sleep disturbance, including abnormal dreams, insomnia. • Neuromuscular and skeletal: Back pain, myalgia. • Renal: Increased serum creatinine • Respiratory: Upper respiratory tract infection • Miscellaneous: Fever
Monitoring Parameters	• Liver chemistries; signs/symptoms of hypersensitivity and/or skin reactions; mood changes. • HIV-1 preexposure prophylaxis (PrEP): Documented negative HIV-1 RNA assay (≤1 week before initiating or reinitiating PrEP, at 1-month post-initiation, then every 2 months while taking PrEP, and following discontinuation of PrEP), assess symptoms of acute HIV infection (before initiation of PrEP at 1-month post-initiation, then every 2 months while taking PrEP).
Drug Interactions	**Risk X: Avoid combination** Atidarsagene Autotemcel, Betibeglogene Autotemcel, Elivaldogene Autotemcel, Etuvetidigene Autotemcel, Lovotibeglogene Autotemcel, Nirmatrelvir and Ritonavir, Oxcarbazepine, Rifapentine, UGT1A1 Inducers. **Risk D: Consider therapy modification** Atazanavir, Belumosudil, Polyvalent Cation Containing Products, Rifabutin
Pregnancy and Lactation	**Pregnancy** • **Not recommended** during pregnancy due to limited human data and unknown effects, and should be used only if the potential benefit outweighs the potential risk to the fetus. • Women of childbearing potential should be counselled that cabotegravir **injection** has prolonged systemic persistence (up to 12 months or longer) after discontinuation, with potential fetal exposure, and the risks and benefits of initiating or continuing cabotegravir PrEP should be carefully discussed when planning pregnancy **Lactation** • Based on animal data, cabotegravir is expected to be excreted in human milk; therefore, breastfeeding is recommended only if the expected benefit outweighs the potential risk to the infant. • Women living **with HIV** are advised **not** to breastfeed their infants to prevent HIV transmission.
Administration	**Tablets** • Cabotegravir tablet may be administered with or without food, • Polyvalent cation-containing antacids are recommended to be taken at least 2 hours before and 4 hours after taking cabotegravir tablets. • When taken at the same time as rilpivirine tablets, cabotegravir should be taken with a meal. **Injection:** • For intramuscular use, administer injections in the ventrogluteal (preferred) or dorsogluteal site with care to avoid intravascular injection, and give the

	dose as soon as possible after preparation (discard if held in the syringe for more than 2 hours).
Warnings/ Precautions	• Individuals should be reconfirmed to be **HIV negative** at each subsequent injection. • To reduce the risk of cabotegravir resistance (**when taken as prophylaxis**), it should be used only in confirmed HIV-negative, anti-retroviral therapy (**ART**) should be started immediately if HIV is diagnosed. Cabotegravir must **not be used alone** to treat HIV-1, and alternative PrEP should be initiated within 2 months after discontinuation in those at ongoing risk. • Hypersensitivity reactions, including rash, systemic symptoms (e.g fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial oedema, hepatitis, eosinophilia or angioedema), or organ dysfunction (e.g., liver injury), may occur with cabotegravir; so cabotegravir and other suspected drugs should be stopped immediately if these occur, with clinical and liver monitoring and appropriate treatment initiated. • Hepatotoxicity has been reported with cabotegravir; clinical and laboratory monitoring is recommended, and it should be discontinued if hepatotoxicity is confirmed, with appropriate clinical management. • Adolescents should be counselled about the potential risk of suicidal ideation or behavior with cabotegravir, especially those with pre-existing psychiatric conditions, and monitored periodically with appropriate clinical management. • Before initiating **treatment therapy**, note that virological failure risk increases in patients with at least two of the following baseline factors—archived rilpivirine resistance, HIV-1 subtype A6/A1, or BMI ≥30 kg/m²—particularly with every-2-month dosing, and caution is advised when treatment history or resistance data are incomplete. • Patients should be informed that (cabotegravir for treatment) does not cure HIV, and they may still develop opportunistic infections or HIV-related complications, requiring ongoing monitoring by experienced healthcare providers. • In **HIV** patients with severe immune deficiency, initiation of combination antiretroviral therapy (**CART**), especially within the first few weeks or months of initiation, may trigger immune reactivation syndrome or autoimmune disorders, requiring evaluation and appropriate management of inflammatory or autoimmune symptoms.
Storage	**Tablet**: Store below 30°C **Injection**: Do not freeze. Do not store above 25°C. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

10. Dolutegravir (DTG)

Generic Name	Dolutegravir
Dosage Form/Strengths	Film Coated Tablets: 50 mg, 10mg.
Route of Administration	Oral
Pharmacologic Category	Antiretroviral, Integrase Inhibitor (Anti-HIV) ATC: J05AJ03
Indications	Treatment of HIV-1 infection in combination with other antiretroviral agents for treatment naïve or experienced adult or pediatric patients
Dosage Regimen	**Adults:** Patients infected with HIV-1 without documented or clinically suspected resistance to the integrase class • The recommended dose of dolutegravir is **50 mg** orally once daily. • Dolutegravir should be administered **twice daily** in this population when co-administered with some medicines (e.g. efavirenz, nevirapine, tipranavir/ritonavir, or rifampicin). Patients infected with HIV-1 with resistance to the integrase class (documented or clinically suspected) • The recommended dose of dolutegravir is **50 mg** twice daily. **Pediatrics:** N.B., it is used for adolescents, children and infants aged 4 weeks and above and weighing at least 3 kg a) Treatment-naive or treatment-experienced and integrase strand transfer inhibitor (INSTI)-naive*:* 1- Soluble tablets for oral suspension (infants and Children weighing 3 to ≥20 kg)

Body weight	Daily dose	Number of 10 mg tablets
3 - < 6 kg	5 mg once daily	1/2
6 - < 10 kg	15 mg once daily	1.5
10 - < 14kg	20 mg once daily	2
14 - < 20 kg	25 mg once daily	2.5
20 kg and greater	30 mg once daily	3

2- Tablets

14 to <20 kg: 40 mg once daily.

