Conitec

Recomendation report

DRUGS

Nº 515

March/2020

Dolutegravir for the treatment of pregnant women living with HIV

Brasília – DF
2020

Technology: Dolutegravir sodium 50 mg (Tivicay®)

Indication: Antiretroviral therapy in pregnant women living with Human Immunodeficiency Virus (HIV)

Applicant: Health Surveillance Department of the Ministry of Health of Brazil

Background: HIV, which stands for Human Immunodeficiency Virus, is a retrovirus that causes AIDS (Acquired Immune Deficiency Syndrome). In 2018, a total of 4,026 pregnant women living with HIV were identified, with the indication to start antiretroviral therapy (ART). The timely initiation of ART, with improved adherence and tolerability, is critical for achieving an undetectable viral load, and, consequently, preventing vertical transmission (VT) of HIV.

Question: Is the use of dolutegravir 50 mg, in combination with other antiretroviral drugs, effective, safe and cost-effective for the treatment of pregnant women living with HIV in initiation of ART, when compared with raltegravir 400 mg?

Scientific evidence: The use of integrase inhibitors in pregnancy was not recommended in the Clinical Protocol and Therapeutic Guidelines for the Management of HIV Infection in Adults, 2017, due to uncertainties about their safety – initial studies had highlighted a possible link between dolutegravir (DTG) and neural tube defects in infants born to women using the drug at the time of conception. In a study conducted in Botswana by Zash et al. (2019), the prevalence of neural tube defects associated with using DTG was 0.30%. The National Cohort Study of Dolutegravir and Pregnancy Outcomes in Brazil was conducted on women living with HIV (WLHIV) who became pregnant while taking ART regimens containing DTG, efavirenz (EFZ) or raltegravir (RAL). Of the 1,468 women included in the study, 382 were DTG-exposed, compared with 1,086 EFZ- or RAL-exposed, and no neural tube defects (NTDs) were detected in either exposure group. Modeling studies on the risks and benefits of DTG in WLHIV of reproductive potential in initiation of ART suggested that the advantages of DTG of greater and more rapid maternal viral suppression, and reduction of both sexual and vertical transmission of HIV, outweigh the risks related to NTDs.

International recommendations: In 2019, the World Health Organization (WHO) published the updated Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. In the current recommendation, the role of DTG as the preferred first-line antiretroviral therapy (ART) regimen has been reaffirmed, due to the decline in NTDs reported in the above-mentioned observational studies. Moreover, it has been demonstrated the efficacy of DTG in achieving greater viral suppression and lower chance of discontinuation compared with regimens containing efavirenz.

Economic evaluation: There are no direct comparison studies between dolutegravir 50 mg and raltegravir 400 mg for the treatment of pregnant women living with HIV who start treatment during pregnancy; however, studies in non-pregnant population have shown non-inferiority of DTG compared with RAL. Therefore, a cost-minimization analysis was conducted, and found that dolutegravir 50 mg replacing raltegravir 400 mg was less expensive, with a saving of BRL 6,566.78 per pregnant woman living with HIV who starts treatment during pregnancy.

Budget impact analysis: The budget impact of replacing raltegravir 400 mg twice daily with dolutegravir 50 mg once daily, in the initial ART regimen in pregnant women, has been estimated at a saving of BRL 24,908,344.38 in the first year (2020), which would continue for the next four years. Thus, at the end of five years (2020-2024), the accumulated savings would be BRL 124,846,181.19 with dolutegravir 50 mg as the drug of choice to start ART during pregnancy.

Considerations: Dolutegravir 50 mg is an antiretroviral drug already incorporated into the Brazilian Public Health System (SUS) for the treatment of people living with HIV. In the study by Zash et al. (2019), dolutegravir 50 mg showed a risk of neural tube defects of 0.3%, compared with 0.1% in the general population. But in the study by Pereira et al. (2019), in Brazil there were no NTDs among the 382 cases of periconceptional exposure to DTG, and similar results have been found in studies conducted in France and Canada. In regard to the economic evaluation, dolutegravir 50 mg replacing raltegravir 400 mg proved to be less expensive in the cost-minimization analysis.

Initial Recommendation: The members of CONITEC's plenary session considered recent safety studies, published including in Brazil, which reported that there were no cases of neural tube defects or other serious adverse events with the use of dolutegravir, as well as the WHO recommendation on the use of this drug as the preferred first- and second-line treatment for both pregnant women and women with the potential to become pregnant. Thus, Conitec, at its 83rd Ordinary Meeting, decided that the subject matter should be made available in a public consultation with a favorable preliminary recommendation to the expansion of the use of dolutegravir for antiretroviral therapy in pregnant women living with HIV, in the scope of SUS.

Public consultation: The Conitec's Recommendation Report was made available through the Public Consultation No. 74/2019, between December 16th, 2019 and January 16th, 2020. Ninety-one contributions were received, four of which were technical-scientific contributions, and 87 were experience or opinion contributions. After analyzing the contributions received in the Public Consultation, CONITEC's plenary session decided that there was not sufficient reason to change the preliminary recommendation, which was to expand the use of dolutegravir in pregnant women living with HIV, from the second trimester of pregnancy, in the scope of SUS.

Final Recommendation: The Conitec's members present at the 85th Ordinary Meeting, on February 5th, 2020, unanimously decided to recommend the expansion of the use of dolutegravir for the treatment of pregnant women living with HIV from the second trimester of pregnancy. The Deliberation Record No. 506/2020 was signed.

Decision: To expand the use of dolutegravir for the treatment of pregnant women living with HIV, in the scope of SUS, according to Ordinance No. 4, published in the Official Gazette of the Federal Executive No. 44, Section 1, page 130, on March 5th, 2020.