Study Protocol

P3-C1-020

Use of antiretroviral therapies in paediatric patients

12/01/2026

Version 5.0

Contents

Study title	DARWIN EU® - Use of antiretroviral therapies in paediatric patients
Protocol version	V5.0
Date	12/01/2026
EU PAS number	EUPAS1000000545
Active substance	J05AE Protease inhibitors J05AF Nucleoside and nucleotide reverse transcriptase inhibitors J05AG Non-nucleoside reverse transcriptase inhibitors J05AJ Integrase inhibitors J05AR Antivirals for treatment of HIV infections, combinations J05AX Other antivirals: J05AX09 maraviroc J05AX07 enfuvirtide J05AX29 fostemsavir J05AX31 lenacapavir V03AX03 cobicistat
Medicinal product	Not applicable
Research question and objectives	The aim of this study is to gain insight into the prevalence and incidence of HIV and use of antiretroviral therapies in paediatric patients with HIV in the EU. The specific objectives of this study are: 1. To describe the prevalence and incidence of HIV in the paediatric general population in a sample of European countries (Spain, Germany and Norway), overall (and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year 2. To describe the prevalence and incidence of use of HIV-specific medication in the paediatric HIV population in a sample of European countries (Germany and Norway) particularly fixed-dose combinations, overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year. 3. To describe the prevalence and incidence of use of HIV-specific medication in the paediatric general population in a sample of European countries (Germany, Norway, and the United Kingdom) particularly fixed-dose combinations, overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year
Countries of study	This study will include 4 databases, representing 4 countries in Europe: • Spain: BIFAP • Germany: InGef RDB • Norway: NLHR •
Author(s)	Guido van Leeuwen (g.vanleeuwen@darwin-eu.org) Katia Verhamme (k.verhamme@darwin-eu.org)

LIST OF ABBREVIATIONS

Acronyms/terms	**Description**
AIDS	Acquired Immunodeficiency Syndrome
ART	Anti-Retroviral Therapy
BIFAP	Base de Datos para la Investigacíon Farmacoepidemiológica en el Ámbito Público
CDM	Common Data Model
CC	Coordinating centre
DARWIN EU®	Data Analysis and Real-World Interrogation Network
DQD	Data Quality Dashboard
DOI	Declaration of Interests
DRE	Digital Research Environment
EHR	Electronic Health Records
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
FDC	Fixed-Dose Combinations
GDPR	General Data Protection Regulation
HIV	Human Immunodeficiency Virus
ICD	International Classification of Diseases
InGef RDB	InGef Research Database
IP	Inpatient
NLHR	Norwegian Linked Health Registry data
OHDSI	Observational Health Data Sciences and Informatics
OMOP	Observational Medical Outcomes Partnership
OP	Outpatient
PDCO	Paediatric committee
PrEP	Pre-Exposure Prophylaxis
PIP	Paediatric Investigation Plan
RWD	Real-World Data
SNOMED	Systematized Nomenclature of Medicine
WHO	World Health Organisation

1. TITLE

DARWIN EU® - Use of antiretroviral therapies in paediatric patients

2. RESPONSIBLE PARTIES – STUDY TEAM

Study team role	Names	Organisation
Principal Investigator	Guido van Leeuwen Katia Verhamme	Erasmus MC
Data Scientist	Ross Williams Maarten van Kessel Cesar Barbosa Ger Inberg Adam Black	Erasmus MC
Epidemiologist/ Clinical Domain Expert	Guido van Leeuwen Katia Verhamme	Erasmus MC
Study Manager	Natasha Yefimenko	Erasmus MC
Data Partner*	**Names**	**Organisation**
BIFAP	Miguel Angel Macia Martinez Elisa Martin-Merino Hermenegildo Martínez-Alcalá Ana Llorente-Garcia	Agencia Española de Medicamentos Y Productos Sanitarious (AEMPS)
InGef RDB	Josephine Jacob Raeleesha Norris Annika Vivirito Alexander Harms	Institut für angewandte Gesundheitsforschung Berlin GmbH
NLHR	Hedvig Marie Egeland Nordeng Nhung Trinh	University of Oslo

*Data partners' role is only to execute code at their data source, review and approve their results. They do not have an investigator role. Data analysts/programmers do not have an investigator role and thus declaration of interests (DOI) for them is not needed.

3. ABSTRACT

Title

DARWIN EU® – Use of antiretroviral therapies in paediatric patients

Rationale and background

Human immunodeficiency viruses (HIV) are retroviruses that can cause acquired immunodeficiency syndrome (AIDS), a condition that leads to progressive failure of the immune system making an individual vulnerable to opportunistic infections and cancers.(1-3)

The optimisation of HIV treatment has been facilitated by a long-term joint collaborative effort between international organizations, academic institutions, innovator and generic manufacturers and other stakeholders, particularly over the last decade. The WHO PADO initiative for instance marks progress and discusses also paediatric needs. Several FDCs have been authorised for use in paediatric patient in the latest years.

This study is intended to help the assessment of a current request for a paediatric investigation plan (PIP) waiver and future similar requests, submitted under the assumption that studies in paediatrics are not possible as HIV infection is very low in this population and that the treatments needs of such patients are already met by existing medications in first line.

To support this paediatric waiver request, real-world data (RWD) from prescription data from Germany and Spain indicating very low number of children living with HIV in EU countries was submitted. And although there may be very few young patients living with HIV infection in the EU, it is relevant for the PDCO to know more about prevalent cases of HIV in in this population and better understand prescription patterns in various age groups and understand the prevalence of the use of fix-dose combination (FDC) products.

This study will establish the prevalence of HIV infection amongst paediatric patients as well as the prevalence and incidence of antiretroviral therapy within this paediatric population particularly for FDC products, to estimate the current utilisation of some active substances.

Research question and objectives

The aim of this study is to gain insight into the prevalence and incidence of HIV and use of antiretroviral therapies in paediatric patients

The specific objectives of this study are:

1) To describe the prevalence and incidence of HIV in the paediatric general population in a sample of European countries (Spain, Germany and Norway), overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year
2) To describe the prevalence and incidence of use of HIV-specific medication in the paediatric HIV population in a sample of European countries (Germany and Norway) particularly fixed-dose combinations, overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year.
3) To describe the prevalence and incidence of use of HIV-specific medication in the paediatric general population in a sample of European countries (Germany, Norway, and the United Kingdom) particularly fixed-dose combinations, overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year

Methods

Study design

This is a descriptive population-level epidemiology study and population-level drug utilisation study (DUS).

Population

The study population will include all children (<18 years of age) present in the database during the study period 01/01/2010 to 31/12/2024 overall, or to the end of available data, and with at least 365 days of database history prior to index date (i.e., start of follow-up). This requirement of 1 year of database history did not hold for children aged 0–2 years. The study period for InGef RDB started on 01/01/2016 and on 01/01/2019 for NLHR, due to the absence of (reliable) data prior to those dates.

Outcomes of interest

- Prevalence and incidence of HIV infection in a sample of European countries (Spain, Germany, and Norway), overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year
- Prevalence and incidence of use of HIV-specific medication in the paediatric HIV population in a sample of European countries (Germany and Norway) overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year and type of regimen, particularly as FDCs.
- Prevalence and incidence of use of HIV-specific medication in the paediatric general population in a sample of European countries (Germany, Norway and the UK) overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year and type of regimen, particularly as FDCs.

  Antiretroviral drugs of interest are the following:

  - J05AE Protease inhibitors
  - J05AF Nucleoside and nucleotide reverse transcriptase inhibitors
  - J05AG Non-nucleoside reverse transcriptase inhibitors
  - J05AJ Integrase inhibitors
  - J05AR Antivirals for treatment of HIV infections, combinations
  - J05AX Other antivirals:
    - J05AX09 maraviroc
    - J05AX07 enfuvirtide
    - J05AX29 fostemsavir
    - J05AX31 lenacapavir
    - V03AX03 cobicistat

Data source

- Base de Datos para la Investigacíon Farmacoepidemiológica en el Ámbito Público (BIFAP), Spain (objective 1 only)
- InGef Research Database (InGef RDB), Germany
- Norwegian Linked Health Registry data

Sample size

No sample size has been calculated as this is a descriptive disease and drug epidemiology study where we are interested in the prevalence and incidence rates of HIV and prevalence and incidence of antiretroviral drugs in each database, irrespective of the sample size.

Based on a preliminary feasibility assessment, the expected number of persons counts for HIV in the databases included in this study were 1,800 (InGef RDB), 4,600 (NLHR) and 17,200 (BIFAP). Preliminary counts for ART were 4,200 (InGef RDB), 5,900 (NLHR), while no counts were present in BIFAP (will contribute to objective 1 only).

Statistical analysis

Yearly incidence rates per 1,000 person-years and period prevalence of HIV infection and use of HIV-specific medications will be estimated in children, overall and stratified by age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year.

The statistical analyses will be performed based on OMOP-CDM mapped data using *"IncidencePrevalence"* R package.

A minimum cell counts of 5 will be used when reporting results, with any smaller count reported as "<5".

4. AMENDMENTS AND UPDATES

Amendment number	Previous approved version of the report	Date	Section of the study	Amendment or update	Reason
1	Not applicable	28-11-2025	Concept sets	Refinement of ART combination concept set and refinement of individual ART class concept sets. There are now 3 concepts sets per Individual ART class, overall, monotherapy, and combinations related to the ingredients.	Advice from requesters to get more accurate and correct results for ARTs.
2	Not applicable	28-11-2025	Data partners	NNRD (National Neonatal Research Database removed) from study	Umbrella IRB approval not received in time

5. MILESTONES

Study milestones and deliverables	Planned dates*
Draft Study Protocol	06/01/2025
Final Study Protocol	07/03/2025
Creation of Analytical code	January/February/March 2025
Execution of Analytical Code on the data	March 2025
Draft Interim Study Report	30/05/2025
Draft Final Study Report	01/09/20205
Final Study Report	01/10/2025

*Planned dates are dependent on obtaining approvals from the internal review boards of the data sources.

6. RATIONALE AND BACKGROUND

Human immunodeficiency viruses (HIV) are retroviruses that can cause acquired immunodeficiency syndrome (AIDS), a condition that leads to progressive failure of the immune system making an individual vulnerable to opportunistic infections and cancers. (1-3)

Generally, HIV is a sexually transmitted infection that follows from contact with blood, semen or vaginal fluid. However, non-sexual transmission can occur from an infected mother to her infant during pregnancy or during childbirth by exposure to her blood or vaginal fluid. (4-7)

The average survival time after infection without treatment is estimated to be 9 to 11 years.(8) At this moment HIV is treated with antiretroviral therapy (ART) and usually a combination of various ART medications are given.(9) Studies have shown that early treatment initiation and factors such as younger

age and female sex are associated with a better treatment effect.(10) ART has changed the course of HIV and often lead to a near-normal lifespan, especially when treatment is initiated early. (11, 12)

This study is intended to help the assessment of requests for a paediatric investigation plan (PIP) and/or waivers. Overall the assumption is that clinical studies in paediatrics are of difficult feasibility as HIV infection is very low in this population in the EU and that the treatments needs of such patients are already met by existing medications.

To support this paediatric waiver request, real-world data (RWD) from prescription data from Germany and Spain indicating very low number of children living with HIV in EU countries was submitted. And although there may be very few young patients living with HIV infection in the EU, it is relevant for the PDCO to know more about prevalent cases of HIV in in this population and better understand prescription patterns in various age groups.

7. RESEARCH QUESTION AND OBJECTIVES

The aim of this study is to gain insight into the prevalence and incidence of HIV and use of antiretroviral therapies in paediatric patients with HIV.

The specific objectives of this study are:

1. To describe the prevalence and incidence of HIV in the paediatric general population in a sample of European countries (Spain, Germany and Norway), overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year
2. To describe the prevalence and incidence of use of HIV-specific medication in the paediatric HIV population in a sample of European countries (Germany and Norway) particularly fixed-dose combinations, overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year.
3. To describe the prevalence and incidence of use of HIV-specific medication in the paediatric general population in a sample of European countries (Germany, Norway, and the United Kingdom) particularly fixed-dose combinations, overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12, 12-<18) and calendar year.

Table 1 provides more details on the specific objectives.

Table 1. Primary and secondary research questions and objective.

A. Primary research question and objective.

Objective:	1. To describe the prevalence and incidence of HIV in the paediatric population in a sample of European countries (Spain, Germany and Norway),overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year. 2. To describe the prevalence and incidence of use of HIV-specific medication in the paediatric HIV population in a sample of European countries (Germany and Norway) particularly FDCs, overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and stratified by calendar year 3. To describe the prevalence and incidence of use of HIV-specific medication in the paediatric population in a sample of European countries (Germany, Norway and the United Kingdom) particularly

	FDCs, overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and stratified by calendar year.
Hypothesis:	None.
Population *(mention key inclusion-exclusion criteria):*	Objective 1 and 3: All children (<18 years of age) present in the databases between 2010 and 2024 and with at least 365 days of prior history in the database. Objective 2: All children (<18 years of age) present in the databases with a diagnosis of HIV between 2010 and 2024 and with at least 365 days of prior history in the database. For outpatient HIV diagnoses in InGef, we move the cohort entry date to 3 months before diagnoses or to date of birth, whichever occurs first. For children within the age group of 0-<2 years, the need to have 365 days of prior database history will be dropped.
Exposure:	None.
Comparator:	None.
Outcome:	HIV diagnosis (objective 1) Antiretroviral drugs (objective 2)
Time *(when follow up begins and ends):*	Study period will be from 1st January 2010 to 31st December 2024 in children <18 years of age. Follow-up for Objective 1 will start at the beginning of the study period until the earliest of the following: 1) censoring (i.e. diagnosis of HIV), 2) loss to follow-up, 3) end of data availability, 4) occurrence of death or 5) end of study period. Follow-up for Objectives 2 and 3 will start at the beginning of the study period until the earliest of the following: 1) loss to follow-up, 2) end of data availability, 3) occurrence of death or 4) end of study period.
Setting:	Routinely collected data from 4 databases in 4 European countries
Main measure of effect:	<u>Objective 1:</u> Annual prevalence rates of a HIV diagnosis in children aged <18. Results will be presented by database overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year Annual incidence rates, expressed as number of new HIV diagnoses in children aged <18, per 1,000 person years. Results will be presented by database overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year. <u>Objective 2:</u> Annual prevalence rates of ART use in children aged <18 (with a HIV diagnosis). Results will be presented by database and drug overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year Annual incidence rates, expressed as number of new ART users in children aged <18 (with a HIV diagnosis), per 1,000 person years. Results will be presented by database and drug overall and

	stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year Objective 3: Annual prevalence rates of ART use in children aged <18. Results will be presented by database and drug overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year Annual incidence rates, expressed as number of new ART users in children aged <18, per 1,000 person years. Results will be presented by database and drug overall and stratified by sex, age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year

8. RESEARCH METHODS

8.1 Study type and study design

The proposed designs for this study are a population-level descriptive epidemiology study and population-level DUS study as "Off-the-shelf", as described in the DARWIN EU® Complete Catalogue of Standard Data Analyses.(13)

Table 2. Description of potential study types and related study designs.