≥20 kg: 50 mg once daily.

b) INSTI-experienced with any INSTI-associated resistance mutation or clinically suspected INSTI resistance:
There are insufficient data to recommend a dose for dolutegravir in integrase inhibitor resistant adolescents, children and infants, but some references recommend the dose of 50 mg twice daily in children and Adolescents

	weighing ≥40 kg. Note: Dolutegravir Tablets for Oral Suspension and Dolutegravir Tablets are not interchangeable on a milligram per milligram basis. The relative bioavailability of dispersible tablets is approximately 1.6-fold higher as compared to film-coated tablets. Thus, a 50 mg dolutegravir dose administered as film-coated tablet(s) will have similar exposure to a 30 mg dolutegravir dose administered as six 5 mg dispersible tablets. Similarly, a 40 mg dolutegravir dose administered as four 10 mg film-coated tablets will provide comparable exposure to a 25 mg dolutegravir dose administered as five 5 mg dispersible tablets. **Missed doses:** If the patient misses a dose of DTG, the patient should take it as soon as possible, providing the next dose is not due within 4 hours. If the next dose is due within 4 hours, the patient should not take the missed dose and simply resume the usual dosing schedule.
Dosage Adjustment	**Dosing: Renal Impairment** • *No dosage adjustment is required in patients with mild, moderate or severe (CrCl <30 mL/min, not on dialysis) renal impairment. No data are available in subjects receiving dialysis although differences in pharmacokinetics are not expected in this population* **Dosing: Hepatic Impairment** • No dosage adjustment is necessary for patients with mild to moderate hepatic impairment (Child-Pugh Score A or B). • The effect of severe hepatic impairment (Child-Pugh Score C) on the pharmacokinetics of dolutegravir has not been studied. Therefore, dolutegravir is not recommended for use in patients with severe hepatic impairment
Contra-indications	Hypersensitivity to dolutegravir or any other component in the formulation.
Major Adverse Drug Reactions	**>10%:** Gastrointestinal: Increased serum lipase (2% to 11%) **1% to 10%:** • **Dermatologic**: Pruritus (<2%) • **Endocrine & metabolic**: Hyperglycemia (≤9%) • Gastrointestinal: Abdominal distress (<2%), abdominal pain (<2%), diarrhea (≤2%), flatulence (<2%), nausea (≤1%), upper abdominal pain (<2%), vomiting (<2%) • **Hematologic & oncologic**: Neutropenia (4%; grades 3/4: 2% to 3%). • **Hepatic**: Hepatitis (<2%), hyperbilirubinemia (≤3%), increased serum alanine aminotransferase (1% to 4%), increased serum aspartate aminotransferase (1% to 5%). • **Nervous system**: Depression (≤1%), fatigue (≤2%), headache (≤2%), insomnia (≤7%), suicidal ideation (<2%), suicidal tendencies (<2%). • **Neuromuscular & skeletal**: Increased creatinine phosphokinase in blood specimen (2% to 7%), myositis (<2%). • **Renal**: Renal insufficiency (<2%).
Monitoring	Viral load, CD4 count, lipid profile; liver aminotransferases (baseline and

Parameters	during therapy); monitor for hypersensitivity.
Drug Interactions	**Risk X: Avoid combination** • Atidarsagene Autotemcel, Betibeglogene Autotemcel, Dofetilide, Elivaldogene Autotemcel, Fosphenytoin-Phenytoin, Lovotibeglogene Autotemcel, Oxcarbazepine, Phenobarbital, Primidone, St John's Wort **Risk D: Consider therapy modification** • Aluminum Hydroxide, Atazanavir, Belumosudil, Calcium Salts, Carbamazepine, Dalfampridine, Efavirenz, Etravirine, Fosamprenavir, Iron Preparations, Magnesium Salts, Metformin, Multivitamins/Minerals (with ADEK, Folate, Iron), Multivitamins/Minerals (with AE, No Iron), Nevirapine, Pilsicainide, Rifampin, Selenium, Sucralfate, Tipranavir, Zinc Salts
Pregnancy and Lactation	▪ **Pregnancy**: An alternative treatment to dolutegravir should be considered at the time of conception through the first trimester due to the risk of neural tube defects. ▪ **Lactation** - Dolutegravir is excreted in human milk in small amounts - There is insufficient information on the effects of dolutegravir in neonates/infants. - Breastfeeding is not recommended due to the potential for HIV-1 transmission
Administration	▪ Administer without regard to meals. ▪ Administer 2 hours before or 6 hours after cation-containing antacids or laxatives, sucralfate, oral supplements containing iron or calcium, or buffered medications. Alternatively, dolutegravir and supplements containing calcium or iron can be taken together with food. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**
Warnings/ Precautions	Hepatotoxicity, hypersensitivity reactions, and immune reconstitution syndrome.
Storage	Store at 15°C to 30°C, protect from moisture. **N.B. Refer to the manufacturer's PIL if there are specific considerations**.

11. Raltegravir (RAL)

Generic Name	Raltegravir
Dosage Form/Strengths	Tablet 400 mg, 25 mg
Route of Administration	*Oral*
Pharmacologic Category	Antiretroviral, Integrase Inhibitor (Anti-HIV) **ATC**: J05AJ01
Indications	Treatment of HIV-1 infection in combination with other antiretroviral agent's HIV-1 (alternative to the first line regimen) in adults and in pediatric patients weighing at least 3 kg.
Dosage Regimen	**HIV-1 infection, treatment: Adults, oral** • 400 mg twice daily. **Dosage modifications:** when co-administered with rifampin 800 mg (two 400-mg tabs) twice daily. **HIV-1 infection, treatment: Pediatrics** Pediatric patients at least 4 weeks of age and weighing at least 3 kg and less than 25 kg: • 3 kg to less than 6: 25 mg twice daily (1 x 25 mg twice daily). • 6 kg to less than 10: 50 mg twice daily (2 x 25 mg twice daily). • 10 kg to less than 14: 75 mg twice daily (3 x 25 mg twice daily). • 14 to less than 20: 100 mg twice daily. • 20 to less than 25: 150 mg twice daily Children and adolescents ≥25 kg: 400 mg twice daily.
Dosage adjustment	**Renal impairment** • **Mild, moderate, and severe impairment:** No dosage adjustment necessary. • **End-stage renal disease (ESRD) on intermittent hemodialysis (IHD):** Dose after dialysis on dialysis days. **Hepatic impairment** • **Mild-to-moderate impairment**: No dosage adjustment necessary. • **Severe impairment**: There are no dosage adjustments (has not been studied); use with caution.
Contra-indications	Hypersensitivity to raltegravir or any other component of the formulation.
Adverse Drug Reactions	**>10%** • Hepatic: Increased serum alanine aminotransferase (grade 2 to 4: ≤11%) **1% to 10%** • **Endocrine and metabolic**: Increase in fasting plasma glucose (grade 2: 126 to 250 mg/dL: 7% to 10%; grade 3: 251 to 500 mg/dL: 2% to 3%) • **Gastrointestinal**: Abdominal pain (<2%), decreased appetite (≥2%), diarrhea (≥2%), dyspepsia (<2%), flatulence (≥2%), gastritis (<2%), increased serum amylase (grade 2 to 4: ≤4%), increased serum lipase (grade 2 to 4: 1% to 7%), nausea (1% to 3%), vomiting (<2%) • **Genitourinary**: Genital herpes simplex (<2%) • **Hematologic and oncologic**: Decrease in absolute neutrophil count (grade 2 to 4: ≤4%), decreased hemoglobin (grade 2 to 4: ≤1%) • **Hepatic**: Hepatitis (<2%), increased serum alkaline phosphatase (grade

