

# Economic Evaluation of the Co-Formulated Antiretroviral Efavirenz 400 mg/ Lamivudine/Tenofovir Disoproxil Fumarate for the Treatment of HIV-1 Infection in Adult Patients from the Perspective of the Mexican Public Health System

María Miroslava, Palecek-Rodríguez, MSc+; Erick Jael, Palomo-Paz, BSc+; Fernando, Gómez-Martínez, Econ+; Yazmin, Escobar-Juárez, MSc+; Herman, Soto-Molina, Mecon+; María Guadalupe, Mendoza-Medrano, Mecon+; Malgorzata, Rozycka, MD\*. +MSR Health Consulting, Mexico; \*VIATRIS Healthcare México.

## Introduction

The human immunodeficiency virus (HIV) causes the acquired immunodeficiency syndrome (AIDS), which is the last stage of the HIV infection disease. AIDS is mainly characterized by the presence of opportunistic infections and tumors, which can be deadly if untreated<sup>1</sup>. Currently, there is no cure for HIV infection, however, it has become a treatable chronic health condition that allows persons who have contracted the virus to live long lives in good health under antiretroviral treatment (ART)<sup>2</sup>.

In Mexico, by 2018 reports stated that 80% of persons living with HIV had been diagnosed, and only 90% of them were receiving ART<sup>3</sup>. Considering this, a public health need to meet the goals for AIDS eradication in Mexico can be identified. To achieve this, the treatment with Efavirenz/Lamivudine/Tenofovir disoproxil fumarate on a single tablet formulation with a dosage of 400 mg/ 300 mg/ 300 mg (EFV400+TDF+3TC), can result in a viable alternative to complement ART options available at Mexico's General Health Council (CNIS for the Spanish abbreviation)<sup>4</sup>.

This study aimed to evaluate the cost-savings of a co-formulated tablet containing 400 mg of Efavirenz, along with Lamivudine and Tenofovir disoproxil fumarate (referred to as EFV400/3TC/TDF), as an antiretroviral treatment (ART) for HIV-1 infections in adults. The evaluation was conducted in comparison to other ARTs used in the Mexican public health system.

## Methods

A systematic review (SR) and a network meta-analysis (NMA) were performed to evaluate the efficacy and safety of EFV400/3TC/TDF and its comparators for the treatment of HIV-1 infection in adults. The comparators included were: BIC+FTC+TAF, DTG+ABC+3TC, DTG+FTC+TAF, DTG+((FTC+TAF) or (XTC+TDx)), DTG+3TC, DOR+TDx+3TC, EFV+TDx, DRV+cobi+ ((TAF+FTC) or (TDx+FTC or 3TC)), DOR+((TAF+FTC) or (TDx+XTC)), EFV+((TAF+FTC) or (TDx+XTC)), RAL+((TAF+FTC) or (TDx+XTC)), DRV+cobi+3TC. The outcomes considered for the NMA were viral suppression <50 copies/mL of HIV-1 ARN and serious adverse events.

With the information obtained, a complete economic evaluation of the cost minimization analysis (AMC) type was carried out. The AMC compared the direct medical costs associated with the use of EFV400/3TC/TDF and its comparators, contemplating a time horizon of 1 year.

A five-year (2024-2028) budget impact analysis evaluated the economic impact of EFV400/3TC/TDF as a treatment option. A market penetration rate of 50% for the first year and annual increases of 12.5% for subsequent years were considered.

## Results

The SR included 18 RTCs<sup>5-22</sup>, with efficacy data (viral suppression <50 copies/mL of HIV-1 ARN) and safety data (serious adverse events) for EFV400/3TC/TDF and its comparators. Results showed no statistically significant differences in efficacy or safety between EFV400/3TC/TDF and the compared treatments.