Study type	Study design	Study classification
Population-level descriptive epidemiology	Population-level cohort	Off the shelf
Population-level DUS study	Population-level cohort	Off the shelf

8.2 Study setting and data sources

This study will use routinely collected health data from 4 databases in the DARWIN EU® network of data partners from 4 countries. All databases were previously mapped to the OMOP CDM.

Data source

- Base de Datos para la Investigacíon Farmacoepidemiológica en el Ámbito Público (BIFAP), Spain (objective 1)
- InGef Research Database (InGef RDB), Germany (all 3 objectives)
- Norwegian Linked Health Registry data (all 3 objectives)

These databases fulfil the criteria required in terms of data quality, completeness, timelines, and representativeness for population-level descriptive epidemiology and population-level DUS while covering different regions of Europe.

BIFAP will only be included in the final version of the report due to delays in CDM updates and IRB approval, respectively. The interim version of the report will only include data from InGef RDB and NLHR. Detailed information on the selected data sources is described in **Table 3**. When it comes to assessing the reliability of data sources, the data partners are asked to describe their internal data quality process on the

source data as part of the DARWIN EU® onboarding procedure. To further ensure data quality, we utilised the Achilles tool,(14) which systematically characterises the data and generates data characteristics such as age distribution, condition prevalence per year, data density. Data density includes information on 1) monthly record counts by data domain (which offers insights into data collection patterns and the start date of each data source), 2) measurement value distribution (i.e. min, max, quartiles for numeric values per measurement concept and per unit and counts for discrete measurement-value pairs). The latter can be compared against expectations for the data based on predefined standards, historical trends, or known epidemiological patterns to identify potential anomalies or inconsistencies. Additionally, the data quality dashboard (DQD) provides more objective checks (see Section D1.3.5.2 on Complete Data Quality Assurance Package) on plausibility of data completeness, consistency, and conformity across the data sources.

In terms of relevance, the selection of databases was based on the availability of data on the selected condition (HIV), the drug treatments (antiretroviral drugs) to perform the described analyses. In addition, the databases were chosen considering their ability to support timely IRB approvals, thus ensuring alignment with the timeline established by stakeholders for the conduct of this study. The DARWIN EU® portal as well as information from the onboarding documents were used to assess whether databases have information on use of drugs treatments and indications of interest. Data within the DARWIN EU® portal is maintained up to date by extracting the release dates for each dataset in the network and monitoring when data are out-of-date with the expected refresh cycle (typically quarterly or half-yearly). In addition, it is important to have a clear understanding of the time covered by each released database, as this can vary across different domains. To facilitate this, the CDMOnboarding (and Achilles) packages contain a 'data density' plot.(14) This plot displays the number of records per OMOP domain monthly. This allows to get insights when data collection started, when new sources of data were added and until when data was included. In addition, at time of inviting data partners, they were informed about study objectives and asked whether they could participate in the study.

More general-purpose diagnostic tools, *CohortDiagnostics* and *DrugExposureDiagnostics*, have been developed.(15, 16) The *CohortDiagnostics* package provides additional insights into cohort characteristics, record counts and index event misclassification.(15) The *DrugExposureDiagnostics* package evaluates ingredient-specific attributes and patterns in drug exposure records.(16) Upon finalisation of the study protocol and creation of the disease and drug cohorts of interest by DARWIN EU® Coordination Centre, these packages will be executed in each data sources by each data partners.

Table 3. Description of the selected data sources.

Country	Name of Database	Justification for Inclusion	Health Care setting	Type of Data	Number of active subjects	Feasibility counts of antiretroviral drugs in children*	Feasibility counts of HIV in children*	Data lock for the last update
Spain	BIFAP	Presence of children (<18 years of age) with diagnosis of HIV. Able to perform study and meet study deadline.	Primary care, pharmacists, hospital inpatient care,	Claims, EHR, registries	22.6M	Not available and BIFAP will not be used for objective 2 and 3	17,200	17/02/2025
Germany	InGeF RDB	Presence of children (<18 years of age) with diagnosis of HIV and information on antiretroviral drug use. Able to perform study and meet study deadline	Primary care, pharmacy, secondary care (inpatient and outpatient), hospital inpatient care, claims data	Claims	10.4M	4,200	1,800	30/09/2024
Norway	NLHR	Presence of children (<18 years of age) with diagnosis of HIV and information on antiretroviral drug use. Able to perform study and meet study deadline	Primary care, secondary care (inpatient and outpatient), hospital inpatient care	Registries	7.34M	5,900	4,600	31/12/2023

*Record counts only as numbers are provided in children only. When looking at specific age categories, the portal only provides record counts and not person counts.

Base de Datos para la Investigacíon Farmacoepidemiológica en el Ámbito Público (BIFAP), Spain

BIFAP is a longitudinal population-based data source of medical patient records of the Spanish National Health Service (SNS) from 12 participating Regions throughout Spain out of the 17 Spanish Regions. Population currently included represents 50% of the total Spanish population. Spain has a SNS that provides universal access to health services through the Regional Healthcare Services. Primary care physicians (PCPs), both general practitioners and paediatricians, have a central role. They act as gatekeepers of the system and exchange information with other levels of care to ensure the continuity of care. Most (98.9%) of the population is registered with a PCP and BIFAP includes a collection of databases linked at individual patient level. The main one is the Primary care Database given the central role of PCPs in the SNS. Linked, there are additional important structural databases like the medicines dispensed at community pharmacies and the patients' hospital diagnosis at discharge. Additional databases are also linked for a subset of patients (hospital pharmacy, cause of death registry). BIFAP program is a non-profit program financed by the Spanish Agency of Medicines and Medical Devices (AEMPS), a government agency belonging to the Ministry of Health in collaboration with the regional health authorities. The main use of BIFAP is for research purposes in order to evaluate the adverse and beneficial effects of drugs and drug utilization patterns in the general population under real conditions of use.

InGef Research Database (InGef RDB), Germany

The InGef database comprises anonymized longitudinal claims data of about 10 million individuals across more than 70 statutory health insurance providers (SHIs) throughout Germany. Data are longitudinally linked over a period of currently ten years. Patients can be traced across health care sectors. All patient-level and provider-level data in the InGef research database are anonymised to comply with German data protection regulations and German federal law. German SHI claims data available in the InGef database includes information on demographics (year of birth, gender, death date if applicable, region of residence on administrative district level); hospitalizations; outpatient services (diagnoses, treatments; specialities of physicians); dispensing of drugs; dispensing of remedies and aids; and sick leave and sickness allowance times. In addition, costs or cost estimates from SHI perspective are available for all important cost elements. All diagnoses in Germany are coded using the International Classification of Diseases, version 10 in the German Modification (ICD-10-GM). The persistence (membership over time) is rather high in the InGef database: During a time period of 5 years (2009 to 2013), 70.6% of insurance members survived and remained insured with the same SHI without any gap in their observational time. Persons leaving one of the participating SHIs and entering another participating SHI, can be linked during yearly database consistency updates and are thus not lost over time. The InGef database is dynamic in nature, i.e. claims data are updated in an ongoing process and new SHIs may join or leave the database. By law, only the last 10 years of data are allowed to be used. At every new release this window shifts, dropping older data and adding new data.

Norwegian Linked Health Registry Data (NLHR), Norway

Norway has a universal public health care system consisting of primary and specialist health care services covering a population of approximately 5.4 million inhabitants. Many population-based health registries were established in the 1960s with use of unique personal identifiers facilitating linkage between registries. Data in these health registries are used for health analysis, health statistics, improving the quality of healthcare, research, administration and emergency preparedness. We harmonized data from the following registries: the Medical Birth Registry of Norway (MBRN), the Norwegian Prescription Registry (NorPD), the Norwegian Patient Registry (NPR), Norway Control and Payment of Health Reimbursement (KUHR), the Norwegian Surveillance System for Communicable Diseases (MSIS), the Norwegian Immunisation Registry (SYSVAK), the National Death Registry, and the National Registry (NR). Linkage between the registries was

facilitated using project-specific person ID generated from unique personal identification assigned at birth or immigration for all legal residents in Norway.

8.3 Study period

The study period is from 01/01/2010 to 31/12/2024. When the study end date is not reached in a data source, the study end for that source will be the last date of available data. (See **Table 3** for more details). InGef RDB only has available data from 01/01/2015 onwards and NLHR only has drug prescription data from 01/01/2018 onwards (with reliable rates starting 01/01/2019). Therefore, the study period for InGef will start in 2015 and in 2019 for NLHR.

8.4 Follow-up

For objective 1: Follow-up will start at the beginning of the study period until the earliest of the following: 1) censoring (i.e. diagnosis of HIV), 2) loss to follow-up, 3) end of data availability, 4) occurrence of death or 5) end of study period.

For objective 2 and 3: Follow-up will start at the beginning of the study period until the earliest of the following: 1) loss to follow-up, 2) end of data availability, 3) occurrence of death or 4) end of study period.

The operational definitions of time 0 (index date) are presented by means of **Table 4.**

Table 4. Operational definition of time 0 (index date) and other primary time anchors.

Study population name(s)	Time Anchor Description (e.g. time 0)	Number of entries	Type of entry	Washout window	Care Setting[1]	Code Type[2]	Diagnosis position	Incident with respect to…
Children < 18 years of age (objective 1 and 3)	Study entry date	Multiple	Incident, prevalent	Prevalent: n/a Incident: [inf, -1]	OP, IP	SNOMED	Primary	HIV diagnosis (Objective 1) or Antiretroviral drugs (Objective 3)
Children < 18 years of age with HIV diagnosis (objective 2)	Study entry date	Multiple	Incident, prevalent	Prevalent: n/a Incident: {-inf, -1]	OP, IP	RxNorm	Any	Antiretroviral drugs

[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable

An example of entry and exit into the denominator population is shown in **Figure 1**. In this example, person ID 1 already has sufficient prior history before the study start date and the observation period ends after the study end date, so this person will contribute during the complete study period. Person IDs 2 and 4 enter the study only when they have sufficient prior history. Person ID 3 leaves when exiting the database (the end of the observation period). Lastly, person ID 5 has two observation periods in the database. The first period contributes time from study start until end of observation period, the second starts contributing time again once sufficient prior history is reached and exits at study end date.

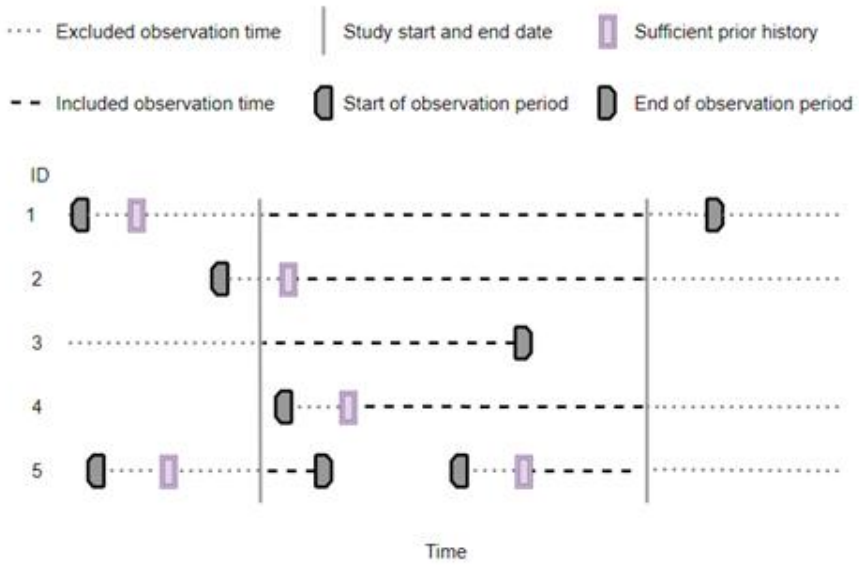


Figure 1. Included observation time for the denominator population.

8.5 Study population with inclusion and exclusion criteria

The study population will include all individuals observed in one of the participating data sources during the study period (1st January 2010 to 31st December 2024) and having at least 1 year of database history. For children within the age group of 0-<2 years, the need to have 365 days of prior database history will be dropped.

The operational definitions of the inclusion and exclusion criteria are presented by means of **Table 5** and **6**, respectively.

Table 5. Operational definitions of inclusion criteria.