	2 to 4: ≤2%), increased serum aspartate aminotransferase (grade 2 to 4: ≤9%), increased serum bilirubin (grade 2 to 4: ≤6%) • Hypersensitivity: Hypersensitivity reaction (<2%) • Infection: Herpes zoster infection (<2%) • Nervous system: Abnormal dreams (≥2%), asthenia, depression, dizziness (≤2%), fatigue (2%), headache (≤4%), insomnia (≤4%), nightmares (≥2%), suicidal ideation (<2%), suicidal tendencies (<2%) • Neuromuscular & skeletal: Increased creatine phosphokinase in blood specimen (grade 2 to 4: 2% to 5%) • Renal: Increased serum creatinine (grade 2 to 3: ≤1%), nephrolithiasis (<2%), renal failure syndrome (<2%).
Monitoring Parameters	• Viral load, CD4 count, signs of skin rash, signs/symptoms of depression, and suicidal ideation.
Drug Interactions	**Risk X: Avoid combination** • Aluminum Hydroxide, Atidarsagene Autotemcel, Betibeglogene Autotemcel, Elivaldogene Autotemcel, Fosamprenavir, Lovotibeglogene Autotemcel, Magnesium Salts. **Risk D: Consider therapy modification** • Belumosudil, Calcium Carbonate, Polyvalent Cation Containing Products, Rifampin.
Pregnancy and Lactation	**Pregnancy** • Raltegravir 400 mg twice daily can be used during pregnancy if clinically needed. **Lactation** • Breastfeeding is not recommended while taking Raltegravir. • It is recommended that women living with HIV not breastfeed their infants to avoid transmission of HIV.
Administration	• May be administered without regard to meals. **Refer to the manufacturer's PIL if there are specific considerations**
Warnings/ Precautions	• Immune reconstitution syndrome, myopathy, skin, and hypersensitivity reactions. • At birth, the enzyme responsible for the metabolism of raltegravir (UGT1A1) is low and Raltegravir elimination in neonates may be prolonged. • The activity of UGT1A1 increases rapidly over the first 4 to 6 weeks of life. • Do not use in combination with darunavir and ritonavir in patients with HIV RNA ≥100,000 copies/mL and/or CD4 count≤200 cells/mm3, or in combination with abacavir and lamivudine in patients with HIV RNA ≥100,000 copies/mL.
Storage	• Store at 20°C to 25°C; excursions are permitted between 15°C and 30°C. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

e) Combinations

12. Abacavir and Lamivudine

Generic Name	Abacavir and Lamivudine
Dosage Form/Strengths	• **Tablet:** Abacavir and Lamivudine 600 mg/300 mg (was in the EDA drug database but cancelled) • **Tablets for oral suspension:** Abacavir and lamivudine 60 mg/30 mg, 120 mg/60 mg.
Route of Administration	Oral
Pharmacologic Category	• Antiretroviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HIV) • **(ATC) Classification**: J05AR02
Indications	**Tablet** antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infection in adults, adolescents, and children weighing at least 25 kg. **Tablets for oral suspension** Is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in pediatric patients aged 3 months and older and weighing at least 5 kg.
Dosage Regimen	• **Adults, adolescents, and children weighing at least 25 kg**: One tablet 600mg/300 mg once daily. • **Pediatric patients** aged 3 months and older and weighing **at least 5 kg**: - **Once daily dosing**: abacavir 16 mg/kg and lamivudine 8 mg/kg, OR - **Twice daily dosing**: abacavir 8 mg/kg and lamivudine 4 mg/kg in combination with other antiretroviral agents. The maximum daily dose of abacavir is 600 mg, and the maximum daily dose of lamivudine is 300 mg.
Dosage Adjustment	**Renal impairment:** • **CrCl ≥50 mL/minute:** No dosage adjustment necessary. • **CrCl ≥30 to <50 mL/minute:** No dosage adjustment necessary. • **CrCl <30 mL/minute:** Use is not recommended (use dose-adjusted individual components). **Hepatic impairment:** **Mild impairment (Child-Pugh class A)** Use is not recommended (close monitoring is required, including monitoring of abacavir plasma levels if feasible) **Moderate and severe impairment (Child-Pugh class B or C)** Use is contraindicated. **Tablets for oral suspension**: There are no data available on using in pediatric patients with renal impairment.
Contra-indications	• Hypersensitivity to the active substances or to any of the excipients. • Moderate or severe hepatic impairment. • Presence of HLA-B*5701 allele.
Adverse Drug Reactions	**1% to 10%**

	• **Central nervous system**: Abnormal dreams, anxiety, depression, dizziness, fatigue, headache, insomnia, malaise, migraine, vertigo • **Dermatologic:** Skin rash • **Gastrointestinal:** Abdominal pain, diarrhea, gastritis • **Hypersensitivity:** Hypersensitivity (including multiorgan failure and anaphylaxis) • **Miscellaneous:** Fever
Monitoring Parameters	• *HLA-B*5701* genotype status **before initiation** of therapy; signs and symptoms of hypersensitivity. • Bilirubin, liver enzymes • Blood glucose, fasting lipid panel • Hematologic parameters, viral load, and CD4 count; amylase, serum creatine kinase (as clinically indicated).
Drug Interactions	**Risk X: Avoid** Atidarsagene Autotemcel, Betibeglogene Autotemcel, Cladribine, Elivaldogene Autotemcel, Etuvetidigene Autotemcel, Lovotibeglogene Autotemcel. **Risk D: Consider Therapy Modification** • Fexinidazole, Risdiplam, Sorbitol, Tafenoquine, Vimseltinib.
Pregnancy and Lactation	**Pregnancy** • Administration in pregnancy should be considered only if the benefit to the mother outweighs the possible risk to the foetus. • Available clinical data indicate that abacavir use during pregnancy is **not** associated with an increased risk of congenital malformations or adverse fetal outcomes, despite animal findings and the theoretical risk of mitochondrial toxicity associated with nucleoside analogues) **Lactation** Abacavir is excreted into human breast milk, and due to the lack of safety data in infants under three months of age and the risk of HIV transmission, breastfeeding is **not recommended** for women living with HIV.
Administration	**Tablet:** Oral use, may be administered with or without food. **Tablets for Oral Suspension** • Can be taken **with or without food**, dispersed in water, or split **along the score**, **but not chewed**; **do not use if damaged, broken, or expired**. • **For children unable to swallow tablets**, - Place tablets in a container and add **10 mL of water per tablet** (5 mL per half tablet). - **Stir or swirl 2–3 minutes** until broken into swallowable pieces; **do not chew**. - **Drink immediately** (within 1 hour); if delayed, stir again before use. Discard after 1 hour. - **Rinse container with a little water** and drink to ensure full dose.
Warnings/ Precautions	• Abacavir is associated with potentially serious hypersensitivity reactions (**HSR**), characterized by fever and/or rash with symptoms of multi-organ involvement, which may be life-threatening or fatal if not properly managed. *Treatment must be **stopped immediately** if HSR is suspected, regardless of*

*HLA-B*5701 status. **Abacavir must never be restarted** after a suspected HSR, as re-exposure can cause rapid, more severe reactions, including hypotension and death; patients should be instructed to discard any remaining tablets.