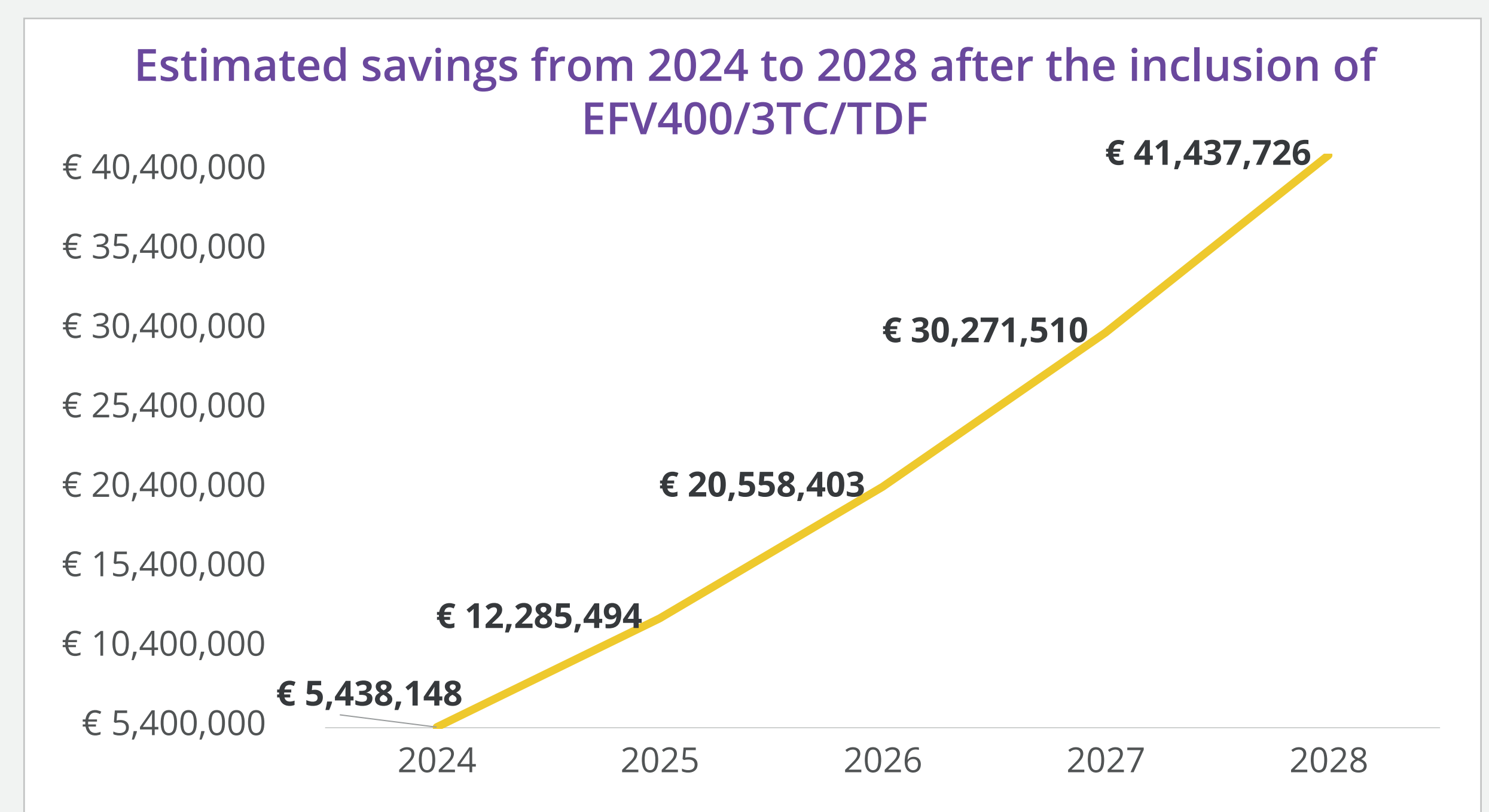
**EFV400/3TC/TDF is a cost-saving option**, in monetary terms, representing an average annual savings of € 1,462 per patient, which equates to a savings of 75.1% compared to all available options.

