Drug Profile of Emtricitabine and Tenofovir AF

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ABSTRACT

Emtricitabine and Tenofovir alafenamide (tenofovir AF) is a novel oral prodrug of the nucleos(t)ide reverse transcriptase inhibitor (NRTI) tenofovir that has several pharmacological advantages over tenofovir disoproxil fumarate (tenofovir DF), including increased plasma stability and reduced tenofovir systemic exposure. Tenofovir AF has been coformulated with emtricitabine for the treatment of adults and adolescents with HIV-1 infection.

Keywords: Emtricitabine, Tenofovir alafenamide, NRTI.

I. INTRODUCTION

Drug Profile of Emtricitabine

Molecular structure

Figure 1. Structure of Emtricitabine

IUPAC Name 4-amino-5-fluoro-1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one.

CAS Number 143491-57-0

Drug Bank DB00879 (APRD00226)

Molecular formula C₈H₁₀FN₅O₃S

Molecular weight 247.248 gm/mol

Category Antiretroviral

Description Emtricitabine is a nucleoside reverse transcriptase inhibitor for the treatment of HIV infection in adults.
Solubility
Soluble in water

pKₐ value
2.65

Mechanism of action
Emtricitabine works by inhibiting reverse transcriptase, the enzyme that copies HIV RNA into new viral DNA. Emtricitabine is a synthetic nucleoside analogue of cytidine. It is phosphorylated by cellular enzymes to form Emtricitabine 5’-triphosphate, which is responsible for the inhibition of HIV-1 reverse transcriptase.

Pharmacokinetic data

Absorption
Rapidly absorbed mean absolute bioavailability of 93% for capsules and 75% for solution. Food does not effect absorption.

Protein Binding
Very low (less than 4%)

Metabolism
Minimally transformed (13%), most appears unchanged in urine (86%). The biotransformation of Emtricitabine includes oxidation of the thiol moiety to form the 3’-sulfoxide diastereomers and conjugation with glucuronic acid to form 2′-O-glucuronide.

Route of elimination
The renal clearance of Emtricitabine is greater than the estimated creatinine clearance, suggesting elimination by both glomerular filtration and active tubular secretion.

Half life
\[ t_{1/2} = \text{Approximately 10 hours} \]

Adverse effects
- Chest pain or tightness
- Cough or Hoarseness
- Fever Or Chills
- Lower Back Or Side Pain
- Painful Or Difficult Urination

Uses
- Emtricitabine is indicated in combination with other antiretroviral agents for the treatment of HIV infection in adults.
- Emtricitabine exhibits clinical activity against the hepatitis B virus (HBV)
- Emtricitabine treatment results in significant histologic, virologic and biochemical improvement.
- Drugs used to treat HBV infection may have to be used in combination to prevent the evolution of drug resistant strains

Storage
Should be kept in a tightly closed container and protect from moisture. Keep out of reach of children.

Dosage
It consists of 200mg/1 tab.
Marketed formulation
Truvada - Emtricitabine + Tenofovir AF

Drug Profile of Tenofovir AF

Molecular structure

![Molecular structure of Tenofovir AF](image)

Figure 2. Structure of Tenofovir AF

<table>
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<tr>
<th>Property</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>CAS Number</td>
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<tr>
<td>Drug Bank</td>
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<tr>
<td>Molecular formula</td>
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<td>Molecular weight</td>
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<tr>
<td>Category</td>
<td>Anti retro viral drug</td>
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<tr>
<td>Description</td>
<td>Tenofovir AF is a nucleotide reverse transcriptase inhibitor and a novel ester prodrug of the antiretroviral. Following oral administration, TAF is converted in vivo to Tenofovir, an acyclic nucleoside phosphonate (nucleotide) analog of adenosine 5’-monophosphate</td>
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<tr>
<td>Solubility</td>
<td>Very soluble in alcohol, slightly soluble in water.</td>
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<td>pKₐ value</td>
<td>3.8</td>
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Mechanism of action
Tenofovir AF is a nucleotide reverse transcriptase inhibitor (NRTI) and a novel ester prodrug of the antiretroviral Tenofovir AF. Following oral administration, TAF is converted in vivo to Tenofovir, an acyclic nucleoside phosphonate (nucleotide) analog of adenosine 5’-monophosphate. Tenofovir AF mimics normal DNA building blocks but is lacking a 3’-OH molecule required for phosphodiester bond linkage.

II. PHARMACOKINETIC DATA

Absorption
Tmax is observed at 1 hour post oral administration

Distribution
Tenofovir AF is ~80% bound to human plasma proteins.

Metabolism
In vivo, Tenofovir AF is hydrolyzed within cells to form Tenofovir (major metabolite), which is phosphorylated to the active metabolite, Tenofovir AF diphosphate. In vitro studies have shown that TAF is
metabolized to Tenofovir by cathepsin A (also known as Lysosomal Protective Protein) in peripheral blood mononuclear cells (PBMCs) and macrophages and by Carboxylesterase 1 (CES1) in hepatocytes.

**Elimination Route**
The renal clearance of Emtricitabine is greater than the estimated creatinine clearance, suggesting elimination by both glomerular filtration and active tubular secretion.

**Half life** \( t_{1/2} \) = Approximately 0.5 hours

**Adverse effects**
- Abdominal Or Stomach Discomfort
- Decreased Appetite
- Diarrhea
- Fast, Shallow Breathing
- General Feeling Of Discomfort

**Uses**
- It is used for HIV-1 infection and chronic hepatitis B treatment
- For HIV-1 infection, Tenofovir AF is indicated in combination with other antiretroviral agents
- Drugs used to treat HBV infection may have to be used in combination to prevent the evolution of drug resistant strains

**Storage**
Should be kept in a tightly closed container and store at room temperature. Keep out of reach of children.

**Dose**
It consists of 25mg/1 tab

**Marketed formulation**
Truvada - Tenofovir AF + Emtricitabine

**III. COCLUSION**

Truvada is successful as part of an antiretroviral treatment. There is also convincing data that it has less undesirable effects on bone mineral density. Even though approved for use in those with predictable filtration rates as low as 30 mL/min, data is somewhat limited in this group.

**IV. REFERENCES**