- Increases in **body weight**, **blood lipid, and glucose levels** may occur during antiretroviral therapy. These changes may be partly related to **improved disease control and lifestyle factors**. While there is some evidence of a **treatment-related effect on lipids**, no strong evidence links weight gain to any specific antiretroviral drug.
- Pancreatitis has been reported, but a causal relationship to lamivudine and abacavir is uncertain.
- An increased risk of **virological failure** has been reported with **triple-nucleoside therapy**, particularly when **abacavir and lamivudine are combined with tenofovir disoproxil fumarate** as a once-daily regimen, with early development of resistance. Overall, the **abacavir/lamivudine combination may carry a higher risk of virological failure** compared with other available treatment options.
- **Patients co-infected with hepatitis B or C** are at increased risk of **severe, potentially fatal hepatic adverse reactions**. When used with HBV therapy, refer to the relevant product information. If **lamivudine** is used for both HIV and HBV, additional information can be found in HBV-specific Summary of Product Characteristics (SmPCs). **Discontinuation** of abacavir/lamivudine in HBV-coinfected patients requires **ongoing monitoring of liver function and HBV markers**, as stopping lamivudine may trigger **acute hepatitis exacerbation**.
- In utero exposure to **nucleoside/nucleotide analogues** may cause **mitochondrial dysfunction** in infants, mainly **transient hematologic and metabolic abnormalities**, with **rare neurological effects**. This does **not change recommendations** for antiretroviral use in pregnancy to prevent **HIV transmission**.
- **Immune Reactivation Syndrome** may occur after starting combination antiretroviral therapy (CART) in severely immunodeficient HIV patients, causing inflammatory reactions to asymptomatic or residual opportunistic infections (e.g., CMV, mycobacterial infections, Pneumocystis jirovecii pneumonia), usually within the first weeks to months. **Autoimmune disorders (such as Graves' disease and autoimmune hepatitis)** may also develop, with variable onset, sometimes many months after treatment initiation.
- **Osteonecrosis** has been reported, particularly in patients with **advanced HIV** and/or **long-term CART**, with a **multifactorial etiology** (e.g., corticosteroid use, alcohol intake, severe immunosuppression, high BMI). Patients should seek medical attention if they develop **joint pain, stiffness, or difficulty in movement**.
- The combination of **abacavir and lamivudine** does **not cure HIV**; patients may still develop **opportunistic infections** and other HIV-related complications and should remain under **close medical supervision**.
- Some studies suggest an **increased risk of cardiovascular events** (especially myocardial infarction) with **abacavir/lamivudine**. **Modifiable risk factors** (e.g., smoking, hypertension, hyperlipidemia) should be managed, and **alternative regimens should be considered** for patients with high cardiovascular risk.
- In **moderate renal impairment (CrCl 30 – 49 mL/min)**, lamivudine levels rise, increasing risk of **anemia and neutropenia**; monitor closely, and **switch**

	to individual components with dose adjustment if needed. **Concurrent drug therapy issues** The combination of abacavir and lamivudine **should not be** taken with any other medicinal products containing lamivudine or medicinal products containing **emtricitabine**.
Storage	Store at 25°C; excursions permitted to 15° to 30°C. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

13. Emtricitabine; tenofovir disoproxil

Generic Name	Emtricitabine; tenofovir disoproxil
Dosage Form/Strengths	Emtricitabine 200 mg; tenofovir disoproxil fumarate 300 mg equivalent to 245 mg tenofovir disoproxil (film-coated tablet)
Route of Administration	*Oral*
Pharmacologic Category	**Pharmacologic category** Antiretroviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HIV); **ATC Classification**: J05AR03
Indications	• Indicated in adults and pediatric patients 12 years of age and older in combination with other antiretroviral agents for the treatment of HIV-1 infection. • Indicated in infected adolescents, for the treatment of HIV-1, in case of NRTI resistance or toxicities precluding the use of first-line agents. • Pre-exposure prophylaxis (PrEP)
Dosage Regimen	***Adults and Adolescents >12 years Dosing (weighing at least 35kg)*** **Treatment and Prevention: One tablet once daily**
Dosage Adjustment	**Dosing Renal Impairment** • CrCl 50-80 mL/min: **treatment** limited clinical data support a once daily dose. • CrCl 60-80 mL/min: **Prophylaxis,** limited clinical data support a once daily dose. • Crcl < 60ml/min: **Prophylaxis,** no data in uninfected patient, use is not recommended. • CrCl 30-49 mL/min: **treatment,** the recommended dose is every 48 hr **Prophylaxis** Not recommended • CrCl < 30 mL/min) and haemodialysis patients: Not recommended in treatment and prophylaxis • Not recommended for use in individuals under the age of 18 years with renal impairment **Dosing Hepatic Impairment** No dosage adjustments are needed.
Contra-indications	• Hypersensitivity to the active ingredient or any component of the formulation. • Use for pre-exposure prophylaxis in individuals with unknown or positive HIV-1status **N.B. Refer to the manufacturer's PIL if there are specific considerations**
Adverse Drug Reactions	>10% • **Neuromuscular and skeletal**: Decreased bone mineral density (13%), elevated creatine kinase • **Gastrointestinal:** diarrhea, nausea, vomiting. 1% to 10% • **Endocrine and metabolic**: Abnormal phosphorus levels (<2.0 mg/dL: 10%), weight loss (3%), hyperglycemia, hypertriglyceridemia • **Gastrointestinal:** Abdominal pain (4%), dyspepsia, elevated amylase, including elevated pancreatic amylase, and elevated serum lipase. • **Hepatobiliary disorders:** elevated serum aspartate aminotransferase (AST) and/or elevated serum alanine aminotransferase (ALT),

