21 August 2025
EMADOC-1700519818-2216398
Human Medicines Division

Assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006

Triumeq

Dolutegravir / Abacavir / Lamivudine

Procedure no.: EMA/PAM/0000279528

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Status of this report and steps taken for the assessment			
Current step	**Description**	**Planned date**	**Actual Date**
☐	Start of Procedure	23 June 2025	23 June 2025
☐	CHMP Rapporteur AR	28 July 2025	31 July 2025
☐	CHMP comments	11 August 2025	N/A
☐	Updated CHMP Rapporteur AR	14 August 2025	N/A
☒	CHMP outcome	21 August 2025	21 August 2025

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Abbreviations

Abbreviation	Definition
ABC/DTG/3TC	Abacavir/dolutegravir/lamivudine
AE	Adverse event
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
CIOMS	Council for International Organizations of Medical Sciences
COVID-19	Coronavirus disease 2019
CRO	Contract research organization
DAIDS	Division of AIDS (United States)
DT	Dispersible tablet
DTG	Dolutegravir
FDC	Fixed dose combination
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human immunodeficiency virus
HIV-1	Human immunodeficiency virus type 1
ICF	Informed consent form
ICH	International Council for Harmonisation
IEC	Independent Ethics Committee
IRB	Institutional Review Board
Max	Maximum
Min	Minimum
SAE	Serious adverse event
SD	Standard deviation

1. Introduction

On 10 June 2025, the MAH submitted a completed paediatric study for Triumeq, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

The MAH stated that the Open-label access to dolutegravir for HIV-1 infected children and adolescents completing IMPAACT Studies P1093 and P2019 (Study Number: 205858) is a standalone study.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

2.2. Information on the pharmaceutical formulation used in the study

The study utilized two primary pharmaceutical formulations of dolutegravir (DTG):

1: Single Entity DTG (Tivicay or Tivicay DT): This formulation contained dolutegravir as the sole active ingredient in dispersible tablet form. The dose of DTG was 5 mg for the dispersible tablet and 10 mg, 25 mg, or 50 mg for the film-coated tablet. Tablets were taken once daily, unless the participant was taking concomitant medications known for enzyme induction, in which case DTG was taken twice daily.

2: Fixed-Dose Combination (FDC) ABC/DTG/3TC (Triumeq or ABC/DTG/3TC DTs): This formulation combined abacavir (ABC), dolutegravir (DTG), and lamivudine (3TC) into a single tablet or dispersible tablet form. For the ABC/DTG/3TC FDC, the dose was 60 mg/5 mg/30 mg for the dispersible tablet and 600 mg/50 mg/300 mg for the film-coated tablet, also taken once daily, with the option for twice-daily dosing if the participant was taking concomitant medications.

Both formulations were available in dispersible tablet and film-coated tablet formulations. Tablets were taken orally, with or without food, and the dosing regimen was based on the participant's weight. The batch numbers for the study interventions were documented.

The dispersible tablet formulation of DTG and ABC/DTG/3TC was deemed suitable for paediatric use. The study did not provide information on conditions for extemporaneous formulations.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

Study 205858: Open-label access to dolutegravir for HIV-1 infected children and adolescents completing IMPAACT Studies P1093 and P2019.

EudraCT, CTIS: 2011-001646-16, ClinicalTrials.gov: NCT03016533

Description

The study is an open-label, multi-centre, non-comparative rollover study designed to provide continued access to age-appropriate formulations of DTG for eligible participants who have completed either the P1093 or IMPAACT 2019 parent studies. The study was conducted in compliance with GCP and involved

18 centres across the following countries: Botswana, Brazil, Kenya, South Africa, Tanzania, Thailand, Uganda, United States, and Zimbabwe.

The Applicant submitted a statement that the study was conducted in compliance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP).

Methods

Study participants

Paediatric participants with HIV-1 who had completed one of the parent studies (P1093 or IMPAACT 2019) and demonstrated virologic control at screening.

Key exclusion criteria included confirmed virologic failure with evidence of resistance to DTG or ABC/DTG/3TC, presence of any active AIDS-defining opportunistic infection, or other known laboratory toxicity or clinically relevant exclusionary findings.

Treatments

Participants received either single entity DTG (Tivicay) or the fixed-dose combination (FDC) of abacavir, dolutegravir, and lamivudine (ABC/DTG/3TC, Triumeq), based on their participation in the parent studies. The study intervention was taken orally at weight-based doses, with or without food, and the dose of DTG was adjusted based on the participant's weight.

The study intervention was planned to be provided to each participant in this Rollover study until an age-appropriate formulation was available from some other source, a participant was no longer deriving benefit, protocol-defined reason for discontinuation or termination of the development of the study intervention.

Other antiretrovirals were not provided by the Rollover study, were not considered part of the Rollover study, and were supplied locally.

Objective(s)

The primary objective was to provide access to age-appropriate formulations of DTG for eligible participants. The secondary objective was to assess serious adverse events (SAEs) and adverse events (AEs) leading to discontinuation of the study intervention.

Outcomes/endpoints

Incidence and severity of SAEs and AEs leading to discontinuation of study intervention.

Laboratory chemistry and hematology assessments, vital signs, height, weight and BMI were performed per local practice and not entered in the clinical database unless the result(s) were considered to be an SAE by the investigator or led to discontinuation of study intervention.

Sample size

Based on the design of the parent studies, target enrolment was a maximum of 300 participants.

Randomisation and blinding (masking)

Non-randomized, open label.

Statistical Methods

No formal hypothesis testing was performed. Available data were analysed descriptively to provide information on safety and tolerability. The analysis population (Safety Population) included all participants who received at least one dose of the study intervention.

Results

Participant flow

115 paediatric participants with HIV-1 were screened, of which 100 were enrolled.