Criterion	Details	Order of application	Assessment window	Care Settings[1]	Code Type	Diagnosis position[2]	Applied to study populations:
Prior database history	Study participants will be required to have 365 days of prior history observed before the index date (start of follow-up). For children within the age group of 0-<2 years, the need to have 365 days of prior database history will be dropped.	After	365 days	OP, IP	N/A	N/A	All individuals within selected databases
Observation period in the database during the study period	All individuals present in 2010-2024 (or latest date available)	After	N/A	OP, IP	N/A	N/A	All individuals within selected databases
Children (<18 years of age)	All individuals present in the study period, aged <18 years	After	N/A	OP, IP	N/A	N/A	All individuals within selected databases
Diagnosis of HIV (Objective 2)	All individuals present in the study period, aged <18 years	after	N/A	OP, IP	SNOMED	N/A	All individuals within selected databases

[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable

[2] Specify whether a diagnosis code is required to be in the primary position (main reason for encounter)

Table 6. Operational definitions of exclusion criteria.

Criterion	Details	Order of application	Assessment window	Care Settings[1]	Code Type	Diagnosis position[2]	Applied to study populations:
None.							

[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable
[2] Specify whether a diagnosis code is required to be in the primary position (main reason for encounter)

8.6 Variables

Preliminary concept/code lists used for the identification of exposures and /or outcomes are included in the supplementary Documents in **Appendix I.**

These will be refined during the study execution following the DARWIN EU® Phenotyping standard processes, which involve the review of code lists by clinical experts, and the review of phenotypes after their execution in the participating databases.

8.6.1 Exposure/s

For this study, exposure will be a prescription of ART and prophylactic use of ART. All ART ingredient drug classes will be split into three separate concept sets, an overall concept set including the ingredients with all descendant ingredient concepts, a monotherapy concept set, including the ingredients and all monotherapy concepts, and a combination concept set, including only the fixed dose combinations concepts related to the included ingredients. In the previously approved version of the protocol all ART ingredients drug classes only consisted of a overall concept set including the ingredients with all descendant ingredient concepts. The list of medications of interest are described in **Appendix I**.

The operational definition of exposure is described in **Table 7**.

Table 9. Operational definitions of exposure(s).

Exposure group name(s)	Details	Washout window	Assessment Window	Care Setting[1]	Code Type	Diagnosis position[2]	Applied to study populations	Incident with respect to…
Antiretroviral therapy (ART) use	A prescription of antiretroviral drugs (Specified in Appendix I)	[-inf,-1]	Calendar year	OP, IP	RxNorm	n/a	Children < 18 years of age with a HIV diagnosis (objective 2)	Previous ART use
antiretroviral therapy (ART) use	A prescription of antiretroviral drugs (Specified in Appendix I)	[-inf, -1]	Calendar year	OP, IP	RxNorm	n/a	Children < 18 years of age (objective 3)	Previous ART use

[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable
[2] Specify whether a diagnosis code is required to be in the primary position (main reason for encounter)

8.6.2 Outcome/s

The outcome of this study will be the prevalence and incidence of a HIV diagnosis.

In InGef RDB, HIV diagnoses consist of both inpatient and outpatient diagnoses. For outpatient HIV diagnoses in InGef RDB, patients are required to have 2 HIV diagnoses in a year for it to count as an actual diagnosis, since that criterion is commonly used in analyses of German claims data to indicate a higher degree of diagnostic validity compared to patients with a single diagnosis.

The operational definition of the outcomes is presented in the **Table 9**.

Table 8. Operational definitions of outcome.

Outcome name	Details	Primary outcome?	Type of outcome	Washout window	Care Settings[1]	Code Type	Diagnosis Position[2]	Applied to study populations
HIV diagnosis	A diagnosis of HIV	Yes	Count	n/a	OP, IP	SNOMED	Any	Children < 18 years of age (objective 1)

[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable
[2] Specify whether a diagnosis code is required to be in the primary position (main reason for encounter).

8.6.3 Other covariates, including confounders, effect modifiers and other variables

The study covariates are described conceptually, and the context or rationale for the choices are provided in this section.

Covariates for the population-level descriptive epidemiology (objective 1)

- Sex
- Calendar year
- Age categories:
  - 0-<1 year
  - 1-<2 years
  - 2-<5 years
  - 5-<12 years
  - 12-<18 years

Covariates for the population-level drug utilisation study (objective 2)

- Sex
- Calendar year
- Age categories:
  - 0-<1 year
  - 1-<2 years
  - 2-<5 years
  - 5-<12 years
  - 12-<18 years

The operational definition of the covariates is described in **Table 9**.

Table 9. Operational definitions of covariates.

Characteristic	Details	Type of variable	Assessment window	Care Settings[1]	Code Type	Diagnosis Position[2]	Applied to study populations
Age, sex, calendar year	Age, sex and calendar year at start of follow-up	Categorical	Assessed at start of follow-up	n/a	n/a	n/a	Objective 1 and 3: Individuals<18 years of age and with 365 days of database history Objective 2: Individuals<18 years of age, with 365 days of database history and diagnosed with HIV For children within the age group of 0-<2 years, the need to have 365 days of prior database history will be dropped.

[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable

[2] Specify whether a diagnosis code is required to be in the primary position (main reason for encounter).

8.7 Study size

No sample size has been calculated as this is a descriptive drug utilisation study where we are interested in all the prevalent and incident paediatric HIV cases in each database. Based on a preliminary feasibility assessment, the expected number of persons counts for HIV in the databases included in this study were 1,800 (InGef RDB), 4,600 (NLHR), and 17,200 (BIFAP). Preliminary counts for ART were 4,200 (InGef RDB), 5,900 (NLHR),while no counts were present in BIFAP.

8.8 Analysis

All analyses will be conducted separately for each database, and will be carried out in a federated manner, allowing analyses to be run locally without sharing patient-level data.

Before sharing the study package, test runs of the analytics will be performed on a subset of the data sources and quality control checks will be performed. After all the tests are passed, the final package will be released in a version-controlled study repository for execution against all the participating data sources.

The data partners will locally execute the analytics against the OMOP-CDM in R Studio and review and approve the default aggregated results. They will then be made available to the Principal Investigators and study team in secure online repository (Data Transfer Zone). All results will be locked and timestamped for reproducibility and transparency.

Cell counts <5 will be suppressed to comply with the database's privacy protection regulations.

The type of analysis in this study is described in **Table 10**.

Table 10. Description of study types and types of analysis.

Study type	Study classification	Type of analysis
Population-level descriptive epidemiology	Off-the-shelf	- Incidence rates of the condition of interest - Prevalence rates of the condition of interest
Population Level DUS	Off-the-shelf	- Population-based incidence rates - Population-based prevalence of use of a drug/drug class

8.8.1 Statistical model specification and assumptions of the analytical approach considered

R-packages

We will use the R package "IncidencePrevalence" to calculate the prevalence and incidence of the paediatric HIV population and the antiretroviral drug use.

Drug exposure calculations

Drug eras will be defined as follows: Exposure starts at date of the first prescription after an infinite washout. For each prescription, the estimated duration of use is retrieved from the drug exposure table in the CDM, using the start and end date of the exposure. Subsequent prescriptions will be combined into continuous exposed episodes (drug eras) using the following specifications:

Two drug eras will be merged into one continuous drug era if the distance in days between end of the first era and start of the second era is ≤ 30 days. The time between the two joined eras will be considered as exposed by the first era as shown in **Figure 2**, first row.

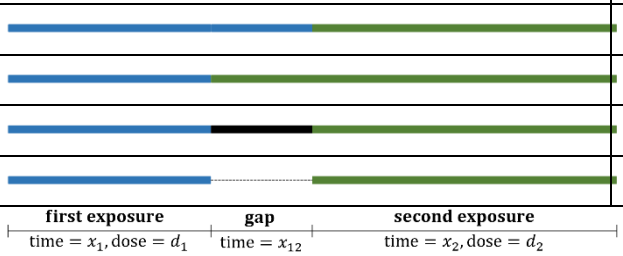
Gap era joint mode	**Schematics**	**Dose in between**	**Cumulative dose**	**Cumulative time**
"first"		d_1	$d_1 \cdot (x_1 + x_{12}) + d_2 \cdot x_2$	$x_1 + x_{12} + x_2$
"second"		d_2	$d_1 \cdot x_1 + d_2 \cdot (x_2 + x_{12})$	$x_1 + x_{12} + x_2$
"zero"		0	$d_1 \cdot x_1 + d_2 \cdot x_2$	$x_1 + x_{12} + x_2$
"join"		NA	$d_1 \cdot x_1 + d_2 \cdot x_2$	$x_1 + x_2$

Figure 2. Gap era joint mode.

8.8.2 Methods to derive parameters of interest

Calendar time

Calendar time will be based on the calendar year of the index prescription.

Age

Age will be calculated using January 1st of the year of birth as a proxy for the actual birthday. The prevalent and incident paediatric HIV population stratified within age groups 0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years .

8.8.3 Population-level prevalence calculations

Prevalence rates of the outcomes of interest namely paediatric HIV and ART use will be calculated as the proportion of study participants who were diagnosed with HIV on a yearly basis (objective 1), proportion of study participants with HIV who were prescribed antiretroviral drugs on a yearly basis (objective 2) or proportion of study participants who were prescribed antiretroviral drugs on a yearly basis. There will be no restriction based on patients' observability within calendar years in the database (i.e. participants will be considered even if they were not present in the database for the entire year).

Prevalence will be presented by database and drug (in case of ART use) overall and stratified by age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year. Overall values will be presented for age groups 0-<2 years and 2-<18 years since the age-groups 0-1 and 1-<2 years do not have a prior database history of 365 days requirement and overall values will also be presented for all calendar years together in the study period.

8.8.4 Population-level incidence calculations

8.8.4.1 Paediatric HIV

Annual incidence rates of the selected pre-specified condition of interest will be calculated as the number of new users after 1 year of no use per 100,000 person-years of the population at risk of getting exposed during the period for each calendar year. Those study participants who enter the denominator population will then contribute time at risk up to their diagnosis during the study period. If they do not have a HIV diagnosis, they will contribute time at risk up as described above. Time-at-risk of subjects who die will be censored at the time of death. Similarly, time at risk of subjects who are lost to follow-up will be censored at the time of loss to follow-up [last contact]. Subjects with data until the end of the study period without experiencing exposure will be administratively censored at the end of the study period. Incidence rates will be given together with 95% Poisson confidence intervals. Incidence of HIV will be presented by database overall and stratified by age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year. Overall values will be presented for age groups 0-<2 years and 2-<18 since the age-groups 0-1 and 1-<2 years do not have a prior database history of 365 days requirement and overall values will also be presented for all calendar years together in the study period.

An illustration of the calculation of incidence of HIV diagnosis is shown below in **Figure 3**. Patient ID 1 and 4 contribute time at risk up to the point at which they become incident HIV patients. Patient ID 2 do not get HIV and so contribute time at risk but no incident outcome. Meanwhile, patient ID 3 does not contribute time at risk since there was a HIV diagnosis before the study start.

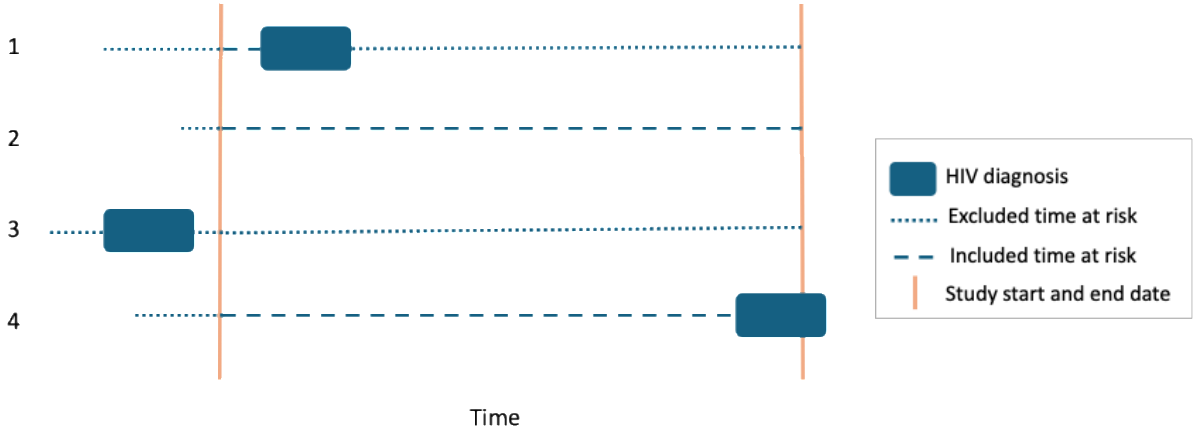


Figure 3. Example of incidence rate estimation.

8.8.4.2 ART use

Annual incidence rates of the selected pre-specified medication of interest will be calculated as the number of new users after 1 year of no use per 1,000 person-years of the population at risk of getting exposed during the period for each calendar year. Those study participants who enter the denominator population will then contribute time at risk up to their first prescription during the study period. If they do not have a drug exposure, they will contribute time at risk up as described above. Time-at-risk of subjects who die will be censored at the time of death. Similarly, time at risk of subjects who are lost to follow-up will be censored at the time of loss to follow-up [last contact]. Subjects with data until the end of the study period without experiencing exposure will be administratively censored at the end of the study period. Incidence rates will be given together with 95% Poisson confidence intervals. Patients are allowed to switch to a

different treatment. Incidence of ART use will be presented by database and drug overall and stratified by age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year. Overall values will be presented for age groups 0-<2 years and 2-<18 years since the age-groups 0-1 and 1-<2 years do not have a prior database history of 365 days requirement and overall values will also be presented for all calendar years together in the study period.

An illustration of the calculation of incidence of selected pre-specified medication of interest is shown below in **Figure 4**. Patient ID 1 and 4 contribute time at risk up to the point at which they become incident users of selected pre-specified medication of interest. Patient ID 2 is not seen to use pre-specified medication of interest and so contributes time at risk but no incident outcomes. Meanwhile, patient ID 3 is not included since he/she has ART use before the start of the study period. This is not allowed since an infinite washout window for ART was used, i.e. not prior use of the same ART drug class was allowed. For person ID 4, both the first and second exposure of pre-specified medication of interest were registered, since the second exposure is a different ART drug class.