	hyperbilirubinemia • **Hematologic and oncologic**: Decreased neutrophils (5%) • **Nervous system:** Headache (7%), dizziness • **Neuromuscular and skeletal**: Bone fracture (2%) • **Immune system:** allergic reaction. • **Psychiatric disorders**: insomnia, abnormal dreams • **Skin and subcutaneous tissue**: vesiculobullous rash, pustular rash, maculopapular rash, pruritus, urticaria, skin discoloration (increased pigmentation) • **Miscellaneous**: pain, asthenia.
Monitoring Parameters	• CBC with differential, reticulocyte count • Creatine kinase • CD4 count • HIV RNA plasma levels • Serum phosphorus (individuals with chronic kidney disease) or at risk of kidney dysfunction with persistent or worsening bone or muscle symptoms) • Serum creatinine, urine glucose, and urine protein (before initiation and as clinically indicated during therapy) • hepatic function tests, • Bone density (patients with a history of bone fracture or who have risk factors for bone loss or kidney dysfunction with persistent or worsening bone or muscle symptoms) • Testing for the hepatitis B virus (HBV) is recommended before the initiation of antiretroviral therapy • Weight (children). • Patients with HIV and HBV coinfection should be monitored for several months following tenofovir discontinuation. **HIV-1 preexposure prophylaxis (PrEP)** - Documented negative HIV test (≤1 week before initiating or reinitiating PrEP, at least every 3 months while taking PrEP, and following discontinuation of PrEP). - Screen for acute viral infections and potential exposure events (eg, condomless sex/condom breaking during sex with a partner of unknown HIV-1 status or unknown viremic status, or a recent STI) within 1 month of starting PrEP; if infections or events exist, reconfirm HIV-1 negative status. - Assess symptoms of side effects and acute HIV infection (every 3 months); renal function (before initiation, then every 6 to 12 months); testing for HBV (before initiation). **HIV occupational postexposure prophylaxis (PEP):** -Documented HIV test (at baseline and 6 weeks, 12 weeks, and 6 months after exposure); If confirmation that a fourth-generation HIV p2 antigen-HIV antibody test is being used, monitor at baseline, 6 weeks, and 4 months after exposure. -CBC, renal, and hepatic function assessments at baseline and 2 weeks after exposure.
Drug Interactions	**Category X: Avoid combination** • Adefovir, Atidarsagene Autotemcel, Betibeglogene Autotemcel, Cladribine, Elivaldogene Autotemcel, Etuvetidigene Autotemcel, Leniolisib, Lovotibeglogene Autotemcel, Sparsentan, Taurursodiol. **Category D: Consider therapy modification**

	• Atazanavir, Belumosudil, Ledipasvir, Nonsteroidal Anti-Inflammatory Agents, Vimseltinib.
Pregnancy and Lactation	**Pregnancy** • A large amount of data on pregnant women indicates no malformations or foetal/neonatal toxicity associated with emtricitabine and tenofovir disoproxil. Therefore, the use of emtricitabine/tenofovir disoproxil may be considered during pregnancy, if necessary. **Lactation** • There is insufficient information on the effects of emtricitabine and tenofovir in newborns/infants. Therefore, emtricitabine/tenofovir disoproxil should not be used during breastfeeding.
Administration	**Administration** • Can be administered with or without food (preferably with food). • If a patient has difficulty swallowing, they can use the tip of a spoon to crush the tablet. Then mix the powder with about 100 mL (half a glass) of water, orange juice, or grape juice, and drink immediately. • Missed dose within 12 hours of the usual dose, the dose should be taken as soon as possible, and the normal schedule should be continued. • In case of a missed dose by more than 12 hours and it is almost time for the next dose, the missed dose shouldn't be taken, and the usual dosing schedule should be resumed. • If vomiting occurs within 1 hour of taking the dose, another The tablet should be taken. • If vomiting occurs more than 1 hour after taking emtricitabine/tenofovir disoproxil, a second dose should not be taken. **N.B Refer to the manufacturer's PIL if there are specific considerations**.
Warnings/ Precautions	**1- Patients with hepatitis B or C virus infection** • Chronic hepatitis B or C patients who are co-infected with HIV-1 treated with antiretroviral therapy have an increased risk of fatal liver adverse effects. • There is no evidence about the safety profile and efficacy of emtricitabine and tenofovir for pre-exposure prophylaxis in co-infected patients with HBV or HCV. **2- Patients with HIV-1 harboring mutations** • Emtricitabine; tenofovir disoproxil should be avoided in patients with HIV-1 with the K65R mutation. **3- Overall HIV-1 infection prevention strategy** • Emtricitabine; tenofovir disoproxil does not always prevent the acquisition of HIV-1. • The protection time after administration of Emtricitabine; tenofovir disoproxil is unknown. **4- Risk of resistance with undetected HIV-1 infection** • Individuals who used Emtricitabine; tenofovir disoproxil for pre-exposure prophylaxis should be confirmed HIV-1 negative, with reconfirmation at least every 3 months using a combined antigen/antibody test. • Using Emtricitabine; tenofovir disoproxil is not a complete treatment regimen, detection of resistance mutations in individuals with undetected HIV-1 infection who are only on emtricitabine; tenofovir disoproxil. • Delay the use of emtricitabine and tenofovir for at least one month if

	the individual has consistent clinical symptoms with acute, present, and recent viral infection (< 1 month). HIV-1 status should be reconfirmed before starting the drug for pre-exposure prophylaxis. **5- Liver disease** • HIV-1-infected patients with pre-existing liver dysfunction, including chronic active hepatitis, have an increased frequency of liver function abnormalities during combination antiretroviral therapy (CART) and should be monitored according to standard practice. • If there is evidence of worsening liver disease in such patients, interruption or discontinuation of treatment must be considered. **6- Renal effects** • Renal failure, renal impairment, elevated creatinine, hypophosphatemia, and proximal tubulopathy (including Fanconi syndrome) have been reported with the use of tenofovir disoproxil. • It is recommended to calculate CrCL for all individuals before initiating the treatment of HIV-1 or in prophylaxis. • It is recommended to monitor renal function tests (creatinine clearance and serum phosphate) after two to four weeks of use, after three months of use, and every three to six months thereafter in case individuals without risk factors for renal disease. • More frequent monitoring is recommended for individuals at risk for renal disease. • Emtricitabine; tenofovir disoproxil should not be initiated in pediatric patients with renal impairment and should be discontinued in pediatric patients who develop renal impairment **7- Bone effects** • Bone abnormalities such as osteomalacia, which can manifest as persistent or worsening bone pain and, which can infrequently contribute to fractures, may be associated with tenofovir disoproxil-induced proximal renal tubulopathy. • Alternative treatment regimens should be considered for patients with osteoporosis or with a history of bone fractures. 8- **Immune reconstitution syndrome**: an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune disorders (e.g., Graves' disease, polymyositis, Guillain-Barré syndrome, autoimmune hepatitis) later in therapy; further evaluation and treatment may be required. **9- Opportunistic infections** **10- Co-administration of other medicinal products** Other nephrotoxic drugs and boosted protease inhibitors **11- Elderly:** Caution should be exercised **12- Importance of adherence** The adherence to the drug is correlated with the drug level in blood, and so the effectiveness in reducing the risk of acquiring HIV-1. **N.B. Refer to the manufacturer's PIL if there are specific considerations**.
Storage	Store in the original package in order to protect from moisture, at a temperature below 30 C. Keep the bottle tightly closed. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

