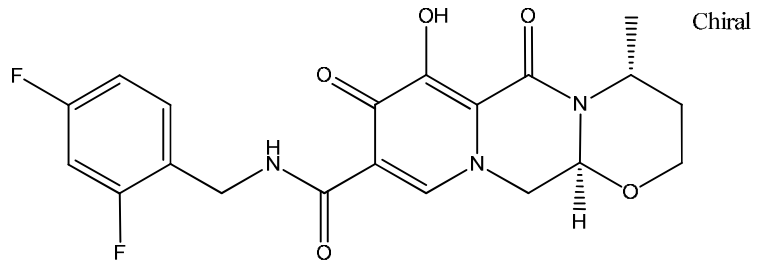
MODULE 2.6.1. INTRODUCTION

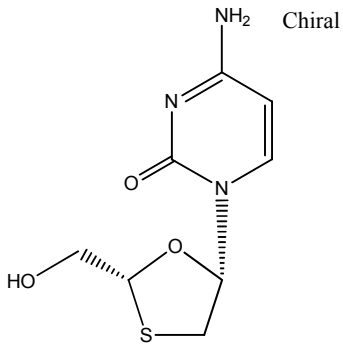
1. INTRODUCTION

Dolutegravir (DTG) is an integrase inhibitor (INI) and abacavir (ABC) and lamivudine (3TC) are nucleoside reverse transcriptase inhibitors (NRTIs). A once daily fixed dose combination (FDC) single tablet regimen (STR) that combines DTG with ABC and 3TC is being developed for use in the treatment of human immunodeficiency virus (HIV) infection.

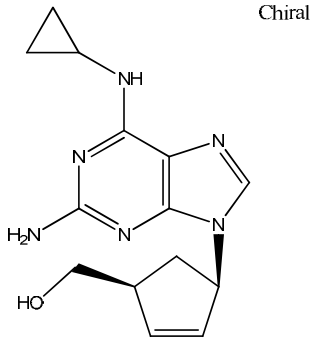
Figure 1 Structure of DTG, ABC and 3TC



Dolutegravir (DTG)



Lamivudine (3TC)



Abacavir (ABC)

In agreement with ICH Guidance M3 (R2), nonclinical combination studies with DTG/ABC/3TC were not considered warranted to support the current application.

To support marketing, DTG, ABC and 3TC have been tested individually in comprehensive nonclinical development programs. Reports of these studies have been previously submitted and reviewed as part of the marketing application approvals.

Since the submission of the original New Drug Application for dolutegravir (NDA 204-790), 2 new pharmacokinetic studies have been completed In one study, dolutegravir interactions with additional transporters were investigated in vitro and in the other study, an assessment of the renal transport inhibition potential by dolutegravir on

the kidney exposure to tenofovir was conducted using a physiological based pharmacokinetic model.

No new previously unsubmitted nonclinical studies have been conducted with ABC (NDA 020-977) or 3TC (NDA 020-564).

A full description of the 2 new pharmacokinetic studies is provided in proceeding sections [m2.6.4 and m2.6.5]. The corresponding company reports are located in m4.2, Study Reports.