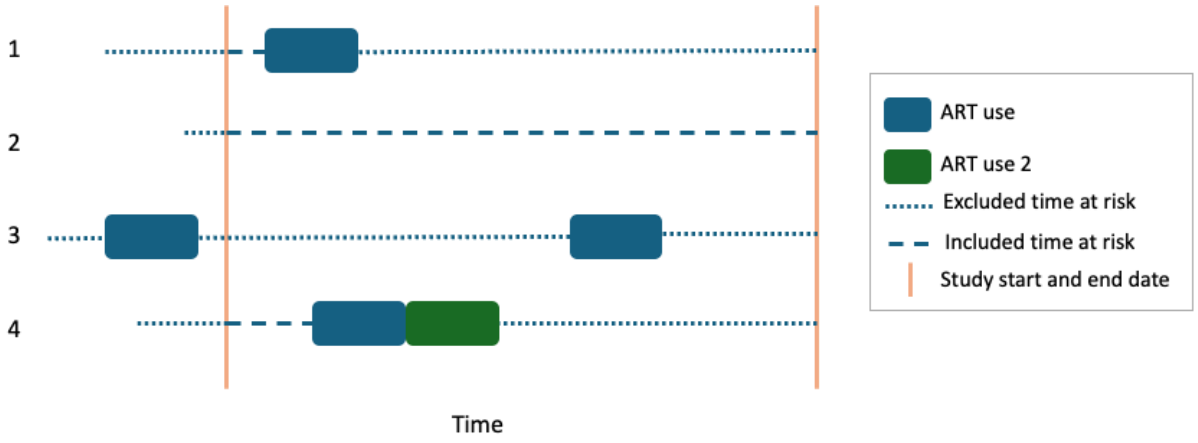


Figure 4. Example of incidence rate estimation.

8.8.5 Output

- Table 1. Study attrition of individuals included in each cohort per database.
- Table 2. Prevalence and incidence of HIV in paediatric general population, overall and stratified by calendar year, sex and age group (0-1 year, 1 -2 years, 3-4 years, 5-11 years, 12-17 years).
- Table 3. Prevalence and incidence of antiretroviral drug use in paediatric HIV population,overalland stratified by type of antiretroviral drug class, sex and by age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year.
- Table 4. Prevalence and incidence of antiretroviral drug use in paediatric general population, overalland stratified by type of antiretroviral drug class, sex and by age group (0-<1, 1-<2, 2-<5, 5-<12 and 12-<18 years) and calendar year..

8.9 Evidence synthesis

Results from analyses described in section 8.8 will be presented separately for each database. No meta-analysis will be conducted.

9. DATA MANAGEMENT

9.1 Data management

All databases are mapped to the OMOP common data model. This enables the use of standardised analytics and tools across the network since the structure of the data and the terminology system is harmonised. The OMOP CDM is developed and maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative and is described in detail on the wiki page of the CDM: https://ohdsi.github.io/CommonDataModel and in The Book of OHDSI: http://book.ohdsi.org.

The analytic code for this study will be written in R. Each data partner will execute the study code against their database containing patient-level data and will then return the results set which will only contain aggregated data. The results from each of the contributing data sites will then be combined in tables and figures for the study report.

9.2 Data storage and protection

For this study, participants from various EU member states will process personal data from individuals which is collected in national/regional electronic health record databases. Due to the sensitive nature of this personal medical data, it is important to be fully aware of ethical and regulatory aspects and to strive to take all reasonable measures to ensure compliance with ethical and regulatory issues on privacy.

All databases used in this study are already used for pharmaco-epidemiological research and have a well-developed mechanism to ensure that European and local regulations dealing with ethical use of the data and adequate privacy control are adhered to. In agreement with these regulations, rather than combining person level data and performing only a central analysis, local analyses will be run, which generate non-identifiable aggregate summary results.

The output files are stored in the DARWIN Digital Research Environment (DRE). These output files do not contain any data that allow identification of subjects included in the study. The DRE implements further security measures in order to ensure a high level of stored data protection to comply with the local implementation of the General Data Protection Regulation (GDPR) (EU) 679/20161 in the various member states.

10. QUALITY CONTROL

General database quality control

A number of open-source quality control mechanisms for the OMOP CDM have been developed (see Chapter 15 of The Book of OHDSI http://book.ohdsi.org/DataQuality.html). In particular, data partners have run the OHDSI Data Quality Dashboard tool (https://github.com/OHDSI/DataQualityDashboard). This tool provides numerous checks relating to the conformance, completeness and plausibility of the mapped data. Conformance focuses on checks that describe the compliance of the representation of data against internal or external formatting, relational, or computational definitions, completeness in the sense of data quality is solely focused on quantifying missingness, or the absence of data, while plausibility seeks to determine the

believability or truthfulness of data values. Each of these categories has one or more subcategories and are evaluated in two contexts: validation and verification. Validation relates to how well data align with external benchmarks with expectations derived from known true standards, while verification relates to how well data conform to local knowledge, metadata descriptions, and system assumptions.

Study specific quality control

When defining specific drugs, conditions, and co-morbidities, a systematic search of possible codes for inclusion was previously identified using CodelistGenerator R package (https://github.com/darwin-eu/CodelistGenerator). This software allows the user to define a search strategy and, using this will then query the vocabulary tables of the OMOP CDM to find potentially relevant codes. The codes returned will then be reviewed by two clinical epidemiologists to consider their relevance. In addition, the CohortDiagnostics R package (https://github.com/OHDSI/CohortDiagnostics) will be run to assess the use of different codes across the databases contributing to the study and identify any codes potentially omitted in error. This will allow for a consideration of the validity of the study cohort of patients with the selected conditions, drugs, and co-morbidities in each of the databases and inform decisions around whether multiple definitions are required.

11. LIMITATIONS OF THE RESEARCH METHODS

This study will be informed by 4 different data sources from 4 countries and will only reflect outcomes occurring in the healthcare settings covered by each database. Results obtained will likely differ across countries and health settings. It is also likely that some results will vary due to differences in how databases handle observations periods, which might vary across different database types and even within the same type.

In some data sources the start of data availability is after the start of the study period. Namely, InGef RDB only has available data from 01/01/2015 onwards and NLHR only has drug prescription data from 01/01/2018 onwards. To have reliable incidence rates for ART use in NLHR its study period will start from 01/01/2019 since the history of ART use before 2018 is also mapped to 2018 leading to unrealistically high incidence rates in 2018.

In this study in particular, counts for HIV and ART in children are low therefore we might encounter difficulties to calculate prevalence and incidence especially when looking into specific strata. Moreover, counts might not be disclosed for governance reasons (if they are <5). Of note, not all databases have counts for both HIV diagnosis and ART. BIFAP for instance does not have counts for ART Therefore, BIFAP will only be used for objective 1.

Lastly, InGeF RDB outpatient data is dated to the end of every quarter, i.e. all observations between January 1st and March 31st are dated on March 31st. This will result in potential misclassification in diagnosis and treatment, where date of treatment might fall prior to the date of HIV diagnosis as recorded in the database. To account for this, the date of HIV diagnosis will be moved to the beginning of the quarter, therefore ensuring that ART use will start after HIV diagnosis. This approach could potentially lead to a small-time increase (maximum 3 months) for the time contributed by the HIV patients towards the corresponding denominator cohort. Lastly, outpatient data patients in InGef RDB are required to have 2 HIV diagnoses in a year for it to count as an actual diagnosis. This is standard practice for German claims data to avoid misclassification and increase specificity. In InGef RDB, a first record of HIV might relate to the indication of HIV testing which is later either confirmed or rejected.

12. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

Adverse events/adverse reactions will not be collected or analysed as part of this evaluation. The nature of this non-interventional evaluation, through the use of secondary data, does not fulfil the criteria for reporting adverse events, according to module VI, VI.C.1.2.1.2 of the Good Pharmacovigilance Practices (https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-good-pharmacovigilance-practices-gvp-module-vi-collection-management-submission-reports_en.pdf).

Only in case of prospective data collection, there is a need to describe the procedures for the collection, management and reporting of individual cases of adverse events/adverse reactions.

13. GOVERNANCE BOARD ASPECTS

All data sources require approval from their respective IRB boards.

14. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

14.1 Study report

A PDF report, including an executive summary and the specified tables and/or figures, will be submitted to EMA by the DARWIN EU® CC upon completion of the study.

An interactive dashboard incorporating all the results (tables and figures) will be provided alongside the PDF report. The full set of underlying aggregated data used in the dashboard will also be made available if requested.

15. OTHER ASPECTS

None.

16. REFERENCES

1. Levy JA. HIV pathogenesis and long-term survival. AIDS. 1993;7(11):1401-10.

2. Powell MK, Benková K, Selinger P, Dogoši M, Kinkorová Luňáčková I, Koutníková H, et al. Opportunistic Infections in HIV-Infected Patients Differ Strongly in Frequencies and Spectra between Patients with Low CD4+ Cell Counts Examined Postmortem and Compensated Patients Examined Antemortem Irrespective of the HAART Era. PLOS ONE. 2016;11(9):e0162704.

3. Weiss RA. How Does HIV Cause AIDS? Science. 1993;260(5112):1273-9.

4. Beyrer C. HIV epidemiology update and transmission factors: risks and risk contexts--16th International AIDS Conference epidemiology plenary. Clin Infect Dis. 2007;44(7):981-7.

5. Cohen MS, Council OD, Chen JS. Sexually transmitted infections and HIV in the era of antiretroviral treatment and prevention: the biologic basis for epidemiologic synergy. J Int AIDS Soc. 2019;22 Suppl 6(Suppl Suppl 6):e25355.

6. Tshivuila-Matala COO, Honeyman S, Nesbitt C, Kirtley S, Kennedy SH, Hemelaar J. Adverse perinatal outcomes associated with antiretroviral therapy regimens: systematic review and network meta-analysis. Aids. 2020;34(11):1643-56.

7. UNAIDS. Joint United Nations Programme on HIV/AIDS. Fast-Track. Ending the AIDS Epidemic by 2030. 2014.

8. UNAIDS. UNAIDS. Global AIDS update 2019. 2019.

9. Langford SE, Ananworanich J, Cooper DA. Predictors of disease progression in HIV infection: a review. AIDS Res Ther. 2007;4:11.

10. Gandhi RT, Spritzler J, Chan E, Asmuth DM, Rodriguez B, Merigan TC, et al. Effect of baseline- and treatment-related factors on immunologic recovery after initiation of antiretroviral therapy in HIV-1-positive subjects: results from ACTG 384. J Acquir Immune Defic Syndr. 2006;42(4):426-34.

11. Siddiqi AE, Hall HI, Hu X, Song R. Population-Based Estimates of Life Expectancy After HIV Diagnosis: United States 2008-2011. J Acquir Immune Defic Syndr. 2016;72(2):230-6.

12. Teeraananchai S, Kerr SJ, Amin J, Ruxrungtham K, Law MG. Life expectancy of HIV-positive people after starting combination antiretroviral therapy: a meta-analysis. HIV Med. 2017;18(4):256-66.

13. EU D. Catalogue of Standard Data Analyses [Available from: https://www.darwin-eu.org/index.php/methods/standardised-analytics.

14. DeFalco F RP, Schuemie M, Huser V, Knoll C, Londhe A, at al. Achilles: Achilles Data Source Characterization. R Package verzion 1.7.2. 2023.

15. Gilbert J RG, Schuemie M, Ryan P, Weaver J. CohortDiagnostics: Diagnostics for OHDSI Cohorts. R package version 3.3.0. https://github.com/OHDSI/CohortDiagnostics,2024.

16. Inberg G BE, Burkard T. DrugExposureDiagnostics: Diagnostics for OMOP Common Data Model Drug Records. R package version 1.0.9. https://github.com/darwin-eu/DrugExposureDiagnostics2024.

17. Battersby C, Statnikov Y, Santhakumaran S, Gray D, Modi N, Costeloe K. The United Kingdom National Neonatal Research Database: A validation study. PLoS One. 2018;13(8):e0201815.