**Table 1: Results of the Cost Minimization Analysis.**

Treatment	Cost per treatment	Saving	Saving (%)
EFV400/3TC/TDF	€ 486	--	--
RAL+(TAF+FTC or TDx+XTC)	€ 4,459	€ 3,973	89%
DTG+FTC+TAF	€ 2,876	€ 2,390	83%
DTG+ABC+3TC	€ 2,075	€ 1,589	77%
DRV+cobi+(TAF+FTC or TDx+XTC)	€ 2,010	€ 1,524	76%
DTG+ (FTC+TAF or XTC+TDx)	€ 1,870	€ 1,384	74%
DTG+3TC	€ 1,825	€ 1,339	73%
DOR+(TAF+FTC or TDx+XTC)	€ 1,793	€ 1,307	73%
DRV+cobi+3TC	€ 1,776	€ 1,290	73%
EFV+(TAF+FTC or TDx+XTC)	€ 1,364	€ 878	64%
DOR+TDF+3TC	€ 1,169	€ 683	58%
EFV+TDx+XTC	€ 1,085	€ 600	55%
BIC+FTC+TAF	€ 1,069	€ 583	55%
<b>Average</b>		<b>€ 1,462</b>	<b>75%</b>

Source: PAAASOP ISSSTE 2023, PAAASOP IMSS 2023<sup>23,24</sup>

Regarding the Budget Impact Analysis, introducing EFV400/3TC/TDF over a 5-year period is an option that represents an average annual savings of €21,998,256, which in terms of percentage of the budget represents 0.314% of the NHS medicines budget.



## Conclusion

EFV400/3TC/TDF shows no statistically significant differences in viral suppression and safety. It is a cost-saving option with savings of up to 75.1% compared to some of its competitors, making it a valuable option for the National Health System in Mexico for treating HIV-1 infection in adult patients.

## Sponsorship

This work was financed by an unrestricted grant from Viatrix Healthcare México S. de R.L de C.V. the company that markets EFV400/3TC/TDF in Mexico.

## Abbreviations

BIC: Bictegravir; FTC: emtricitabine; TAF: tenofovir alafenamide, DTG: dolutegravir; ABC: abacavir; 3TC: Lamivudine; XTC: Lamivudine or emtricitabine; TDx: tenofovir disoproxil; DOR: doravirine; EFV: efavirenz 600 mg; EFV400: efavirenz 400 mg; DRV: darunavir; cobi: cobicistat; RAL: raltegravir.