14. Lamivudine/Zidovudine

Generic Name	Lamivudine/Zidovudine
Dosage Form/Strengths	**Film-coated tablet:** Lamivudine/Zidovudine 150 mg/300 mg
Route of Administration	*Oral*
Pharmacologic Category	• Antiretroviral, Reverse Transcriptase Inhibitor, Nucleoside (Anti-HIV) • **ATC classification**: J05AR01
Indications	Indicated in antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infection
Dosage Regimen	• **Adults and adolescents weighing ≥ 30 kg:** one tablet twice daily. • **Children (21 kg - 30 kg):** one-half tablet taken in the morning and one whole tablet taken in the evening. • **Children (14 kg- 21 kg)**: one-half tablet taken twice daily. • **Children < 14 kg:** tablets should **not** be used.
Dosage Adjustment	**Renal impairment** • **CrCl ≥50 mL/minute**: No dosage adjustment necessary. • **CrCl <50 mL/minute:** Use is not recommended (use dose-adjusted individual components). **Severe hepatic impairment** Use is not recommended (use dose-adjusted individual components). ▪ **Limited data in patients with cirrhosis suggest that accumulation of zidovudine may occur in patients with hepatic impairment because of decreased glucuronidation.** ▪ **Data obtained in patients with moderate to severe hepatic impairment show that lamivudine pharmacokinetics are not significantly affected by hepatic dysfunction.** ▪ **However, as dosage adjustments for zidovudine may be necessary, it is recommended that separate preparations of lamivudine and zidovudine be administered to patients with severe hepatic impairment**
Contra-indications	• Hypersensitivity to the active substances or to any of the excipients • Zidovudine is contraindicated in patients with abnormally low neutrophil counts (<0.75 x 109/L), or abnormally low haemoglobin levels (<7.5 g/dL or 4.65 mmol/L).
Adverse Drug Reactions	**Lamivudine** **>10%** **Dermatologic:** Skin rash **Gastrointestinal:** Diarrhea, nausea, vomiting **Hepatic:** Hepatomegaly (infants, children, adolescents) **Nervous system:** Fatigue, headache, malaise, neuropathy, sleep disturbance **Neuromuscular and skeletal:** Musculoskeletal pain **Respiratory:** Cough, ENT infection, nasal signs and symptoms, pharyngitis **Miscellaneous:** Fever **1% to 10%** **Gastrointestinal:** Abdominal cramps, abdominal pain, anorexia, decreased appetite, dyspepsia, increased serum amylase, increased serum lipase, stomatitis

	Hematologic & oncologic: Decrease in absolute neutrophil count, lymphadenopathy, thrombocytopenia **Hepatic**: Increased serum alanine aminotransferase, increased serum aspartate aminotransferase **Immunologic:** Splenomegaly **Nervous system**: Chills, depression, dizziness **Neuromuscular & skeletal:** Arthralgia, increased creatine phosphokinase in blood specimen, myalgia **Respiratory:** Abnormal breath sounds, wheezing. **Zidovudine** **>10%** **Gastrointestinal:** Anorexia, nausea, vomiting. **Hematologic and oncologic:** Anemia **Nervous system:** Headache, malaise **1% to 10%** **Gastrointestinal:** Abdominal cramps, abdominal pain, constipation, dyspepsia **Nervous system**: Asthenia, chills, fatigue, insomnia, neuropathy **Neuromuscular and skeletal:** Arthralgia, musculoskeletal pain, myalgia.
Monitoring Parameters	• Amylase, bilirubin, signs and symptoms of pancreatitis. • Monitor CBC with differential and platelet count at least every 2 weeks, liver function tests (including signs/symptoms of hepatomegaly), MCV, serum creatinine kinase, viral load, and CD4 count; observe for appearance of opportunistic infections; signs of muscle weakness or pain; blood lactate levels and signs of acidosis.
Drug Interactions	**Risk X: Avoid combination** • Atidarsagene Autotemcel, Bacillus Calmette Guerin (BCG) (Intravesical), Betibeglogene Autotemcel, Chloramphenicol (Systemic), Cladribine, Elivaldogene Autotemcel, Etuvetidigene Autotemcel, Fexinidazole, Lovotibeglogene Autotemcel, Stavudine, Thiamphenicol. **Risk D: Consider therapy modification** • Amodiaquine, Clarithromycin, Deferiprone, Doxorubicin (Conventional, liposomal), Levamisole, Ribavirin (Oral Inhalation, systemic), Risdiplam, Ropeginterferon Alfa-2b, Sorbitol, Tafenoquine, Vimseltinib.
Pregnancy and Lactation	**Pregnancy** • Extensive data indicate that lamivudine and zidovudine are generally **safe in pregnancy** and reduce maternal-fetal HIV transmission, Though potential risks such as mitochondrial dysfunction in infants, transplacental carcinogenicity in animals, and hepatitis recurrence in co-infected patients should be considered, clinical use should balance maternal benefit and fetal risk. **Lactation** • Lamivudine and zidovudine are excreted in breast milk, with low infant exposure for lamivudine, but women living with HIV are **advised not to breastfeed** to prevent HIV transmission.
Administration	• Lamivudine/Zidovudine may be administered with or without food. • The tablet(s) should ideally be swallowed without crushing. For patients who are unable to swallow tablets, tablets may be crushed and added to a

	small amount of semi-solid food or liquid, all of which should be consumed immediately
Warnings/ Precautions	• Patients receiving lamivudine/zidovudine or other antiretroviral therapy may still develop opportunistic infections and HIV-related complications, and should remain under close monitoring by experienced healthcare providers. • Zidovudine may cause anemia, neutropenia, or leukopenia, especially at higher doses (1200-1500 mg/day) or in patients with advanced HIV or poor bone marrow reserve; therefore, hematologic parameters should be **regularly** monitored, and separate lamivudine and zidovudine preparations should be used if severe anemia or myelosuppression occurs. • Rare cases of pancreatitis have been reported with lamivudine/zidovudine, and treatment should be discontinued immediately if clinical signs, symptoms, or lab abnormalities suggest pancreatitis. • Zidovudine may cause lactic acidosis, often with hepatomegaly and hepatic steatosis, which can be **life-threatening**; treatment should **be discontinued** if symptomatic **hyperlactatemia,** metabolic acidosis, or rapidly rising liver enzymes occur, and patients with liver disease risk factors should be monitored closely. **Hyperlactatemia symptoms** include: - Nausea, vomiting, and abdominal pain - Non-specific malaise, loss of appetite, weight loss - Respiratory symptoms (rapid and/or deep breathing) - Neurological symptoms (including motor weakness). • Zidovudine treatment may cause lipoatrophy—loss of subcutaneous fat, especially in the face, limbs, and buttocks—related to cumulative exposure and mitochondrial toxicity; patients should be regularly monitored, and therapy switched to an alternative regimen if lipoatrophy is suspected. • Antiretroviral therapy may cause increases in weight, blood lipids, and glucose, partly due to disease control or lifestyle; lipid and glucose levels should be monitored according to HIV treatment guidelines, and lipid disorders managed as clinically appropriate. • Immune reactivation syndrome may occur after initiation of combination antiretroviral therapy (CART) in severely immunocompromised HIV patients, presenting with inflammatory reactions to opportunistic infections or autoimmune disorders, requiring prompt evaluation and appropriate management. • Osteonecrosis has been reported in patients with advanced HIV or long-term CART, and patients should seek medical advice for joint symptoms; additionally, lamivudine/zidovudine should not be co-administered with other lamivudine- or emtricitabine-containing products, and use with cladribine is not recommended.
Storage	Store in a dry place at a temperature not exceeding 30° C. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