17. ANNEXES

Appendix I:

Table S1. Code list for condition of interest. (preliminary codes – might change during study execution based on cohort diagnostics)

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs
HIV	Human immunodeficiency virus infection Human immunodeficiency virus Finding of HIV status	439727 4078242 4276586	False positive serology for HIV False positive serology for human immunodeficiency virus antibody HIV negative	3200792 37017660 4013105

Table S2. Code list for exposure definitions. (preliminary codes – might change during study execution based on drug exposure diagnostics)

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
J05AF Nucleoside and Nucleotide Reverse transcriptase inhibitors	Zidovudine Zalcitabine Tenofovir disoproxil Tenofovir alafenamide Telbivudine Stavudine Lamivudine Entecavir Emtricitabine Didanosine Clevudine Abacavir	1710612 1724827 1710281 35605546 1758392 1781406 1704183 1711246 1703069 1724869 43009047 1736971	Interferon alfa-2b and Zidovudine	35803592
J05AF Nucleoside and Nucleotide Reverse transcriptase inhibitors (Monotherapy)	Zidovudine Zalcitabine Tenofovir disoproxil Tenofovir alafenamide Telbivudine Stavudine Lamivudine Entecavir Emtricitabine Didanosine Clevudine Abacavir	1710612 1724827 1710281 35605546 1758392 1781406 1704183 1711246 1703069 1724869 43009047 1736971	abacavir / dolutegravir / Lamivudine Delayed Release Oral Tablet abacavir / dolutegravir / lamivudine Oral Liquid Product abacavir / dolutegravir / lamivudine Oral Product abacavir / dolutegravir /	43211100 779346 36247224 45775746 36247225 779347 43211101 36219266 40097200 36219267 43156335 36219268 40097202 36219269

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			lamivudine Oral Tablet	44094321 43821524
			abacavir / dolutegravir / lamivudine Pill	19120798 41236246 779349
			abacavir / dolutegravir / lamivudine Tablet for Oral Suspension	2928973 45775749 36784669 1831243
			abacavir / Lamivudine / Zidovudine Delayed Release Oral Tablet	44029600 44120245 2918563
			abacavir / lamivudine / zidovudine Oral Product	19122307 21053216 44042631
			abacavir / lamivudine / zidovudine Oral Tablet	44120244 44042630 40923765
			abacavir / lamivudine / zidovudine Pill	41298103 36236510
			abacavir / Lamivudine Delayed Release Oral Tablet	36236511 43026139 964012
			abacavir / lamivudine Oral Product	964014 964013
			abacavir / lamivudine Oral Tablet	702170 964017
			abacavir / lamivudine Pill	964019 964020
			abacavir 300 MG / Lamivudine 150 MG / Zidovudine 300 MG [Apo-Abacavir-Lamivudine-Zidovudine]	42543876 42543877 36788486 1560076 1560078 1560077
			abacavir 300 MG / Lamivudine 150 MG / Zidovudine 300 MG [Triplead-Ratiopharm]	21149330 43149972 36248152 35605551
			abacavir 300 MG / lamivudine 150 MG / zidovudine 300 MG [Trizivir]	36248153 43180174 36243625 36243626
			abacavir 351 MG / Lamivudine 150 MG / Zidovudine 300 MG [Trizivir]	36893513 1560081 21060949 35605554
			abacavir 60 MG / dolutegravir 5 MG / lamivudine 30 MG [Triumeq]	21051155 42874226 36219437 36219438
			abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Trelavue]	36220376 36220377 35200460 35200461

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Triumeq]	36249554 36249555 1511082 1511084
			abacavir 600 MG / Lamivudine 300 MG [Abacavir / Lamivudin Sandoz]	1511083 1511087 1511085 43026751
			abacavir 600 MG / lamivudine 300 MG [Abacavir / Lamivudine Mylan Pharma]	35200462 35200464 35200463 43026753 43200066
			abacavir 600 MG / Lamivudine 300 MG [Apo-Abacavir-Lamivudine]	36226563 40134707 36226564 36226561
			abacavir 600 MG / Lamivudine 300 MG [Auro-Abacavir/Lamivudine]	40166595 36226562 35201132 21043604
			abacavir 600 MG / lamivudine 300 MG [Bezort]	1831213 782837 36788477
			abacavir 600 MG / lamivudine 300 MG [Epzicom]	19124373 1510223 36788493
			abacavir 600 MG / Lamivudine 300 MG [Kivexa]	36788492 36249077 35605920
			abacavir 600 MG / Lamivudine 300 MG [Mylan-Abacavir/Lamivudine]	36249078 43212854 36226580 40241980
			abacavir 600 MG / Lamivudine 300 MG [Pms-Abacavir-Lamivudine]	36226581 21094460 35411176 36249552
			abacavir 600 MG / Lamivudine 300 MG [Teva-Abacavir/Lamivudine]	35604224 36249553 43202121 36225757
			abacavir 703 MG / dolutegravir 50 MG / Lamivudine 300 MG [Triumeq]	40124350 36225758 36882760 35803592
			abacavir 703 MG / Lamivudine 300 MG [Kivexa]	36245184 40146970 36218347
			Atripla Oral Product	40173162
			Atripla Pill	36218348
			bictegravir / emtricitabine / tenofovir alafenamide Delayed Release Oral	36218349 40137867 36218350 36218351

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			Tablet bictegravir / emtricitabine / tenofovir alafenamide Oral Product bictegravir / emtricitabine / tenofovir alafenamide Oral Tablet bictegravir / emtricitabine / tenofovir alafenamide Pill bictegravir 30 MG / emtricitabine 120 MG / tenofovir alafenamide 15 MG [Biktarvy] bictegravir 50 MG / emtricitabine 200 MG / tenofovir alafenamide 25 MG [Biktarvy] Biktarvy Oral Product Biktarvy Pill Cimduo Oral Product Cimduo Pill cobicistat / darunavir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Pill cobicistat / elvitegravir / emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet	40142130 36218352 42543869 42543871 42543870 43189263 36218353 40051161 36218354

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Pill cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Pill cobicistat / elvitegravir / emtricitabine / Tenofovir Oral Tablet cobicistat 150 MG / darunavir 800 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Symtuza] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / Tenofovir 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			/ tenofovir disoproxil 250 MG [Stribild] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Stribild] Combivir Oral Product Combivir Pill Complera Oral Product Complera Pill Delstrigo Oral Product Delstrigo Pill Descovy Oral Product Descovy Pill dolutegravir / lamivudine Oral Product dolutegravir / lamivudine Oral Tablet dolutegravir / lamivudine Pill dolutegravir 50 MG / lamivudine 300 MG [Dovato] dolutegravir 50 MG / lamivudine 300 MG Oral Tablet DORAVIRINE / Lamivudine / tenofovir disoproxil Delayed Release Oral Tablet doravirine / lamivudine / tenofovir disoproxil Oral Product doravirine / lamivudine / tenofovir disoproxil Oral Tablet doravirine / lamivudine / tenofovir disoproxil Pill DORAVIRINE 100 MG / Lamivudine 300 MG / tenofovir disoproxil 250 MG [Delstrigo] efavirenz / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			efavirenz / emtricitabine / tenofovir disoproxil Oral Product efavirenz / emtricitabine / tenofovir disoproxil Oral Tablet efavirenz / emtricitabine / tenofovir disoproxil Pill efavirenz / lamivudine / tenofovir disoproxil Oral Product efavirenz / lamivudine / tenofovir disoproxil Oral Tablet efavirenz / lamivudine / tenofovir disoproxil Pill efavirenz 400 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Atripla] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efatriten] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Krka] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Mylan] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Atripla] efavirenz 600 MG / lamivudine 300 MG /	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			tenofovir disoproxil fumarate 300 MG [Symfi] emtricitabine / Rilpivirine / tenofovir alafenamide Delayed Release Oral Tablet emtricitabine / Rilpivirine / tenofovir alafenamide Delayed Release Oral Tablet [Odefsey] emtricitabine / rilpivirine / tenofovir alafenamide Oral Product emtricitabine / rilpivirine / tenofovir alafenamide Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Pill emtricitabine / Rilpivirine / tenofovir disoproxil Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Oral Product emtricitabine / rilpivirine / tenofovir disoproxil Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Pill emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet emtricitabine / tenofovir alafenamide Oral Product emtricitabine / tenofovir alafenamide Oral Tablet emtricitabine / tenofovir alafenamide Pill emtricitabine / tenofovir disoproxil	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			Delayed Release Oral Tablet emtricitabine / tenofovir disoproxil Oral Product emtricitabine / tenofovir disoproxil Oral Tablet emtricitabine / tenofovir disoproxil Pill emtricitabine / Tenofovir Oral Tablet Interferon alfa-2b and Zidovudine lamivudine / nevirapine / stavudine Disintegrating Oral Product lamivudine / nevirapine / stavudine Disintegrating Oral Tablet lamivudine / nevirapine / stavudine Oral Product lamivudine / nevirapine / stavudine Oral Tablet lamivudine / nevirapine / stavudine Pill lamivudine / nevirapine / zidovudine Oral Product lamivudine / nevirapine / zidovudine Oral Tablet lamivudine / nevirapine / zidovudine Pill lamivudine / stavudine Oral Product lamivudine / stavudine Oral Tablet lamivudine / stavudine Pill lamivudine / tenofovir disoproxil Oral Product lamivudine / tenofovir disoproxil Oral Tablet lamivudine / tenofovir	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			disoproxil Pill Lamivudine / Zidovudine Delayed Release Oral Tablet lamivudine / zidovudine Oral Product lamivudine / zidovudine Oral Tablet lamivudine / zidovudine Pill	
J05AF Nucleoside and Nucleotide Reverse transcriptase inhibitors (Combinations)	abacavir / dolutegravir / Lamivudine Delayed Release Oral Tablet abacavir / dolutegravir / lamivudine Oral Liquid Product abacavir / dolutegravir / lamivudine Oral Product abacavir / dolutegravir / lamivudine Oral Tablet abacavir / dolutegravir / lamivudine Pill abacavir / dolutegravir / lamivudine Tablet for Oral Suspension abacavir / Lamivudine / Zidovudine Delayed Release Oral Tablet abacavir / lamivudine / zidovudine Oral Product abacavir / lamivudine / zidovudine Oral Tablet abacavir / lamivudine / zidovudine Pill abacavir / Lamivudine Delayed Release Oral Tablet abacavir / lamivudine Oral Product abacavir / lamivudine Oral Tablet abacavir / lamivudine Pill abacavir 300 MG / Lamivudine 150 MG / Zidovudine 300 MG [Apo-Abacavir-Lamivudine-Zidovudine] abacavir 300 MG / Lamivudine 150 MG / Zidovudine 300 MG [Triplead-Ratiopharm] abacavir 300 MG / lamivudine 150 MG / zidovudine 300 MG [Trizivir] abacavir 351 MG /	43211100 779346 36247224 45775746 36247225 779347 43211101 36219266 40097200 36219267 43156335 36219268 40097202 36219269 44094321 43821524 19120798 41236246 779349 2928973 45775749 36784669 1831243 44029600 44120245 2918563 19122307 21053216 44042631 44120244 44042630 40923765 41298103 36236510 36236511 43026139 964012 964014 964013 702170 964017 964019 964020 42543876	N/A	N/A

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	Lamivudine 150 MG / Zidovudine 300 MG [Trizivir]	42543877 36788486		
	abacavir 60 MG / dolutegravir 5 MG / lamivudine 30 MG [Triumeq]	1560076 1560078 1560077		
	abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Trelavue]	21149330 43149972 36248152 35605551		
	abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Triumeq]	36248153 43180174 36243625 42874221		
	abacavir 600 MG / Lamivudine 300 MG [Abacavir / Lamivudin Sandoz]	36243626 36893513 1560081 21060949		
	abacavir 600 MG / lamivudine 300 MG [Abacavir / Lamivudine Mylan Pharma]	35605554 21051155 42874226 36219437		
	abacavir 600 MG / Lamivudine 300 MG [Apo-Abacavir-Lamivudine]	36219438 36220376 36220377		
	abacavir 600 MG / Lamivudine 300 MG [Auro-Abacavir/Lamivudine]	35200460 35200461 36249554		
	abacavir 600 MG / lamivudine 300 MG [Bezort]	36249555 1511082		
	abacavir 600 MG / lamivudine 300 MG [Epzicom]	1511084 1511083 1511087		
	abacavir 600 MG / Lamivudine 300 MG [Kivexa]	43026751 35200462		
	abacavir 600 MG / Lamivudine 300 MG [Mylan-Abacavir/Lamivudine]	35200464 35200463 43026753		
	abacavir 600 MG / Lamivudine 300 MG [Pms-Abacavir-Lamivudine]	1511089 1511090 43200066		
	abacavir 600 MG / Lamivudine 300 MG [Teva-Abacavir/Lamivudine]	36226563 40134707 36226564		
	abacavir 703 MG / dolutegravir 50 MG / Lamivudine 300 MG [Triumeq]	36226561 40166595 36226562 35201132		
	abacavir 703 MG / Lamivudine 300 MG [Kivexa]	21043604 1831213		
	Atripla Oral Product\ Atripla Pill	782837 36788477		
	bictegravir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet	19124373 1510223 36788493		
	bictegravir / emtricitabine /	36249077		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	tenofovir alafenamide Oral Product	35605920 36249078		
	bictegravir / emtricitabine / tenofovir alafenamide Oral Tablet	43212854 36226580 40241980		
	bictegravir / emtricitabine / tenofovir alafenamide Pill	36226581 21094460		
	bictegravir 30 MG / emtricitabine 120 MG / tenofovir alafenamide 15 MG [Biktarvy]	35411176 36249552 35604224 36249553		
	bictegravir 50 MG / emtricitabine 200 MG / tenofovir alafenamide 25 MG [Biktarvy]	43202121 36225757 40124350 36225758		
	Biktarvy Oral Product	36882760		
	Biktarvy Pill	36222529		
	Cimduo Oral Product	36220688		
	Cimduo Pill	36248154		
	cobicistat / darunavir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet	36248155 36245184 40146970 36218347		
	cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Product	40173162 36218348 36218349		
	cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Tablet	40137867 36218350 36218351		
	cobicistat / darunavir / emtricitabine / tenofovir alafenamide Pill	40142130 36218352 42543869		
	cobicistat / elvitegravir / emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet	42543871 42543870 43189263 36218353		
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet	40051161 36218354 36249079 36249080		
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Product	36243647 36243648 1510225		
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Tablet	1510226 1560083 1560084		
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Pill	1511231 1511232 779350		
	cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet	36247333 36247334 36239208 36239209		
	cobicistat / elvitegravir / emtricitabine / tenofovir	36239226 36239227		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	disoproxil Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Pill cobicistat / elvitegravir / emtricitabine / Tenofovir Oral Tablet cobicistat 150 MG / darunavir 800 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Symtuza] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / Tenofovir 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Stribild] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Stribild] Combivir Oral Product Combivir Pill Complera Oral Product Complera Pill Delstrigo Oral Product Delstrigo Pill Descovy Oral Product Descovy Pill dolutegravir / lamivudine Oral Product dolutegravir / lamivudine Oral Tablet dolutegravir / lamivudine Pill dolutegravir 50 MG / lamivudine 300 MG [Dovato] DORAVIRINE / Lamivudine / tenofovir disoproxil Delayed Release Oral Tablet doravirine / lamivudine / tenofovir disoproxil Oral Product			