All 100 participants who started the study received treatment and were included in the safety analysis.

Overall, 82 (82%) participants completed the study, and 18 (18%) participants withdrew. The most common reasons given for treatment discontinuation overall were physician decision, withdrawal by participant, and protocol deviation. None of the reasons for treatment discontinuation were related to study intervention.

Overall, 65 participants had important protocol deviations (40 participants with ICH/GCP deviations and 54 participants with protocol deviations), none of which were considered to affect analysis of the results.

Recruitment

Participants were recruited from the parent studies P1093 and IMPAACT 2019.

First participant first visit: 07 June 2017

Last participant last visit: 24 December 2024

Database lock date: 21 January 2025.

Baseline data

Characteristic	ABC/DTG/3TC N=39	DTG N=61	Overall N=100
Sex, n(%)			
Male	22 (56)	29 (48)	51 (51)
Female	17 (44)	32 (52)	49 (49)
Age (years)			
Mean (SD)	6.7 (3.14)	7.5 (4.07)	7.2 (3.74)
Median (Min, Max)	7.0 (1.0, 12.0)	6.0 (3.0, 21.0)	7.0 (1.0, 21.0)
Age Group (years), n(%)			
<2	2 (5)	0	2 (2)
2 to <6	15 (38)	22 (36)	37 (37)
6 to <12	20 (51)	29 (48)	49 (49)
12 to <18	2 (5)	8 (13)	10 (10)
≥18	0	2 (3)	2 (2)
Ethnicity, n (%)			
Hispanic or Latino	0	12 (20)	12 (12)
Not Hispanic or Latino	39 (100)	49 (80)	88 (88)
Race, n(%)			
Asian	15 (38)	11 (18)	26 (26)
Black or African American	23 (59)	47 (77)	70 (70)
White	1 (3)	3 (5)	4 (4)
Weight, kg[a]			
Mean (SD)	21.8 (7.78)	23.5 (9.08)	22.9 (8.60)
Median (Min, Max)	20.6 (10.4, 42.8)	20.6 (13.9, 56.0)	20.6 (10.4, 56.0)

Source: Table 1.5

a. Weight was collected at Visit 1

Exposure

The median (range) exposure duration to study intervention in this Rollover study was 1.474 years (0.04 to 4.61 years) in the DTG arm and 1.633 years (0.25 to 2.40 years) in the ABC/DTG/3TC arm.

Efficacy results

There were no efficacy endpoints.

Safety results

Overall, 8 participants (5 participants in the DTG arm and 3 participants in the ABC/DTG/3TC arm) experienced at least 1 SAE; none were considered related to study intervention, none led to treatment discontinuation, and none were fatal. Four out of 8 SAEs had a maximum intensity of Grade 3; the remaining were Grade 2 (n=3) and Grade 1 (n=1). The most common SAE overall was COVID-19 (reported for 2 participants, 1 in each arm), no other SAEs were reported in more than 1 participant.

There were no deaths.

There were no AEs that let to permanent discontinuation of study intervention.

System Organ Class	Preferred Term	ABC/DTG/3TC (N=39)	DTG (N=61)	Overall (N=100)
Any Event	Number of participants with SAEs	3 (8%)	5 (8%)	8 (8%)
	Number of SAEs	3	5	8
Blood and lymphatic system disorders	Anaemia megaloblastic	0	1 (2%)	1 (1%)
Gastrointestinal disorders	Haemoperitoneum	0	1 (2%)	1 (1%)
Infections and infestations	COVID-19	1 (3%)	1 (2%)	2 (2%)
	Dengue fever	1 (3%)	0	1 (1%)
	Epididymitis	0	1 (2%)	1 (1%)
	Gastroenteritis	1 (3%)	0	1 (1%)
Nervous system disorders	Petit mal epilepsy	0	1 (2%)	1 (1%)

Discussion on clinical aspects

Tivicay (dolutegravir) 5 mg dispersible tablets are authorised in the EU in combination with other anti-retroviral medicinal products for the treatment of Human Immunodeficiency Virus (HIV) infected children of at least 4 weeks of age or older and weighing at least 3 kg. Film-coated tablets are authorised for use in children of at least 6 years of age or older and weighing at least 14 kg.

Triumeq (dolutegravir, abacavir, lamivudine) 5 mg/60 mg/30 mg dispersible tablets are authorised in the EU for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infected children of at least 3 months of age and weighing at least 6 kg to less than 25 kg. Film-coated tablets are authorised for use in children weighing at least 25 kg.

Study 205858 is a completed, open-label rollover paediatric study intended to provide continued access to age-appropriate formulations of Tivicay and Triumeq to 100 paediatric patients with HIV-1 infection who had completed IMPAACT Studies P1093 and P2019, for up to 4.61 years on Tivicay and up to 2.40 years on Triumeq. This was a standalone study.

Safety assessment was only a secondary objective and safety endpoints were limited to SAEs and AEs leading to discontinuation of study intervention. Furthermore, the uncontrolled study design, absence of complete, solicited and unsolicited TEAE reporting, and lack of information on comorbidities and concomitant antiretrovirals or other medications limit interpretation of the safety data.

A total of 8/100 (8%) participants in the Safety Population reported SAEs. Review of the case narratives for all 8 SAEs indicates that none of the events were plausibly related to administration of the study intervention. There were no AEs that let to permanent discontinuation of study intervention and no deaths.

Overall, no new safety concerns are raised.

Conclusion on clinical aspects

Study 205858 was designed as a rollover AAF access study and was not intended to provide substantial or standalone clinical safety data. Due to the study design the new safety information provided is very limited. No new safety concerns are raised. No regulatory action is required.

3. Rapporteur's overall conclusion and recommendation

☒ **Fulfilled:**

No regulatory action required.