SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

Contact information

General

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Product identifier	**Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Fumarate Combination Tablet**
Synonyms	**Elvitegravir:** GS-9137; EVG **Cobicistat**: GS-9350, COBI **Emtricitabine**: FTC, *cis*-(-)-FTC **Tenofovir Alafenamide Fumarate**: TAF fumarate, GS-7340-03; Tenofovir phenyl isopropyl L-alaninyl phosphonamidate
Trade names	Genvoya®
Chemical family	Mixture - contains multiple anti-viral compounds / one pharmacoenhancer
Relevant identified uses of the substance or mixture and uses advised against	Bulk formulated pharmaceutical product/Formulated pharmaceutical product packaged in final form for patient use. Used alone or in combination with other antiretroviral agents for the treatment of HIV-1 infection.
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture	**Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada.** Consult prescribing/packaging information. **The classification and labeling listed below is for bulk drug product.**
Globally Harmonized System [GHS]	Not classified

Label elements

SECTION 2 - HAZARDS IDENTIFICATION …continued

GHS hazard pictogram None required

GHS signal word None required

GHS hazard statements None required

GHS precautionary statements None required

Other hazards In clinical trials with the combination formulation containing elvitegravir, emtricitabine, cobicistat, and tenofovir alafenamide over a period of 48 weeks, treatment was generally well tolerated as most adverse effects were mild and not associated with treatment discontinuation. The most frequent treatment-emergent adverse events (>10%) included: nausea, diarrhea, fatigue, upper respiratory tract infection, and headache. In clinical trials in both healthy volunteers and HIV-infected subjects, TAF has been generally well tolerated.

Note This mixture is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ELINCS#	Amount	GHS Classification
Cellulose	9004-34-6	232-674-9	20-25%	Not classified
Emtricitabine	143491-57-0	N/A	17-20%	Not classified
Elvitegravir	697761-98-1	N/A	13-15%	CA3: H412
Cobicistat	1004316-88-4	N/A	13-15%	Not classified
Silicon Dioxide (silica, amorphous)	112945-52-5	231-545-4	10-15%	Not classified
Tenofovir Alafenamide Fumarate	1392275-56-7	N/A	1-2%	STOT-RE2: H373
Sodium lauryl (dodecyl) sulfate	151-21-3	205-788-1	1-2%	ATO4: H302; ATD3: H311; SI2: H315; EI2: H319; FS2: H228; STOT-S3: H335
Magnesium Stearate	557-04-0	209-150-3	1-2%	Not classified
Titanium dioxide	13463-67-7	236-675-5	0.4-1%	Not classified

Note The ingredients listed above are considered hazardous. The ingredients that are designated with GHS classifications are listed because they are classified as hazardous. Cobicistat, emtricitabine, elvitegravir, and tenofovir alafenamide fumarate are pharmacologically active and have OELs. Silicon dioxide, magnesium stearate, titanium dioxide and cellulose are included because they have OELs. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	Yes
Eye Contact	In the event of a chemical exposure, immediately irrigate eyes with copious quantities of water for at least 15 minutes. Remove contact lenses as soon as practical. Do not delay irrigation while waiting for contact lens removal. If irritation occurs or persists, notify medical personnel and supervisor.
Skin Contact	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
Inhalation	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
Ingestion	Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
Protection of first aid responders	See Section 8 for Exposure Controls/Personal Protection recommendations.
Most important symptoms and effects, both acute and delayed	See Sections 2 and 11.
Indication of immediate medical attention and special treatment needed, if necessary	Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug-drug interactions.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
Specific hazards arising from the substance or mixture	No information identified. May emit toxic gases of carbon monoxide, carbon dioxide, oxides of nitrogen, sulfur-containing compounds, and fluorine-containing compounds.
Flammability/Explosivity	No information identified.
Advice for firefighters	In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	If tablets are spilled, scoop up and dispose of in a manner that is compliant with federal, state or local laws. If tablets are crushed/broken, do not raise dust. Clean up spill with HEPA-filtered vacuum if available. If not available, add water to allow for the material to enter solution. Collect material with absorbents. Place spill materials into a leak-proof container suitable for disposal. Decontaminate area a second time. Dispose of material in a manner that is compliant with federal, state and local laws.
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	Follow recommendations for handling bulk formulated/packaged pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). If tablets are crushed or broken, dust containing drug substance may be released. Minimize dust generation and accumulation. Wash thoroughly after handling. Avoid contact with eyes, skin and other mucous membranes.
Conditions for safe storage including any incompatibilities	Store at controlled room temperature of 25 °C. Excursions permitted between 15-30 °C
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Cellulose	ACGIH, Australia, Belgium, Estonia, France, Portugal, Romania, Singapore, Spain	TWA-8 HR	10 mg/m