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	doravirine / lamivudine / tenofovir disoproxil Oral Tablet doravirine / lamivudine / tenofovir disoproxil Pill DORAVIRINE 100 MG / Lamivudine 300 MG / tenofovir disoproxil 250 MG [Delstrigo] Dovato Oral Product Dovato Pill efavirenz / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet efavirenz / emtricitabine / tenofovir disoproxil Oral Product efavirenz / emtricitabine / tenofovir disoproxil Oral Tablet efavirenz / emtricitabine / tenofovir disoproxil Pill efavirenz / lamivudine / tenofovir disoproxil Oral Product efavirenz / lamivudine / tenofovir disoproxil Oral Tablet efavirenz / lamivudine / tenofovir disoproxil Pill efavirenz 400 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Atripla] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efatriten] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Krka] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Mylan] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate			

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	300 MG [Atripla] efavirenz 600 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] emtricitabine / Rilpivirine / tenofovir alafenamide Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Oral Product emtricitabine / rilpivirine / tenofovir alafenamide Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Pill emtricitabine / Rilpivirine / tenofovir disoproxil Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Oral Product emtricitabine / rilpivirine / tenofovir disoproxil Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Pill emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet emtricitabine / tenofovir alafenamide Oral Product emtricitabine / tenofovir alafenamide Oral Tablet emtricitabine / tenofovir alafenamide Pill emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet emtricitabine / tenofovir disoproxil Oral Product emtricitabine / tenofovir disoproxil Oral Tablet emtricitabine / tenofovir disoproxil Pill emtricitabine / Tenofovir Oral Tablet Epzicom Oral Product Epzicom Pill Genvoya Oral Product Genvoya Pill lamivudine / nevirapine /			

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	stavudine Disintegrating Oral Product lamivudine / nevirapine / stavudine Disintegrating Oral Tablet lamivudine / nevirapine / stavudine Oral Product lamivudine / nevirapine / stavudine Oral Tablet lamivudine / nevirapine / stavudine Pill lamivudine / nevirapine / zidovudine Oral Product lamivudine / nevirapine / zidovudine Oral Tablet lamivudine / nevirapine / zidovudine Pill lamivudine / stavudine Oral Product lamivudine / stavudine Oral Tablet lamivudine / stavudine Pill lamivudine / tenofovir disoproxil Oral Product lamivudine / tenofovir disoproxil Oral Tablet lamivudine / tenofovir disoproxil Pill Lamivudine / Zidovudine Delayed Release Oral Tablet lamivudine / zidovudine Oral Product lamivudine / zidovudine Oral Tablet lamivudine / zidovudine Pill Odefsey Oral Product Odefsey Pill Stribild Oral Product Stribild Pill Symfi Oral Product Symfi Pill Symtuza Oral Product Symtuza Pill Temixys Oral Product Temixys Pill Triumeq Oral Liquid Product Triumeq Oral Product Triumeq Pill Trizivir Oral Product Trizivir Pill Truvada Oral Product Truvada Pill			
J05AE Protease inhibitors	Tipranavir Saquinavir Ritonavir	1736999 1746244 1748921	dasabuvir / ombitasvir / paritaprevir / ritonavir Extended	40220795 40220793 44120603

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	Nelfinavir Indinavir Fosamprenavir Darunavir Atazanvir Amprenavir	1715472 1711523 1736829 1756831 1727223 1789428	Release Oral Tablet dasabuvir / ombitasvir / paritaprevir / ritonavir Oral Product dasabuvir / ombitasvir / paritaprevir / Ritonavir Oral Tablet dasabuvir / ombitasvir / paritaprevir / ritonavir Pill dasabuvir 250 MG / ombitasvir 12.5 MG / paritaprevir 75 MG / Ritonavir 50 MG [Holkira] nirmatrelvir / ritonavir Oral Tablet ombitasvir / paritaprevir / Ritonavir Delayed Release Oral Tablet ombitasvir / paritaprevir / ritonavir Oral Product ombitasvir / paritaprevir / ritonavir Oral Tablet ombitasvir / paritaprevir / ritonavir Pill ombitasvir 12.5 MG / paritaprevir 75 MG / ritonavir 50 MG [Technivie] ombitasvir 12.5 MG / paritaprevir 75 MG / Ritonavir 50 MG [Viekira Pak] ombitasvir 12.5 MG / paritaprevir 75 MG / Ritonavir 50 MG [VIEKIRA] ombitasvir 12.5 MG / paritaprevir 75 MG / Ritonavir 50 MG [Viekirax] (nirmatrelvir 150 MG Oral Tablet) / (Ritonavir 100 MG Delayed Release Oral Tablet) Pack (nirmatrelvir 150 MG Oral Tablet) / (ritonavir 100 MG Oral Tablet) Pack	40220794 44067904 1235357 43138759 36248898 45892556 36248899 46275632 43268385 42963129 21061185 36919881 36958852 780185 702577 36933915 1466319

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			10 (nirmatrelvir 150 MG Oral Tablet) / 10 (ritonavir 100 MG Oral Tablet) Pack 20 (nirmatrelvir 150 MG Oral Tablet) / 10 (ritonavir 100 MG Oral Tablet) Pack 4 (nirmatrelvir 150 MG Oral Tablet) / 2 (ritonavir 100 MG Oral Tablet) Pack 6 (nirmatrelvir 150 MG Oral Tablet) / 5 (ritonavir 100 MG Oral Tablet) Pack	
J05AE Protease inhibitors (Monotherapy)	Tipranavir Saquinavir Ritonavir Nelfinavir Indinavir Fosamprenavir Darunavir Atazanvir Amprenavir	1736999 1746244 1748921 1715472 1711523 1736829 1756831 1727223 1789428	(nirmatrelvir 150 MG Oral Tablet) / (Ritonavir 100 MG Delayed Release Oral Tablet) Pack (nirmatrelvir 150 MG Oral Tablet) / (ritonavir 100 MG Oral Tablet) Pack 10 (nirmatrelvir 150 MG Oral Tablet) / 10 (ritonavir 100 MG Oral Tablet) Pack 20 (nirmatrelvir 150 MG Oral Tablet) / 10 (ritonavir 100 MG Oral Tablet) Pack 4 (nirmatrelvir 150 MG Oral Tablet) / 2 (ritonavir 100 MG Oral Tablet) Pack 6 (nirmatrelvir 150 MG Oral Tablet) / 5 (ritonavir 100 MG Oral Tablet) Pack atazanavir / cobicistat Oral Product atazanavir / cobicistat Oral Tablet atazanavir / cobicistat Pill atazanavir 300 MG / cobicistat 150 MG [Evotaz] cobicistat / darunavir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet	36919881 36958852 780185 702577 36933915 1466319 36248760 45892113 36248761 45892116 36788486 1560076 1560078 1560077 36248699 45892973 3624870 45892976 21159260 1560081 40220795 40220793 44120603 40220794 44067904 43215610 40059335 36222583 36222584 40059337 36222585 19048073 19048077 19048071 19048075 1235357 43138759 36248898 36248899

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Pill cobicistat / darunavir Delayed Release Oral Tablet cobicistat / darunavir Oral Product cobicistat / darunavir Oral Tablet cobicistat / darunavir Pill cobicistat 150 MG / darunavir 675 MG [Prezcobix] cobicistat 150 MG / darunavir 800 MG [Prezcobix] cobicistat 150 MG / darunavir 800 MG [Rezolsta] cobicistat 150 MG / darunavir 800 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Symtuza] dasabuvir / ombitasvir / paritaprevir / ritonavir Extended Release Oral Tablet dasabuvir / ombitasvir / paritaprevir / ritonavir Oral Product dasabuvir / ombitasvir / paritaprevir / Ritonavir Oral Tablet dasabuvir / ombitasvir / paritaprevir / ritonavir Pill dasabuvir 250 MG / ombitasvir 12.5 MG / paritaprevir 75 MG / Ritonavir 50 MG [Holkira] lopinavir / Ritonavir	46275632 43268385 42963129 21061185

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			Delayed Release Oral Tablet lopinavir / ritonavir Oral Capsule lopinavir / ritonavir Oral Liquid Product lopinavir / ritonavir Oral Product lopinavir / ritonavir Oral Solution lopinavir / ritonavir Pill lopinavir 100 MG / ritonavir 25 MG [Kaletra] lopinavir 133 MG / ritonavir 33.3 MG [Kaletra] lopinavir 200 MG / ritonavir 50 MG [Kaletra] lopinavir 80 MG/ML / ritonavir 20 MG/ML [Kaletra] nirmatrelvir / ritonavir Oral Tablet ombitasvir / paritaprevir / Ritonavir Delayed Release Oral Tablet ombitasvir / paritaprevir / ritonavir Oral Product ombitasvir / paritaprevir / ritonavir Pill ombitasvir 12.5 MG / paritaprevir 75 MG / ritonavir 50 MG [Technivie] ombitasvir 12.5 MG / paritaprevir 75 MG / Ritonavir 50 MG [Viekira Pak] ombitasvir 12.5 MG / paritaprevir 75 MG / Ritonavir 50 MG [VIEKIRA] ombitasvir 12.5 MG / paritaprevir 75 MG / Ritonavir 50 MG [Viekirax]	
J05AE Protease inhibitors (Combinations)	atazanavir / cobicistat Oral Product atazanavir / cobicistat Oral	36248760 45892113 36248761	N/A	N/A

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	Tablet atazanavir / cobicistat Pill atazanavir 300 MG / cobicistat 150 MG [Evotaz] cobicistat / darunavir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Pill cobicistat / darunavir Delayed Release Oral Tablet cobicistat / darunavir Oral Product cobicistat / darunavir Oral Tablet cobicistat / darunavir Pill cobicistat 150 MG / darunavir 675 MG [Prezcobix] cobicistat 150 MG / darunavir 800 MG [Prezcobix] cobicistat 150 MG / darunavir 800 MG [Rezolsta] cobicistat 150 MG / darunavir 800 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Symtuza] Evotaz Oral Product Evotaz Pill Kaletra Oral Liquid Product Kaletra Oral Product Kaletra Pill lopinavir / Ritonavir Delayed Release Oral Tablet lopinavir / ritonavir Oral Capsule lopinavir / ritonavir Oral Liquid Product lopinavir / ritonavir Oral Product lopinavir / ritonavir Oral Solution lopinavir / ritonavir Oral Tablet lopinavir / ritonavir Pill	45892116 36788486 1560076 1560078 1560077 36783451 36248699 45892973 36248700 1465936 45892976 21159260 1560081 36248762 36248763 36233144 36233142 36233143 43215610 40059335 36222583 36222584 40059337 40128015 36222585 19048073 19048077 19048071 19048075 36248701 36248702 1560083 1560084		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	lopinavir 100 MG / ritonavir 25 MG [Kaletra] lopinavir 133 MG / ritonavir 33.3 MG [Kaletra] lopinavir 200 MG / ritonavir 50 MG [Kaletra] lopinavir 80 MG/ML / ritonavir 20 MG/ML [Kaletra] Prezcobix Oral Product Prezcobix Pill Symtuza Oral Product Symtuza Pill			
J05AG Non-nucleoside reverse transcriptase inhibitors	Rilpivirine Nevirapine Etravirine Efavirenz Doravirine Delavirdine	40238930 1769389 1758536 1738135 35200446 1747157	N/A	N/A
J05AG Non-nucleoside reverse transcriptase inhibitors (Monotherapy)	Rilpivirine Nevirapine Etravirine Efavirenz Doravirine Delavirdine	40238930 1769389 1758536 1738135 35200446 1747157	1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 400 MG / 600 MG] 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva] 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 600 MG / 900 MG] 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva] Atripla Oral Product Atripla Pill Complera Oral Product Complera Pill	740217 740218 2938121 740215 740216 2938119 36236510 36236511 36220376 36220377 35200460 35200461 43028257 793025 793027 793026 793030 43026751 35200462 35200464 35200463 43026753 35200467 43200066 36226563 40134707 36226564 36226561 40166595 36226562 35201132 21043604 1831213 782837 36788477 19124373 1510223

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			Delstrigo Oral Product Delstrigo Pill dolutegravir / Rilpivirine Delayed Release Oral Tablet dolutegravir / rilpivirine Oral Product dolutegravir / rilpivirine Oral Tablet dolutegravir / rilpivirine Pill dolutegravir 50 MG / rilpivirine 25 MG [Juluca] DORAVIRINE / Lamivudine / tenofovir disoproxil Delayed Release Oral Tablet doravirine / lamivudine / tenofovir disoproxil Oral Product doravirine / lamivudine / tenofovir disoproxil Oral Tablet doravirine / lamivudine / tenofovir disoproxil Pill DORAVIRINE 100 MG / Lamivudine 300 MG / tenofovir disoproxil 250 MG [Delstrigo] doravirine 100 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Delstrigo] efavirenz / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet efavirenz / emtricitabine / tenofovir disoproxil Oral Product efavirenz / emtricitabine / tenofovir disoproxil Oral Tablet efavirenz / emtricitabine / tenofovir disoproxil	36788493 36249077 35605920 36249078 43212854 36226580 40241980 36226581 35605923 42965766 21055612 40860485 40241984 793032 793033 36245184 40146970 36218347 40173162 36218348 36218349 40137867 36218350 36249079 36249080 1510225 1510226