15. Tenofovir Disoproxil, Lamivudine, and Efavirenz

Generic Name	Tenofovir Disoproxil, Lamivudine, and Efavirenz
Dosage Form/Strengths	• Efavirenz (EFV) 600 mg/ lamivudine (3TC) 300 mg/tenofovir disoproxil fumarate (TDF) 300 mg (equivalent to 245 mg of tenofovir disoproxil) tablet. • Efavirenz 400 mg/lamivudine 300 mg/ tenofovir disoproxil fumarate 300 mg (equivalent to 245 mg of tenofovir disoproxil) tablet.
Route of Administration	*Oral*
Pharmacologic Category	• **Pharmacologic category**: Antiviral for systemic use; antivirals for treatment of HIV infections, combinations, Antiretroviral (efavirenz (EFV), a non-nucleoside reverse transcriptase inhibitor, and lamivudine (3TC) and tenofovir disoproxil fumarate (TDF), both nucleo(t)side reverse transcriptase inhibitors) • **ATC Classification**: J05AR11
Indications	• Indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adult and pediatric patients weighing at least 40 kg or 35 kg.
Dosage Regimen	***Adults and pediatric patients (weighing at least 40kg)* can swallow a solid tablet. *Dosing*** • Treatment of HIV-1: One tablet once daily (EFV 600 mg/ (3TC) 300 mg/ (TDF) 300 mg) ***Adults and pediatric patients (weighing at least 35 kg) can swallow a solid tablet*** • Treatment of HIV-1: One tablet once daily (EFV 400 mg/ (3TC) 300 mg/ (TDF) 300 mg)
Dosage adjustment	**Dosing Renal Impairment:** • CrCl ≥50 mL/minute: No dosage adjustment needed. • CrCl <50 mL/minute: Not recommended. • End-stage renal disease (ESRD) requiring hemodialysis: Not recommended • Acute kidney injury during treatment: Discontinuing tenofovir disoproxil fumarate is recommended and substituting with alternative antiretroviral therapy. **Dosing Hepatic Impairment:** • Mild hepatic impairment: Use with caution. • Moderate to severe hepatic impairment (Child-Pugh B, C): Not recommended
Contra-indications	• In patients with a previous hypersensitivity reaction (e.g., Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions) to any of the components contained in the formulation. • Coadministration with elbasvir and grazoprevir. **N.B. Refer to the manufacturer's PIL if there are specific considerations**
Adverse Drug Reactions	>10% • **Dermatologic**: Skin rash (18%) • **Endocrine and metabolic**: Hypercholesterolemia (grades 3/4: 19%) • **Gastrointestinal**: Diarrhea (11%)

	• **Nervous system**: Depression (11%), headache (14%), pain (13%) • **Neuromuscular & skeletal**: Decreased bone mineral density (28%), increased creatine phosphokinase in blood specimen (grades 3/4: 12%). 1% to 10%: • **Endocrine & metabolic**: Increased serum triglycerides (grades 3/4: 1%) • **Gastrointestinal**: Abdominal pain (7%), dyspepsia (4%), increased amylase (grades 3/4: 9%), nausea (8%), vomiting (5%) • **Genitourinary**: Hematuria (grades 3/4: 7%) • **Hematologic & oncologic:** Decreased neutrophils (grades 3/4: 3%) • **Hepatic**: Increased serum alanine aminotransferase (grades 3/4: 4%), increased serum aspartate aminotransferase (grades 3/4: 5%) • **Nervous system**: Anxiety (6%), asthenia (6%), dizziness (3%), insomnia (5%), peripheral neuropathy (1%) • **Neuromuscular & skeletal**: Arthralgia (5%), back pain (9%), lipodystrophy (1%), myalgia (3%) • **Respiratory**: Pneumonia (5%) • **Miscellaneous**: Fever (8%)
Monitoring Parameters	• **Prior to initiation:** test all patients for hepatitis B virus (HBV). • **As clinically appropriate:** Assess serum creatinine, serum phosphorus, estimated creatinine clearance, urine glucose, and urine protein in all patients. • **At baseline and during treatment in all patients:** Cholesterol and triglycerides Monitor hepatic function
Drug Interactions	**Category X, Avoid combination:** • Abemaciclib, Acoramidis, Adefovir, Amodiaquine, Antihepaciviral Combination Products, Atidarsagene Autotemcel, Atrasentan, Avacopan, Avapritinib, Bedaquiline, Betibeglogene Autotemcel, Cabotegravir, Capivasertib, Capmatinib, CarBAMazepine, Cladribine, Cobimetinib, Daridorexant, Dasabuvir, Defactinib, Deflazacort, Dordaviprone, DOXOrubicin, Elacestrant, Elbasvir and Grazoprevir, Elinzanetant, Elivaldogene Autotemcel, Ensartinib, Entrectinib, Ergonovine, Etuvetidigene Autotemcel, Fedratinib, Fexinidazole, Finerenone, Ibrexafungerp, Ivabradine, Ketoconazole (Systemic), Lazertinib, Lemborexant, Leniolisib, Letermovir, Levoketoconazole, Lonafarnib, Lovotibeglogene Autotemcel, Lumateperone, Mavacamten, Methoxyflurane, Mobocertinib, Nerandomilast, Neratinib, Nirogacestat, Nisoldipine, Olaparib, Olutasidenib, Omaveloxolone, Palovarotene, Pemigatinib, Pimavanserin, Posaconazole, Pretomanid, Quizartinib, Ranolazine, Remibrutinib, Repotrectinib, Reverse Transcriptase Inhibitors (Non-Nucleoside), Revumenib, Rilzabrutinib, Rimegepant, Sacituzumab Govitecan, Sebetralstat, Selpercatinib, Selumetinib, Sevabertinib, Simeprevir, Sonidegib, Sparsentan, Suzetrigine, Taletrectinib, Taurursodiol, Tazemetostat, Ulipristal, Vanzacaftor, Tezacaftor, and Deutivacaftor, Velpatasvir, Venetoclax, Voclosporin, Vonoprazan, Vorapaxar, Voxilaprevir, Ziftomenib, Zoliflodacin, Zuranolone. **Category D, Consider therapy modification:** • Aficamten, Alfentanil, Atazanavir, Atogepant, Atovaquone, Avanafil, Axitinib, Belumosudil, Brigatinib, Cabozantinib, Cariprazine, Caspofungin, Clarithromycin, Crinecerfont, Daclatasvir, Darunavir, Deferasirox, Dolutegravir, Duvelisib, Erdafitinib, Erlotinib,