## References

- Justiz-Vallant, A. G. (2023). HIV Disease Current Practice. StatPearls Publishing. <https://www.ncbi.nlm.nih.gov/books/NBK534860/>.
- WHO. (2023, 07 13). HIV and AIDS. Retrieved from Data and numbers: <https://www.who.int/es/news-room/fact-sheets/detail/hiv-aids>
- Salas-Ortiz, A. (2022). Coordination and cooperation of the networks formed behind the continuum of care to people living with HIV in Mexico. Salud Pública Mex., 488-497. <https://doi.org/10.21149/13490>.
- Mexico's General Health Council. (2023). Agreement by which the National Compendium of Health Consumables is published version 2023 [Text in Spanish]. México: Official Federal Diary.
- ENCORE1-Study-Group. (2014). Efficacy of 400 mg efavirenz versus standard 600 mg dose in HIV-infected, antiretroviral-naïve adults (ENCORE1): a randomised, double-blind, placebo-controlled, non-inferiority trial. Lancet, 1474-1482. doi: 10.1016/S0140-6736(13)62187-X.
- NAMSAL-ANRS-12313-Study-Group, K. C.-E.-D. (2019). Dolutegravir-Based or Low-Dose Efavirenz-Based Regimen for the Treatment of HIV-1. N Engl J Med., 816-826. doi: 10.1056/NEJMoa1904340.
- Aberg, J.A. (2012). Metabolic effects of darunavir/ritonavir versus atazanavir/ritonavir in treatment-naïve, HIV type 1-infected subjects over 48 weeks. AIDS Res Hum Retroviruses, 1184-1195. doi: 10.1089/aid.2011.0327.
- Cahn P. (2019). Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naïve adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferior. Lancet, 143-155. doi: 10.1016/S0140-6736(18)32462-0.
- Clotet, B. (2014). Once-daily dolutegravir versus darunavir plus ritonavir in antiretroviral-naïve adults with HIV-1 infection (FLAMINGO): 48 week results from the randomised open-label phase 3b study. Lancet, 2222-2231. doi: 10.1016/S0140-6736(14)60084-2.
- Eron, J.J. (2018). A week-48 randomized phase-3 trial of darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-naïve HIV-1 patients. AIDS, 1431-1442. doi: 10.1097/QAD.0000000000001817.
- Gallant, J. (2017). Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial. Lancet, 2063-2072. doi: 10.1016/S0140-6736(17)32299-7.
- Lennox, J.L. (2009). Safety and efficacy of raltegravir-based versus efavirenz-based combination therapy in treatment-naïve patients with HIV-1 infection: a multicentre, double-blind randomised controlled trial. Lancet, 796-806. doi: 10.1016/S0140-6736(09)60918-1.
- Lennox, J.L. (2014). Efficacy and tolerability of 3 nonnucleoside reverse transcriptase inhibitor-sparing antiretroviral regimens for treatment-naïve volunteers infected with HIV-1: a randomized, controlled equivalence trial. Ann Intern Med., 461-471. doi: 10.7326/M14-1084.
- Miro, J.M., (2015). Immune Reconstitution in Severely Immunosuppressed Antiretroviral-Naïve HIV-1-Infected Patients Starting Efavirenz, Lopinavir-Ritonavir, or Atazanavir-Ritonavir Plus Tenofovir/Emtricitabine: Final 48-Week Results (The Advanz-3 Trial). J Acquir Immune Defic Syndr., 206-215. doi: 10.1097/QAI.0000000000000567.
- Molina, J.M. (2018). Doravirine versus ritonavir-boosted darunavir in antiretroviral-naïve adults with HIV-1 (DRIVE-FORWARD): 48-week results of a randomised, double-blind, phase 3, non-inferiority trial. Lancet HIV., e211-e220. doi: 10.1016/S2352-3018(18)30021-3.
- Orkin, C. (2019). Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate is Non-inferior to Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate in Treatment-naïve Adults With Human Immunodeficiency Virus-1 Infection: Week 48 Results of the DRIVE-AHEAD Trial. Clin Infect Dis., 535-544. doi: 10.1093/cid/ciy540.
- Orrell, C. (2017). Fixed-dose combination dolutegravir, abacavir, and lamivudine versus ritonavir-boosted atazanavir plus tenofovir disoproxil fumarate and emtricitabine in previously untreated women with HIV-1 infection (ARIA): week 48 results from a randomised, open-label. Lancet HIV., e536-e546. doi: 10.1016/S2352-3018(17)30095-4.
- Puls, R.L. (2010). Efavirenz versus boosted atazanavir or zidovudine and abacavir in antiretroviral treatment-naïve, HIV-infected subjects: week 48 data from the Altair study. Clin Infect Dis., 855-864. doi: 10.1086/656363.
- Raffi, F. (2013). Once-daily dolutegravir versus raltegravir in antiretroviral-naïve adults with HIV-1 infection: 48 week results from the randomised, double-blind, non-inferiority SPRING-2 study. Lancet, 735-743. doi: 10.1016/S0140-6736(12)61853-4.
- Sax, P.E. (2012). Co-formulated elvitegravir, cobicistat, emtricitabine, and tenofovir versus co-formulated efavirenz, emtricitabine, and tenofovir for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3 trial, analysis of results after 48 weeks. Lancet, 2439-2448. doi: 10.1016/S0140-6736(12)60917-9.
- Sax, P.E. (2017). Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide, for initial treatment of HIV-1 infection (GS-US-380-1490): a randomised, double-blind, multicentre, phase 3, non-inferior. Lancet, 2073-2082. doi: 10.1016/S0140-6736(17)32340-1.
- Walmsley, S.L. (2013). Dolutegravir plus abacavir-lamivudine for the treatment of HIV-1 infection. N Engl J Med., 1807-1818. doi: 10.1056/NEJMoa1215541.
- Programa Anual de Adquisiciones, Arrendamientos, Servicios y Obras Públicas (PAAASOP) del Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE), 2023.
- Programa Anual de Adquisiciones, Arrendamientos, Servicios y Obras Públicas (PAAASOP) del Instituto Mexicano del Seguro Social (IMSS), 2023.