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			Pill efavirenz / lamivudine / tenofovir disoproxil Oral Product efavirenz / lamivudine / tenofovir disoproxil Oral Tablet efavirenz / lamivudine / tenofovir disoproxil Pill efavirenz 400 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Atripla] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efatriten] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Krka] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Mylan] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Atripla] efavirenz 600 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] emtricitabine / Rilpivirine / tenofovir alafenamide Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Oral Product	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			emtricitabine / rilpivirine / tenofovir alafenamide Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Pill emtricitabine / Rilpivirine / tenofovir disoproxil Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Oral Product emtricitabine / rilpivirine / tenofovir disoproxil Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Pill emtricitabine 200 MG / rilpivirine 25 MG / tenofovir alafenamide 25 MG [Odefsey] emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 250 MG [Complera] emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 250 MG [Eviplera] emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 300 MG [Eviplera] emtricitabine 200 MG / rilpivirine 25 MG / tenofovir disoproxil fumarate 300 MG [Complera] Juluca Oral Product Juluca Pill lamivudine / nevirapine / stavudine Disintegrating Oral Product lamivudine / nevirapine / stavudine Disintegrating Oral Tablet lamivudine / nevirapine / stavudine Oral Product	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			lamivudine / nevirapine / stavudine Oral Tablet lamivudine / nevirapine / stavudine Pill lamivudine / nevirapine / zidovudine Oral Product lamivudine / nevirapine / zidovudine Oral Tablet lamivudine / nevirapine / zidovudine Pill Odefsey Oral Product Odefsey Pill Symfi Oral Product Symfi Pill	
J05AG Non-nucleoside reverse transcriptase inhibitors (Combinations)	1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 400 MG / 600 MG] 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva] 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 600 MG / 900 MG] 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva] Atripla Oral Product Atripla Pill Complera Oral Product Complera Pill Delstrigo Oral Product Delstrigo Pill dolutegravir / Rilpivirine Delayed Release Oral Tablet dolutegravir / rilpivirine Oral	740217 740218 2938121 740215 740216 2938119 36236510 36236511 36220376 36220377 35200460 35200461 43028257 793025 793027 793026 793030 43026751 35200462 35200464 35200463 43026753 35200467 43200066 36226563 40134707 36226564 36226561 40166595 36226562 35201132 21043604 1831213 782837 36788477	N/A	N/A

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	Product dolutegravir / rilpivirine Oral Tablet dolutegravir / rilpivirine Pill dolutegravir 50 MG / rilpivirine 25 MG [Juluca] DORAVIRINE / Lamivudine / tenofovir disoproxil Delayed Release Oral Tablet doravirine / lamivudine / tenofovir disoproxil Oral Product doravirine / lamivudine / tenofovir disoproxil Oral Tablet doravirine / lamivudine / tenofovir disoproxil Pill DORAVIRINE 100 MG / Lamivudine 300 MG / tenofovir disoproxil 250 MG [Delstrigo] doravirine 100 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Delstrigo] efavirenz / emtricitabine / tenofovir disoproxil efavirenz / emtricitabine / tenofovir disoproxil Oral Product efavirenz / emtricitabine / tenofovir disoproxil Oral Tablet efavirenz / emtricitabine / tenofovir disoproxil Pill efavirenz / lamivudine / tenofovir disoproxil Oral Product efavirenz / lamivudine / tenofovir disoproxil Oral Tablet efavirenz / lamivudine / tenofovir disoproxil Pill efavirenz 400 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Atripla] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efatriten]	19124373 1510223 36788493 36249077 35605920 36249078 43212854 36226580 40241980 36226581 35605923 42965766 21055612 40860485 40241984 793032 793033 36245184 40146970 36218347 40173162 36218348 36218349 40137867 36218350 36249079 36249080 1510225 1510226		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Krka] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Mylan] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Atripla] efavirenz 600 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] emtricitabine / Rilpivirine / tenofovir alafenamide Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Oral Product emtricitabine / rilpivirine / tenofovir alafenamide Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Pill emtricitabine / Rilpivirine / tenofovir disoproxil Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Oral Product emtricitabine / rilpivirine / tenofovir disoproxil Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Pill emtricitabine 200 MG / rilpivirine 25 MG / tenofovir alafenamide 25 MG [Odefsey] emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 250 MG [Complera] emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 250 MG [Eviplera] emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 300 MG [Eviplera] emtricitabine 200 MG /			

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	rilpivirine 25 MG / tenofovir disoproxil fumarate 300 MG [Complera] Juluca Oral Product Juluca Pill lamivudine / nevirapine / stavudine Disintegrating Oral Product lamivudine / nevirapine / stavudine Disintegrating Oral Tablet lamivudine / nevirapine / stavudine Oral Product lamivudine / nevirapine / stavudine Oral Tablet lamivudine / nevirapine / stavudine Pill lamivudine / nevirapine / zidovudine Oral Product lamivudine / nevirapine / zidovudine Oral Tablet lamivudine / nevirapine / zidovudine Pill Odefsey Oral Product Odefsey Pill Symfi Oral Product Symfi Pill			
J05AJ Integrase inhibitors	Raltegravir Elvitegravir Dolutegravir Cabotegravir	1712889 42874212 43560385 739588	N/A	N/A
J05AJ Integrase inhibitors (Monotherapy)	Raltegravir Elvitegravir Dolutegravir Cabotegravir	1712889 42874212 43560385 739588	1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 400 MG / 600 MG] 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva] 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine	740217 740218 2938121 740215 740216 2938119 43211100 779346 36247224 45775746 36247225 779347 779349 2928973 45775749 40923765 21149330 43149972 36248152 35605551 36248153 43180174 36243625 42874221

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			300 MG/ML Injection) Pack [CABENUVA 600 MG / 900 MG]	36243626 36893513
			1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva]	21060949 35605554 21051155 42874226 1511082 1511084
			abacavir / dolutegravir / Lamivudine Delayed Release Oral Tablet	1511083 43028257 793025 793027
			abacavir / dolutegravir / lamivudine Oral Liquid Product	793026 1511087 793030 1511089
			abacavir / dolutegravir / lamivudine Oral Product	1511090 36248154 36248155 793032 793033
			abacavir / dolutegravir / lamivudine Oral Tablet	36243647 36243648 779350
			abacavir / dolutegravir / lamivudine Pill	36247333 36247334
			abacavir / dolutegravir / lamivudine Tablet for Oral Suspension	
			abacavir 60 MG / dolutegravir 5 MG / lamivudine 30 MG [Triumeq]	
			abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Trelavue]	
			abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Triumeq]	
			abacavir 703 MG / dolutegravir 50 MG / Lamivudine 300 MG [Triumeq]	
			cobicistat / elvitegravir / emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet	
			cobicistat / elvitegravir / emtricitabine /	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			tenofovir alafenamide Delayed Release Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Pill cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Pill cobicistat / elvitegravir / emtricitabine / Tenofovir Oral Tablet cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / Tenofovir 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Genvoya] cobicistat 150 MG /	

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Stribild] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Stribild] dolutegravir / lamivudine Oral Product dolutegravir / lamivudine Oral Tablet dolutegravir / lamivudine Pill dolutegravir / Rilpivirine Delayed Release Oral Tablet dolutegravir / rilpivirine Oral Product dolutegravir / rilpivirine Oral Tablet dolutegravir / rilpivirine Pill dolutegravir 50 MG / lamivudine 300 MG [Dovato] dolutegravir 50 MG / rilpivirine 25 MG [Juluca] Dovato Oral Product Dovato Pill Genvoya Oral Product Genvoya Pill Juluca Oral Product Juluca Pill Stribild Oral Product Stribild Pill Triumeq Oral Liquid Product Triumeq Oral Product Triumeq Pill	
J05AJ Integrase inhibitors (Combinations)	1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 400 MG / 600 MG]	740217 740218 2938121 740215 740216 2938119 43211100 779346 36247224	N/A	N/A

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva] 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 600 MG / 900 MG] 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva] abacavir / dolutegravir / Lamivudine Delayed Release Oral Tablet abacavir / dolutegravir / lamivudine Oral Liquid Product abacavir / dolutegravir / lamivudine Oral Product abacavir / dolutegravir / lamivudine Oral Tablet abacavir / dolutegravir / lamivudine Pill abacavir / dolutegravir / lamivudine Tablet for Oral Suspension abacavir 60 MG / dolutegravir 5 MG / lamivudine 30 MG [Triumeq] abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Trelavue] abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Triumeq] abacavir 703 MG / dolutegravir 50 MG / Lamivudine 300 MG [Triumeq] cobicistat / elvitegravir / emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet	45775746 36247225 779347 779349 2928973 45775749 40923765 21149330 43149972 36248152 35605551 36248153 43180174 36243625 42874221 36243626 36893513 21060949 35605554 21051155 42874226 1511082 1511084 1511083 43028257 793025 793027 793026 1511087 793030 1511089 1511090 36248154 36248155 793032 793033 36243647 36243648 779350 36247333 36247334		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Pill cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Pill cobicistat / elvitegravir / emtricitabine / Tenofovir Oral Tablet cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / Tenofovir 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Stribild] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Stribild] dolutegravir / lamivudine Oral Product dolutegravir / lamivudine Oral Tablet dolutegravir / lamivudine Pill dolutegravir / Rilpivirine Delayed Release Oral Tablet dolutegravir / rilpivirine Oral Product dolutegravir / rilpivirine Oral Tablet			

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	dolutegravir / rilpivirine Pill dolutegravir 50 MG / lamivudine 300 MG [Dovato] dolutegravir 50 MG / rilpivirine 25 MG [Juluca] Dovato Oral Product Dovato Pill Genvoya Oral Product Genvoya Pill Juluca Oral Product Juluca Pill Stribild Oral Product Stribild Pill Triumeq Oral Liquid Product Triumeq Oral Product Triumeq Pill			
J05AX Other antivirals (including V03AX03 Cobicistat)	Maraviroc Enfuvirtide Fostemsavir Cobicistat Lenacapavir	1787101 1717002 1146410 42874220 1301335	N/A	N/A
J05AX Other antivirals (including V03AX03 Cobicistat) (Monotherapy)	Maraviroc Enfuvirtide Fostemsavir Cobicistat Lenacapavir	1787101 1717002 1146410 42874220 1301335	atazanavir / cobicistat Oral Product atazanavir / cobicistat Oral Tablet atazanavir / cobicistat Pill atazanavir 300 MG / cobicistat 150 MG [Evotaz] cobicistat / darunavir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Pill cobicistat / darunavir Delayed Release Oral Tablet cobicistat / darunavir Oral Product cobicistat / darunavir Oral Tablet cobicistat / darunavir	36248760 45892113 36248761 45892116 36788486 1560076 1560078 1560077 36783451 36248699 45892973 36248700 21149330 43149972 36248152 35605551 36248153 43180174 36243625 42874221 36243626 36893513 1465936 45892976 21159260 1560081 21060949 35605554 21051155 42874226 36248701 36248702 36243647 36243648

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			Pill cobicistat / elvitegravir / emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Pill cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Pill cobicistat / elvitegravir / emtricitabine / Tenofovir Oral Tablet cobicistat 150 MG / darunavir 675 MG [Prezcobix]	1560083 1560084

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
			cobicistat 150 MG / darunavir 800 MG [Prezcobix] cobicistat 150 MG / darunavir 800 MG [Rezolsta] cobicistat 150 MG / darunavir 800 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Symtuza] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / Tenofovir 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Stribild] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Stribild] Prezcobix Oral Product Prezcobix Pill Stribild Oral Product Stribild Pill Symtuza Oral Product Symtuza Pill	
J05AX Other antivirals (including V03AX03 Cobicistat) (Combinations)	atazanavir / cobicistat Oral Product atazanavir / cobicistat Oral Tablet atazanavir / cobicistat Pill atazanavir 300 MG / cobicistat 150 MG [Evotaz] cobicistat / darunavir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Product	36248760 45892113 36248761 45892116 36788486 1560076 1560078 1560077 36783451 36248699 45892973 36248700 21149330 43149972		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / darunavir / emtricitabine / tenofovir alafenamide Pill cobicistat / darunavir Delayed Release Oral Tablet cobicistat / darunavir Oral Product cobicistat / darunavir Oral Tablet cobicistat / darunavir Pill cobicistat / elvitegravir / emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Pill cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Product cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Pill cobicistat / elvitegravir / emtricitabine / Tenofovir Oral Tablet cobicistat 150 MG / darunavir 675 MG [Prezcobix] cobicistat 150 MG / darunavir 800 MG [Prezcobix] cobicistat 150 MG / darunavir 800 MG [Rezolsta] cobicistat 150 MG /	36248152 35605551 36248153 43180174 36243625 42874221 36243626 36893513 1465936 45892976 21159260 1560081 21060949 35605554 21051155 42874226 36248762 36248763 36248154 36248155 36248701 36248702 36243647 36243648 1560083 1560084		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	darunavir 800 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Symtuza] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / Tenofovir 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Stribild] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Stribild] Evotaz Oral Product Evotaz Pill Genvoya Oral Product Genvoya Pill Prezcobix Oral Product Prezcobix Pill Stribild Oral Product Stribild Pill Symtuza Oral Product Symtuza Pill			
J05AR Antivirals for treatment of HIV infections, combinations	1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 400 MG / 600 MG] 1 (2 ML cabotegravir 200 MG/ML Injection) / 1 (2 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva] 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack 1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [CABENUVA 600 MG / 900 MG]	740217 740218 2938121 740215 740216 2938119 43211100 779346 36247224 45775746 36247225 779347 43211101 36219266 40097200 36219267 44094321 43821524 41236246 779349 2928973 45775749	N/A	N/A