	Flibanserin, Fosamprenavir, Fruquintinib, Gepotidacin, Glasdegib, Glecaprevir and Pibrentasvir, GuanFACINE, Hormonal Contraceptives, Itraconazole, Ketoconazole (Systemic), Larotrectinib, Ledipasvir, Lefamulin (Intravenous), Lefamulin, Lenacapavir, Lopinavir, Lorlatinib, Lurasidone, Maraviroc, Maribavir, MiFEPRIStone, Mitapivat, Nonsteroidal Anti-Inflammatory Agents, Paltusotine, Perampanel, Pirtobrutinib, Pralsetinib, Praziquantel, Rifabutin, Ripretinib, Risdiplam, Saquinavir, Sorbitol, Sunvozertinib, Tafenoquine, Ubrogepant, Valoctocogene Roxaparvovec, Vimseltinib, Voriconazole, Zanubrutinib.
Pregnancy and Lactation	**Pregnancy** • Because of the potential risk of neural tube defects, EFV should not be used in the first trimester of pregnancy. **Advise pregnant** women of the potential risk to the fetus. • There are no adequate and well-controlled studies with TDF in pregnant women. • Women, so TDF should be used during pregnancy only if clearly needed. • Lamivudine crosses the placenta in humans. • Patients who become pregnant while taking this fixed-dose combination may continue if viral suppression is effective and the regimen is well tolerated**.** • Females of reproductive potential should undergo pregnancy testing before initiation. **Lactation** • Efavirenz, lamivudine, and tenofovir are present in breast milk. • Instruct mothers not to breastfeed if they are receiving.
Administration	**<u>Administration</u>** • Should be taken on an empty stomach, preferably at bedtime (may improve tolerability of CNS symptoms). **N.B. Refer to the manufacturer's PIL if there are specific considerations**.
Warnings/ Precautions	• **Lactic acidosis and severe hepatomegaly with steatosis** - Any Patient who exhibits clinical or laboratory findings of lactic acidosis or severe hepatotoxicity should have their treatment stopped (even in the absence of marked transaminase elevations). - Female gender and obesity may increase the risk for development. • **Severe acute exacerbation of hepatitis B in patients coinfected with HIV-1 and HBV** - Posttreatment Exacerbations of Hepatitis: before initiating antiretroviral therapy, all HIV-1 patients should be tested for chronic HBV. - HBV patients who discontinue the drug should be closely followed up for at least several months. Resume anti-hepatitis B therapy if possible. • **New onset or worsening renal impairment** - Reported cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), with the use of TDF. - All patients before initiating therapy and during therapy with TDF should assess their estimated CrCl.

- Patients at risk of renal dysfunction before initiating therapy and during therapy with TDF: should assess estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein.
- Recent use of a nephrotoxic agent: Avoid using the drug.

- **CNS effects**
- There are reported cases with efavirenz has **(**Insomnia, abnormal dreams, hallucinations); symptoms usually start during the first 1 to 2 days of treatment and generally resolve after 2 to 4 weeks; administration at bedtime may improve the tolerability of CNS symptoms.
- CNS depression also may happen (eg, impaired concentration, dizziness, or drowsiness); avoid driving or operating machinery.
- Treatment with EFV was associated with an increase in the occurrence of these selected psychiatric symptoms (Severe depression (2.4%, 0.9%), suicidal ideation (0.7%, 0.3%), nonfatal suicide attempts (0.5%, 0), aggressive behavior (0.4%, 0.5%), paranoid reactions (0.4%, 0.3%), and manic reactions (0.2%, 0.3%)
- Patients with serious psychiatric adverse experiences should seek immediate medical evaluation to assess the possibility that the symptoms may be related to the use of EFV, and if so, to determine whether the risks of continued therapy outweigh the benefits.

- **Embryo-fetal toxicity**
- Encourage reproductive-age women receiving EFV to avoid getting pregnant, as it may cause fetal harm when administered during the first trimester.

- **Decreased bone mineral density**
- TDF was associated with slightly greater decreases in bone mineral density (BMD) and increases in biochemical markers of bone metabolism.
- Assessment of BMD should be considered for adults who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss.
- Consider calcium and vitamin D supplementation for all patients may be beneficial.
- Reported cases with TDF use of osteomalacia associated with proximal renal tubulopathy, manifested as bone pain or pain in extremities, and which may contribute to fractures.

- **Fat redistribution**
- Combination of antiretrovirals may cause redistribution/accumulation of body fat (eg, central obesity, dorsocervical fat enlargement [buffalo hump], peripheral wasting, facial wasting, breast enlargement, cushingoid appearance).

- **Hepatotoxicity**
- Reported cases in patients treated with efavirenz acquire hepatitis, including fulminant hepatitis, sometimes fatal or progressing to liver failure requiring transplantation.

- **Hypercholesterolemia:** Increases in total cholesterol and triglycerides have been reported with efavirenz.

- **Immune reconstitution syndrome**
- Occurrence with combination antiretroviral therapy as an inflammatory response to an indolent or residual opportunistic infection during initial HIV treatment or activation of autoimmune

	disorders (eg, Graves' disease, polymyositis, Guillain-Barré syndrome, autoimmune hepatitis) later in therapy. • **Pancreatitis** - Has been reported particularly in HIV-infected pediatric patients with a history of antiretroviral nucleoside use, history of pancreatitis, or significant risk factors for pancreatitis, when using lamivudine; in this case, use lamivudine with caution. - Treatment with lamivudine should be discontinued if signs or symptoms of pancreatitis occur. • **QT prolongation** - QT prolongation has been reported with efavirenz. - Consider alternative therapy in patients at risk of torsade de pointes or when administered with medications with known risk of torsade de pointes. • **Convulsions** - Have been observed in patients receiving EFV, generally in the presence of a known medical history of seizures - Caution should be taken in any patient with a history of seizures. - Patients who are receiving concomitant anticonvulsant medications primarily metabolized by the liver, such as phenytoin and phenobarbital, may require periodic monitoring of plasma levels. **N.B. Refer to the manufacturer's PIL if there are specific considerations**.
Storage	Store below 30 °C. Keep the bottle tightly closed, in its original container. **N.B. Refer to the manufacturer's PIL if there are specific considerations.**

References

- The Egyptian Drug Authority database for drugs and pharmaceutical products, available on the official website, https://www.edaegypt.gov.eg/.
- The European Medicines Agency (EMA), https://www.ema.europa.eu/en/homepage.
- The United States Food and Drug Administration, the federal agency of the Department of Health and Human Services, www.accessdata.fda.gov
- Lexicomp Online, reference handbooks, and desktop software, as a source of drug full monographs, by Wolters Kluwer Health, www.lexicomp.com
- The searchable version of the complete Anatomical Therapeutic Classification (ATC) index with Defined Daily Dose (DDDs), by the World Health Organization (WHO), www.whocc.no/atc_ddd_index/
- World Health Organization. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. World Health Organization; 2021 July.