Control Parameters/Occupational Exposure Limit Values
…continued

Compound	Issuer	Type	OEL
Cellulose	Ireland, United Kingdom	TWA-8 HR	10 mg/m (inhalable dust); 4 mg/m (respirable dust)
	Ireland	STEL	20 mg/m (total inhalable dust)
	Latvia	TWA-8 HR	2 mg/m
	Mexico	TWA-8 HR/STEL	10/20 mg/m
	NIOSH	TWA-8 HR	10 mg/m (total dust); 5 mg/m (respirable dust)
	OSHA	TWA-8 HR	15 mg/m (total dust); 5 mg/m (respirable fraction)
	United Kingdom	STEL	20 mg/m (inhalable dust); 12 mg/m (respirable dust)
Emtricitabine	Gilead	TWA-8 HR	1 mg/m
Elvitegravir	Gilead	TWA 8-Hr	600 µg/m
Cobicistat	Gilead	TWA 8-HR	80 µg/m
Silicon Dioxide (silica, amorphous)	United Kingdom	WEL-TWA	6 mg/m^3 (inhalable dust); 2.4 mg/m^3 (respirable dust)
	United Kingdom	WEL-STEL	18 mg/m^3 (inhalable dust); 7.2 mg/m^3 (respirable dust)
	Switzerland	TWA-8 HR	4 mg/m^3 (inhalable dust); 0.3 mg/m^3 (respirable dust)
	Slovakia	TWA-8 HR	4 mg/m^3 (total aerosol)
	Slovenia	TWA-8 HR	4 mg/m^3 (inhalable fraction)
	NIOSH	IDLH (Immediately dangerous to life or health)	3000 mg/m^3
	NIOSH	REL-TWA	6 mg/m^3
	Latvia	TWA-8 HR	1 mg/m^3
	Lithuania	STEL	0.02 mg/m
	Ireland	TWA-8 HR	6 mg/m^3 (total inhalable dust); 2.4 mg/m^3 (respirable dust)

Control Parameters/Occupational Exposure Limit Values
…continued

Compound	Issuer	Type	OEL
Silicon Dioxide (silica, amorphous)	Germany	TWA-8 HR	4 mg/m^3 (inhalable fraction)
	Estonia	TWA-8 HR	2 mg/m^3 (respirable dust)
	Czech Republic	TWA-8 HR	0.1 mg/m^3 (respirable fraction); 4 mg/m^3 (regulated under amorphous silicon dioxide)
	Australia	TWA-8 HR	2 mg/m (respirable dust)
	Austria	TWA-8 HR	4 mg/m^3 (inhalable fraction)
Tenofovir Alafenamide Fumarate	Gilead	TWA-8 HR	15 µg/m
Sodium lauryl (dodecyl) sulfate	--	--	--
Magnesium Stearate	ACGIH	TWA-8 HR	10 mg/m (stearates)
	Lithuania	TWA-8 HR	3 mg/m
	Sweden	TWA-8 HR	5 mg/m
Titanium dioxide	ACGIH, Australia, Belgium, Bulgaria, Latvia, Poland, Portugal, Romania, Singapore, Spain, OSHA (vacated)	TWA-8 HR	10 mg/m
	Austria	TWA-8 HR	5 mg/m (respirable fraction)
	Austria	STEL (2 x 60 min)	10 mg/m (respirable fraction)
	Denmark	TWA-8 HR	6 mg/m (as Ti)
	Estonia, Lithuania, Sweden	TWA-8 HR	5 mg/m
	France, Mexico	TWA-8 HR	10 mg/m (as Ti)

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Control Parameters/Occupational Exposure Limit Values
…continued

Compound	Issuer	Type	OEL
Titanium dioxide	Greece	TWA-8 HR	10 mg/m (inhalable fraction); 5 mg/m (respirable fraction)
	Ireland, United Kingdom	TWA-8 HR	10 mg/m (total inhalable dust); 4 mg/m (respirable dust)
	Mexico	STEL	20 mg/m (as Ti)
	NIOSH	IDLH	5000 mg/m
	Romania	STEL	15 mg/m
	United Kingdom	STEL	30 mg/m (total inhalable); 12 mg/m (respirable)

Exposure/Engineering controls

None required for normal handling of packaged product. If handling bulk tablets or tablets are crushed or broken: control exposures to below the OEL. The objective of containment, controls and work practices should be to contain worker breathing zone concentrations to below the OEL for each task or operation. Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at dust-generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling of powders. High-energy operations such as milling, particle sizing, spraying or fluidizing should be done within an approved emission control or containment system.

Respiratory protection

None required for normal handling of packaged product. If handling bulk tablets or tablets are crushed or broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. An approved and properly fitted air-purifying respirator with HEPA filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a powered air-purifying respirator equipped with HEPA filters or combination filters or a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where a lower level of respiratory protection may not provide adequate protection. The assigned protection factor (APF) of the selected PAPR should be at least 1000.

Hand protection

None required for normal handling of packaged product. Wear nitrile or other impervious gloves if skin contact with tablets is possible.

Skin protection

Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Eye/face protection	Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
Environmental Exposure Controls	Should not be required during normal handling of material. In case of spill, do not release to drains. Avoid release to the environment.
Other protective measures	Wash hands in the event of contact with tablets, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Capsule-shaped, film-coated tablets.
Color	White or green
Odor	No information identified.
Odor threshold	No information identified.
pH	No information identified.
Melting point/freezing point	No information identified.
Initial boiling point and boiling range	No information identified.
Flash point	No information identified.
Evaporation rate	No information identified.
Flammability (solid, gas)	No information identified.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified.
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	No information identified.
Solvent solubility	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

Molecular formula	Not applicable (Mixture)
Molecular weight	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note	The following data describe the active ingredients and/or other ingredients where applicable. The hazards of tenofovir alafenamide fumarate (TAF) are considered to be similar to those of the compound tenofovir alafenamide monofumarate (GS-7340-02).

Information on toxicological effects

Route of entry	None likely for packaged product. Crushed/broken tablets may be absorbed by inhalation, skin contact and ingestion.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Acute toxicity

Compound	Type	Route	Species	Dose
Cellulose	LC_{50}	Inhalation	Rat	>5800 mg/m /4h
	LD_{50}	Oral	Rat	>5000 mg/kg
	LD_{50}	Dermal	Rabbit	>2000 mg/kg
Emtricitabine	LD_{50}	Oral	Rat/Mouse	>4000 mg/kg
Elvitegravir	LD_{50}	Oral	Rat	>2000 mg/kg
	LD_{50}	Oral	Dog (female)	>1000 mg/kg
Cobicistat	--	--	--	--
Silicon Dioxide (silica, amorphous)	LD_{50}	Oral	Rat	>22500 mg/kg
	LD_{50}	Oral	Mouse	>15000 mg/kg
	LC_{50}	Inhalation	Rat	>2.2 mg/L/1 hour
	LD_{50}	Dermal	Rabbit	>2000 mg/kg
Tenofovir Alafenamide Fumarate	--	--	--	--
Sodium lauryl (dodecyl) sulfate	LC_{50}	Inhalation	Rat	>3900 mg/m
	LD_{50}	Oral	Rat	977 - 1427 mg/kg
	LD_{50}	Intravenous	Rat	118 mg/kg
	LD_{50}	Intravenous	Mouse	118 mg/m
	LD_{50}	Dermal	Rabbit	580 mg/kg
	LD_{50}	Oral	Mouse	2700 - 2800 mg/kg
Magnesium Stearate	LC_{50}	Inhalation	Rat	>2000 mg/m
Titanium dioxide	LD_{50}	Oral	Rat	>10000 mg/kg
	LD_{50}	Oral	Mouse	>10000 mg/kg
	LD_{50}	Dermal	Rabbit	>10000 mg/kg

Irritation/Corrosion Cobicistat was mildly irritating to rabbit skin, but not to rabbit eyes. Elvitegravir was not irritating to rabbit skin or eyes. TAF fumarate is not considered corrosive or a severe eye irritant based on an *in vitro* screening assessment of potential eye irritation, and was non- irritating/non-corrosive when tested on the skin of rabbits under semi-occluded conditions. No information identified for emtricitabine.

Sensitization TAF fumarate did not show the potential to cause skin sensitization with repeated application to the dorsal surface of mouse ears (LLNA assay). Elvitegravir and cobicistat were not contact sensitizers in guinea pigs and/or mice. No information identified for emtricitabine.

STOT-single exposure In rats and female dogs, lethal single oral doses of elvitegravir were >2000 and >1000 mg/kg, respectively. No adverse effects were seen in rats given high oral doses of cobicistat.

In single-dose oral toxicity studies, the NOAEL of TAF monofumarate (GS-7340-02) in the rat was at least 1000 mg/kg, and the NOEL of GS-7340-02 in the dog was 30 mg/kg.

STOT-repeated exposure/Repeat-dose toxicity	There were no target organs identified in repeat-dose studies with emtricitabine or elvitegravir. The NOAELs for elvitegravir in chronic toxicology studies were considered to be 2000 mg/kg/day for mice and rats, and 100 mg/kg/day for dogs. Administration of emtricitabine alone at a dose of 20 mg/kg/day was well tolerated by dogs for 4 weeks. Oral NOELs of 500, 600 and 200 mg/kg/day emtricitabine were identified in repeat-dose toxicity studies in mice (6-month), rats (3-month) and monkeys (12-month), respectively. The NOAEL associated with repeat doses of TAF monofumarate in a 28-day oral rat study was 6.25 mg/kg/day (target organ: hematological system). In chronic studies in rats, bone and kidneys were the primary target organs after 26 weeks of treatment with TAF at 100 mg/kg/day. Effects were not seen at lower doses; the NOAEL was 25 mg/kg/day. The NOAEL associated with a 28-day oral study of TAF monofumarate in dogs was >10 mg/kg (target organs: kidney and bone). The NOAEL associated with a 9- month oral study of TAF monofumarate in dogs was 2 mg/kg/day (target organs: kidney and bone); doses of 18 mg/kg/day were lethal to one animal. There were no treatment-related effects observed in monkeys following 28 days of oral dosing with TAF monofumarate; the NOAEL was ≥30 mg/kg/day. Target organs in repeated-dose studies with cobicistat were the liver (mice, rats, and dogs) and thyroid (rats only).
Reproductive toxicity	Elvitegravir, cobicistat, and emtricitabine are not considered to be reproductive toxicants based on fertility studies conducted in laboratory animals at doses ≥ 300 mg/kg/day in all cases. In a TAF monofumarate oral rat fertility study, the NOAEL for reproductive and early embryonic toxicity was 160 mg/kg/day.
Developmental toxicity	Elvitegravir, cobicistat, and emtricitabine are not considered to be developmental toxicants based on studies conducted in laboratory animals at doses ≥ 450 mg/kg/ day in all cases. There was no effect on fetal viability or fetal development in pregnant rats and rabbits administered doses of TAF monofumarate up to 250 mg/ kg/day and 100 mg/kg/day, respectively. The highest doses were maternally toxic. The NOAEL/ NOEL in pregnant rats/rabbits administered oral doses of TAF monofumarate in embryo-fetal development studies was 100 mg/kg/day.
Genotoxicity	The weight of evidence is that these ingredients would not be considered to be genotoxic. Emtricitabine was negative in the *in vitro* Ames assay, an *in vitro* mutation assay in mouse lymphoma cells, and an *in vivo* mouse micronucleus assay. Elvitegravir was negative in the Ames bacterial cell mutagenicity assay and in a micronucleus genotoxicity study and equivocal in an *in vitro* chromosomal aberration test. Cobicistat was negative in several genotoxicity studies. TAF monofumarate was negative for genotoxic effects in an *in vitro* mouse lymphoma assay, in the *in vitro* Ames assay, and in an *in vivo* mouse micronucleus assay.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Carcinogenicity

No drug-related increases in tumor incidence were observed in mice or rats treated with oral doses as high as 750 and 600 mg/kg/day emtricitabine, respectively.

No drug-related increases in tumor incidence were observed in mice or rats treated orally with up to 2000 mg/ kg/day elvitegravir.

In 2-year carcinogenicity studies with cobicistat, no drug-related tumors were observed in mice. Increases in follicular cell adenomas and/or carcinomas in the thyroid gland were observed at doses of ≥25 and 30 mg/kg/day in male and female rats, respectively, but these tumors are considered to be species-specific and not relevant to human exposure.

No studies conducted for TAF fumarate or TAF monofumarate. Long-term oral carcinogenicity studies of tenofovir disoproxil fumarate in mice and rats were carried out at exposures up to approximately 16 (mice) and 5 times (rats), respectively, those observed in humans at the therapeutic dose for HIV-1 infection. At the high dose in female mice, duodenal tumors were increased. In rats, no evidence of carcinogenicity was observed. Carcinogenicity studies are not planned for TAF because of the existing data for TDF.

Titanium dioxide has been classified by the International Agency for Research on Cancer (IARC) as an IARC Group 2B carcinogen "possibly carcinogenic to humans". This classification is based upon animal inhalation studies. Epidemiology studies do not suggest an increased risk of cancer in humans from occupational exposure to titanium dioxide. None of the remaining components of the mixture present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.

Aspiration hazard

No data available.

Human health data

See "Section 2 - Other Hazards".

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Cellulose	--	--	--
Emtricitabine	EC_{50}/72h	Freshwater green algae	>110 mg/L
	EC_{50}/48h	Daphnia magna	>110 mg/L
	LC_{50}/96h	Rainbow trout	>110 mg/L
	NOEC/21 days reproduction	Daphnia magna	110 mg/L
	Early Life Cycle NOEC	Fathead minnow	6.1 mg/L
	NOEC (3-hr)	Activated sludge microorganisms	940 mg/L

SECTION 12 - ECOLOGICAL INFORMATION …continued

Toxicity …continued

Compound	Type	Species	Concentration
Elvitegravir	NOEC	Pimephales promelas	206 µg/L
	NOEC	Daphnia magna	390 µg/L
	NOEC	Pseudokirchneriella subcapitata (algae)	162 µg/L
	NOEC	Activated sludge microorganisms	≥ 500 mg/L
Cobicistat	NOEC	Pimephales promelas	4.84 mg/L
	NOEC	Daphnia magna	17.5 mg/L
	NOEC	Pseudokirchneriella subcapitata (algae)	29.3 mg/L
	NOEC	Activated sludge microorganisms	>1000 mg/L
Silicon Dioxide (silica, amorphous)	EC_{50}/72h	Green algae (Selenastrum capricornutum)	440 mg/L
	LC_{50}/96h	Brachydanio rerio (zebrafish)	5000 mg/L (static)
	EC_{50}/48h	Ceriodaphnia dubia	7600 mg/L
Tenofovir Alafenamide Fumarate	NOEC (3-hr)	Activated sludge microorganisms	≥1,000 mg/L (tenofovir)
	NOEC/28 days (hatch, post-hatch, growth)	Pimephales promelus (fathead minnow)	≥10 mg/L (tenofovir)
	NOEC/21 days (reproduction)	Daphnia magna	≥100 mg/L (tenofovir)
	NOEC (72h)	Pseduokirchneriella subcapitata (green algae)	32 mg/L (tenofovir)
Sodium lauryl (dodecyl) sulfate	EC_{50}/72h	Scenedesmus supspicatus (algae)	53 mg/L
	LC_{50}/96h	Various Fish Species	~ 1.2 - 29 mg/L
	EC_{50}/48h	Daphnia magna	1.8 - 31 mg/L
Magnesium Stearate	--	--	--
Titanium dioxide	LC_{50}/48h	Leuciscus idus	>1000 mg/L

Additional toxicity information

An EC_{50} of >1000 mg a.i./L was identified for emtricitabine in a respiratory inhibition study.

Results from human clinical trials have shown that TAF is not significantly excreted (<2%). The majority of drug excreted occurs as tenofovir (TFV), all other excretion by-products are individually significantly less than 10%. The results of tenofovir early-life stage (ELS) test in fathead minnows (*Pimephales promelas)* led to the following conclusions:

SECTION 12 - ECOLOGICAL INFORMATION …continued

Additional toxicity information …continued	1. Tenofovir did not induce any statistically significant effects on embryonic survival at 10 mg/L. Hence, both the NOEC and LOEC for embryonic survival were >10 mg/L; 2. Tenofovir did not induce any statistically significant effects on larval survival at 10 mg/L. Hence, the both the NOEC and LOEC for larval survival were >10 mg/L; 3. Tenofovir did not induce any statistically significant effects on larval growth at 10 mg/L. Hence, both the NOEC and LOEC for larval growth were >10 mg/L. Tenofovir did not induce any statistically significant effects on parental growth at 100 mg/L. Hence, the NOEC and LOEC for parental growth were 100 and >100 mg/L, respectively. Mean parental body length was not significantly reduced at any of the test concentrations.
Persistence and Degradability	Emtricitabine, cobicistat, elvitegravir, and tenofovir alafenamide fumarate are not readily biodegradable. The environmentally relevant residues of emtricitabine and TAF fumarate (as TFV) are indicated to have sufficiently low concentrations in the sediment environment that their toxicity is unlikely to present a risk to aquatic ecosystems.
Bioaccumulative potential	Emtricitabine, elvitegravir, cobicistat, and TFV are unlikely to bioaccumulate, based on their respective octanol/water partition coefficients and/or bioconcentration studies in fish. The mean log K_{OW} of elvitegravir was 3.39 - 4.33. The mean log K_{OW} of emtricitabine was -0.693 - -0.670. The mean log K_{OW} of cobicistat was 3.05 - 4.10. The mean log K_{OW} of TFV was -3.8 - -4.3.
Mobility in soil	Elvitegravir is highly bound to soil and sludge but not a risk to terrestrial organisms at environmentally relevant concentrations. Cobicistat, emtricitabine, and TFV will bind to soil or sludge to a lesser degree and are below cutoffs triggering a terrestrial assessment..
Adsorption coefficient (Koc)	Emtricitabine did not adsorb significantly to activated sludge with a K_{OC} value from 21.1 - 45.6 L/kg. K_{OC} soil values of cobicistat ranged from 3,624 - 9,012 L/kg, indicating tendency for adsorption to soil. Elvitegravir likely adsorbs to soil, with K_{OC} values in the range of 25,500 - 104,000 L/kg. The soil K_{OC} for TFV ranges from 351-1091.
Results of PBT and vPvB assessment	Emtricitabine, cobicistat, elvitegravir, and TAF fumarate are not considered PBT or vPvB substances
Other adverse effects	No data available.
Note	The environmental characteristics of this product/mixture have not been fully investigated. The above data are for the active ingredients and/or any other ingredient(s) where applicable. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods	Used product should be disposed of according to local, state, and federal regulations. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

SECTION 14 - TRANSPORT INFORMATION

Transport	Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
UN number	None assigned.
UN proper shipping name	None assigned.
Transport hazard classes and packing group	None assigned.
Environmental hazards	Based on the available data, this product/mixture is not regulated as an environmental hazard or a marine pollutant.
Special precautions for users	Avoid release to the environment.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.
Chemical safety assessment	Not conducted.
TSCA status	Drugs are exempt from TSCA.
SARA section 313	Not listed.
California proposition 65	Not listed.

SECTION 15 - REGULATORY INFORMATION …continued

Additional information No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications ATO4 - Acute Toxicity (Oral) Category 4. H302 - Harmful if swallowed. ATD3 - Acute Toxicity (Dermal) Category 3. H311 - Toxic in contact with skin. STOT-RE2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2. H373 - May cause damage to liver, bone, kidneys or lymphoid/hematopoietic system through prolonged or repeated exposure. STOT-SE3 - Specific Target Organ Toxicity Following Single Exposure Category 3. H335 - May cause respiratory irritation. EI2 - Eye irritant Category 2. H319 - Causes serious eye irritation. SI2 - Skin irritant Category 2. H315 - Causes skin irritation. CA3 - Chronic Aquatic Toxicity Category 3. H412 - Harmful to aquatic life with long lasting effects. AA3- Acute aquatic toxicity Category 3. H402 - Harmful to aquatic life. FS2 - Flammable Solid Category 2. H228 - Flammable Solid.

Sources of data Information from published literature and internal company data.

Abbreviations ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System;

Issue Date 3 March 2017

Revisions This is the fourth version of this SDS.

SECTION 16 - OTHER INFORMATION …continued

Disclaimer

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions. No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.