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	1 (3 ML cabotegravir 200 MG/ML Injection) / 1 (3 ML rilpivirine 300 MG/ML Injection) Pack [Cabenuva]	40923765 36236510 36236511 43026139		
	abacavir / dolutegravir / Lamivudine Delayed Release Oral Tablet	964012 964014 964013		
	abacavir / dolutegravir / lamivudine Oral Liquid Product	702170 964017 964019		
	abacavir / dolutegravir / lamivudine Oral Product	964020 42543876		
	abacavir / dolutegravir / lamivudine Oral Tablet	42543877 1560082		
	abacavir / dolutegravir / lamivudine Pill	21149330 43149972		
	abacavir / dolutegravir / lamivudine Tablet for Oral Suspension	36248152 35605551 36248153		
	abacavir / Lamivudine / Zidovudine Delayed Release Oral Tablet	43180174 36243625 42874221		
	abacavir / lamivudine / zidovudine Oral Product	36243626 36893513		
	abacavir / lamivudine / zidovudine Oral Tablet	21060949 35605554		
	abacavir / lamivudine / zidovudine Pill	21051155 42874226		
	abacavir 300 MG / Lamivudine 150 MG / Zidovudine 300 MG [Apo-Abacavir-Lamivudine-Zidovudine]	36220376 36220377 35200460 35200461 36249554		
	abacavir 300 MG / Lamivudine 150 MG / Zidovudine 300 MG [Triplead-Ratiopharm]	36249555 1511082 1511084 1511083		
	abacavir 351 MG / Lamivudine 150 MG / Zidovudine 300 MG [Trizivir]	43028257 793025 793027		
	abacavir 60 MG / dolutegravir 5 MG / lamivudine 30 MG [Triumeq]	793026 1511087 793030		
	abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Trelavue]	43026751 35200462 35200464 35200463		
	abacavir 600 MG / dolutegravir 50 MG / lamivudine 300 MG [Triumeq]	43026753 35200467 1511089 1511090		
	abacavir 703 MG / dolutegravir 50 MG / Lamivudine 300 MG [Triumeq]	43200066 36226563 40134707 36226564		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	Atripla Oral Product	36226561		
	Atripla Pill	40166595		
	bictegravir / emtricitabine / tenofovir alafenamide	36226562		
	Delayed Release Oral Tablet	35201132		
	bictegravir / emtricitabine / tenofovir alafenamide Oral Product	21043604		
	bictegravir / emtricitabine / tenofovir alafenamide Oral Tablet	1831213		
	bictegravir / emtricitabine / tenofovir alafenamide Pill	782837		
	bictegravir 30 MG / emtricitabine 120 MG / tenofovir alafenamide 15 MG [Biktarvy]	36788477		
	bictegravir 50 MG / emtricitabine 200 MG / tenofovir alafenamide 25 MG [Biktarvy]	19124373		
	Biktarvy Oral Product	1510223		
	Biktarvy Pill	36788493		
	Cimduo Oral Product	36249077		
	Cimduo Pill	35605920		
	cobicistat / darunavir / emtricitabine / tenofovir alafenamide Oral Tablet [Symtuza]	36249078		
	cobicistat / elvitegravir / emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet	43212854		
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet	36226580		
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Product	40241980		
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Oral Tablet	36226581		
	cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide Pill	21094460		
	cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet	35411176		
	cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Oral Product	36249552		
	cobicistat / elvitegravir / emtricitabine / tenofovir	35604224		
		36249553		
		36882760		
		21104773		
		1758830		
		35605923		
		42965766		
		21055612		
		40860485		
		40241984		
		782825		
		782824		
		44067769		
		35604227		
		36248154		
		36248155		
		793032		
		793033		
		36245184		
		40146970		
		36218347		
		40173162		
		36218348		
		36218349		
		40137867		
		36218350		
		36218351		
		40142130		
		36218352		
		42543869		
		42543871		
		42543870		
		42543874		
		1511229		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	disoproxil Oral Tablet cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil Pill cobicistat / elvitegravir / emtricitabine / Tenofovir Oral Tablet cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / Tenofovir 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir alafenamide 10 MG [Genvoya] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Stribild] cobicistat 150 MG / elvitegravir 150 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Stribild] Complera Oral Product Complera Pill Delstrigo Oral Product Delstrigo Pill Descovy Oral Product Descovy Pill dolutegravir / lamivudine Oral Product dolutegravir / lamivudine Oral Tablet dolutegravir / lamivudine Pill dolutegravir / Rilpivirine Delayed Release Oral Tablet dolutegravir / rilpivirine Oral Product dolutegravir / rilpivirine Oral Tablet dolutegravir / rilpivirine Pill dolutegravir 50 MG / lamivudine 300 MG [Dovato] dolutegravir 50 MG / rilpivirine 25 MG [Juluca] DORAVIRINE / Lamivudine / tenofovir disoproxil Delayed Release Oral Tablet doravirine / lamivudine / tenofovir disoproxil Oral Product	36249079 36249080 36243647 36243648 1510225 1510226 1560083 1560084 1511231 1511232 21055213 779350 36247333 36247334 36239208 36239209		

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	doravirine / lamivudine / tenofovir disoproxil Oral Tablet doravirine / lamivudine / tenofovir disoproxil Pill DORAVIRINE 100 MG / Lamivudine 300 MG / tenofovir disoproxil 250 MG [Delstrigo] doravirine 100 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Delstrigo] Dovato Oral Product Dovato Pill efavirenz / emtricitabine / tenofovir disoproxil Delayed Release Oral Tablet efavirenz / emtricitabine / tenofovir disoproxil Oral Product efavirenz / emtricitabine / tenofovir disoproxil Oral Tablet efavirenz / emtricitabine / tenofovir disoproxil Pill efavirenz / lamivudine / tenofovir disoproxil Oral Product efavirenz / lamivudine / tenofovir disoproxil Oral Tablet efavirenz / lamivudine / tenofovir disoproxil Pill efavirenz 400 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Atripla] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efatriten] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine / Tenofovir disoproxil Krka] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil 250 MG [Efavirenz / Emtricitabine /			

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	Tenofovir disoproxil Mylan] efavirenz 600 MG / emtricitabine 200 MG / tenofovir disoproxil fumarate 300 MG [Atripla] efavirenz 600 MG / lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Symfi] emtricitabine / Rilpivirine / tenofovir alafenamide Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Oral Product emtricitabine / rilpivirine / tenofovir alafenamide Oral Tablet emtricitabine / rilpivirine / tenofovir alafenamide Pill emtricitabine / Rilpivirine / tenofovir disoproxil Delayed Release Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Oral Product emtricitabine / rilpivirine / tenofovir disoproxil Oral Tablet emtricitabine / rilpivirine / tenofovir disoproxil Pill emtricitabine / Tenofovir / tenofovir disoproxil Oral Tablet emtricitabine / tenofovir alafenamide Delayed Release Oral Tablet emtricitabine / tenofovir alafenamide Oral Product emtricitabine / tenofovir alafenamide Oral Tablet emtricitabine / tenofovir alafenamide Pill emtricitabine / Tenofovir Oral Tablet emtricitabine 10 MG/ML Oral Solution [Emtriva] by Gilead emtricitabine 120 MG / tenofovir alafenamide 15 MG [Descovy] emtricitabine 200 MG / rilpivirine 25 MG / tenofovir alafenamide 25 MG [Odefsey]			

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 250 MG [Complera] emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 250 MG [Eviplera] emtricitabine 200 MG / Rilpivirine 25 MG / tenofovir disoproxil 300 MG [Eviplera] emtricitabine 200 MG / rilpivirine 25 MG / tenofovir disoproxil fumarate 300 MG [Complera] emtricitabine 200 MG / Tenofovir 245 MG [Emtricitabine / Tenofovir disoproxil Krka] emtricitabine 200 MG / Tenofovir 245 MG [Emtricitabine / Tenofovir disoproxil Mylan] emtricitabine 200 MG / tenofovir alafenamide 10 MG [Descovy] emtricitabine 200 MG / tenofovir alafenamide 25 MG [Descovy] Genvoya Oral Product Genvoya Pill Juluca Oral Product Juluca Pill lamivudine / nevirapine / stavudine Disintegrating Oral Product lamivudine / nevirapine / stavudine Disintegrating Oral Tablet lamivudine / nevirapine / stavudine Oral Product lamivudine / nevirapine / stavudine Oral Tablet lamivudine / nevirapine / stavudine Pill lamivudine / nevirapine / zidovudine Oral Product lamivudine / nevirapine / zidovudine Oral Tablet lamivudine / nevirapine / zidovudine Pill lamivudine / stavudine Oral Product lamivudine / stavudine Oral Tablet lamivudine / stavudine Pill			

Concept set name	Included concepts	IDs (including descendants)	Excluded concepts	IDs (including descendants)
	lamivudine / tenofovir disoproxil Oral Product lamivudine / tenofovir disoproxil Oral Tablet lamivudine / tenofovir disoproxil Pill lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Cimduo] lamivudine 300 MG / tenofovir disoproxil fumarate 300 MG [Temixys] Odefsey Oral Product Odefsey Pill Stribild Oral Product Stribild Pill Symfi Oral Product Symfi Pill Symtuza Oral Product Symtuza Pill Temixys Oral Product Temixys Pill Tenofovir / tenofovir disoproxil Oral Tablet Triumeq Oral Liquid Product Triumeq Oral Product Triumeq Pill Trizivir Oral Product Trizivir Pill			

Appendix II: ENCePP checklist for study protocols

Study title: DARWIN EU® - P3-C1-020 - Use of antiretroviral therapies in paedriatic patients

EU PAS Register® number: N/A
Study reference number (if applicable): N/A
EU PAS Register® number:
Study reference number (if applicable):

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1. Does the protocol specify timelines for				
1.1.1 Start of data collection	X			
1.1.2 End of data collection	X			5. Milestones,
1.1.3 Progress report(s)			X	8.2 Data Sources
1.1.4 Interim report(s)			X	
1.1.5 Registration in the EU PAS Register®	X			
1.1.6 Final report of study results.	X			

Comments:

Section 2: Research question	**Yes**	**No**	**N/A**	**Section Number**
2.1 Does the formulation of the research question and objectives clearly explain:				
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	X			7. Research question and objectives
2.1.2 The objective(s) of the study?	X			
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	X			8. Research methods
2.1.4 Which hypothesis(-es) is (are) to be tested?		X		
2.1.5 If applicable, that there is no *a priori* hypothesis?			X	

Comments:

Section 3: Study design	**Yes**	**No**	**N/A**	**Section Number**
3.1 Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	X			8.1 Study type and Study Design

3.2	Does the protocol specify whether the study is based on primary, secondary or combined data collection?	X			8.2 Study Setting and Data Sources
3.3	Does the protocol specify measures of occurrence? (e.g., rate, risk, prevalence)	X			8.8 Analysis
3.4	Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))			X	8.8 Analysis
3.5	Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)			X	

Comments:

Section 4: Source and study populations		**Yes**	**No**	**N/A**	**Section Number**
4.1	Is the source population described?	X			8.5 Study Population
4.2	Is the planned study population defined in terms of:				
	4.2.1 Study time period	X			8.3 Study Period
	4.2.2 Age and sex	X			8.6.3. Other covariates
	4.2.3 Country of origin				8.2 Study Setting and Data Sources
	4.2.4 Disease/indication	X			8.6.1. Exposures
	4.2.5 Duration of follow-up	X			8.4 Follow-up
4.3	Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	X			8.5 Study Population with inclusion and exclusion criteria

Comments:

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.1 Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	X			8.6.1. Exposures And 8.8 Analysis
5.2 Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)			X	
5.3 Is exposure categorised according to time windows?			X	
5.4 Is intensity of exposure addressed? (E.g. dose, duration)			X	
5.5 Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?			X	
5.6 Is (are) (an) appropriate comparator(s) identified?			X	

Comments:

Section 6: Outcome definition and measurement	Yes	No	N/A	Section Number
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	X			8.6.2. Outcomes
6.2 Does the protocol describe how the outcomes are defined and measured?	X			8.6.2. Outcomes
6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)		X		
6.4 Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease or treatment, compliance, disease management)		X		

Comments:

Section 7: Bias	Yes	No	N/A	Section Number
7.1 Does the protocol address ways to measure confounding? (e.g. confounding by indication)			X	
7.2 Does the protocol address selection bias? (e.g. healthy user/adherer bias)			X	
7.3 Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)			X	

Comments:

Section 8: Effect measure modification	Yes	No	N/A	Section Number
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)			X	

Comments:

Section 9: Data sources	Yes	No	N/A	Section Number
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)			X	
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	X			8.2 Study Setting and Data Sources
9.1.3 Covariates and other characteristics?	X			8.6.3. Other covariates
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)			X	

9.2.2 Outcomes? (e.g. date of occurrence, multiple events, severity measures related to event)	X			8.2 Study Setting and Data Sources
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	X			8.2 Study Setting and Data Sources
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	X			
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	X			8.6.2. Outcomes
9.3.3 Covariates and other characteristics?	X			8.6.3. Other covariates
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)			X	

Comments:

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.1 Are the statistical methods and the reason for their choice described?	X			8.8 Analysis
10.2 Is study size and/or statistical precision estimated?			X	
10.3 Are descriptive analyses included?	X			8.8.2 Descriptive statistics
10.4 Are stratified analyses included?	X			8.8 Analysis
10.5 Does the plan describe methods for analytic control of confounding?			X	
10.6 Does the plan describe methods for analytic control of outcome misclassification?			X	
10.7 Does the plan describe methods for handling missing data?			X	
10.8 Are relevant sensitivity analyses described?			X	

Comments:

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	X			9. Data management
11.2 Are methods of quality assurance described?	X			10. Quality Control
11.3 Is there a system in place for independent review of study results?			X	

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of: 12.1.1 Selection bias? 12.1.2 Information bias?	X			11. Limitations of the research methods

12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods).				
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	X			Table 8.2. Description of the selected Data Sources.

Comments:

Section 13: Ethical/data protection issues	**Yes**	**No**	**N/A**	**Section Number**
13.1 Have requirements of Ethics Committee/ Institutional Review Board been described?	X			13. Governance board aspects
13.2 Has any outcome of an ethical review procedure been addressed?			X	
13.3 Have data protection requirements been described?	X			9.2 Data storage and protection

Comments:

Section 14: Amendments and deviations	**Yes**	**No**	**N/A**	**Section Number**
14.1 Does the protocol include a section to document amendments and deviations?	X			4. Amendments and updates

Comments:

Section 15: Plans for communication of study results	**Yes**	**No**	**N/A**	**Section Number**
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	X			14. Plans for disseminating and communicating study results
15.2 Are plans described for disseminating study results externally, including publication?	X			14. Plans for disseminating and communicating study results

Comments:

Name of the main author of the protocol: G. van Leeuwen

Date: 3rd of January 2025

Signature: