SAFETY DATA SHEET

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

Contact information

General

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Product identifier	Bictegravir/Emtricitabine/Tenofovir Alafenamide Tablets
Synonyms	**Bictegravir:** GS-9883-01 (sodium salt); GS-9883 **Emtricitabine**: FTC, *cis*-(-)-FTC **Tenofovir Alafenamide fumarate**: TAF fumarate, GS-7340-03; Tenofovir phenyl isopropyl L-alaninyl phosphonamidate
Trade names	Biktarvy™
Chemical family	Mixture
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.
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	**The classification and labeling listed below is for bulk drug product.**
Globally Harmonized System [GHS]	Specific Target Organ Toxicity (repeated exposure) - Category 2. Aquatic toxicity (chronic) - Category 2.

Label elements

GHS hazard pictogram

GHS signal word Warning

GHS hazard statements H373 - May cause damage to liver, bone, or kidneys through prolonged or repeated exposure. H411 - Toxic to aquatic life with long-lasting effects.

GHS precautionary statements P260 - Do not breathe dust. P273 - Avoid release to the environment. P314 - Get medical advice/attention if you feel unwell. P391 - Collect spillage. P501 - Dispose of contents/container to location in accordance with local/regional/national/ international regulations.

Other hazards

In clinical studies conducted to date with bictegravir, single oral doses (up to 600 mg), multiple doses administered for 14 days (up to 300 mg), and 100 mg co-administered with F/TAF for seven days in healthy adult subjects were generally well tolerated, without evidence of clinically meaningful drug-related adverse effects.

TAF monofumarate has been generally well-tolerated in human clinical trials; adverse effects have included headache, nausea, flatulence, and insomnia, considered mild to moderate in severity.

Common adverse effects seen in clinical trials with emtricitabine alone or in combination with other antiretrovirals include headache, diarrhea, nausea, fatigue, dizziness, depression, insomnia, abnormal dreams, rash, abdominal pain, weakness, increased cough and runny nose. Serious effects including lactic acidosis and effects on the liver have also been reported with the use of nucleoside analogues. Adverse effects generally occur at doses that are not occupationally relevant.

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). The pharmacological, toxicological and ecological properties of this mixture have not been fully characterized.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ELINCS#	Amount	GHS Classification
Cellulose	9004-34-6	232-674-9	45-55%	Not classified
Emtricitabine	143491-57-0	N/A	25-30%	Not classified
Bictegravir	N/A	N/A	5-15%	CA1: H410
Tenofovir Alafenamide Fumarate	1392275-56-7	N/A	3-5%	STOT-RE2: H373
Magnesium Stearate	557-04-0	209-150-3	1-2%	Not classified
Titanium dioxide	13463-67-7	236-675-5	0.5-0.8%	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. Bictegravir, emtricitabine and tenofovir alafenamide fumarate are each pharmacologically active and have OELs. Cellulose, magnesium stearate and titanium dioxide are listed 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 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
	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
Bictegravir	Gilead	8-hour TWA	400 µg/m
Tenofovir Alafenamide Fumarate	Gilead	TWA-8 HR	15 µg/m
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)

Control Parameters/Occupational Exposure Limit Values
…continued

Compound	Issuer	Type	OEL
Titanium dioxide	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)
	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(s). 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.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

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.
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 the 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	Tablet (capsule-shaped).
Color	Purplish-brown or pink
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 are considered to be similar to those of the compounds tenofovir alafenamide monofumarate (GS-7340- 02) and tenofovir disoproxil fumarate (TDF).

Information on toxicological effects

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

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
Bictegravir	--	--	--	--
Tenofovir Alafenamide Fumarate	--	--	--	--
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

Bictegravir (GS-9883-01) has been determined using *in vitro* assays to be noncorrosive and nonirritating to skin, and moderately irritating to 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

Bictegravir is not regarded as a potential skin sensitizer based on the local lymph node assay in mice.

TAF fumarate did not show the potential to cause skin sensitization with repeated application to the dorsal surface of mouse ears (LLNA assay). No information identified for emtricitabine.

STOT-single exposure

In rats and monkeys, single oral doses of up to 300 and 1000 mg/kg GS-9883 (free acid), respectively, were well-tolerated in both species.

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

In two-week repeat dose studies conducted in rats and monkeys at oral doses of up to 300 and 1000 mg/kg/day of GS-9883 (free acid), respectively, there were no test article-related effects on clinical signs, body weights, body weight change, food consumption, ophthalmic examinations, organ weights, or macroscopic or microscopic findings in either species. At the highest doses, administration of GS-9883 was associated with slight changes to blood parameters in rats and a decrease in the activity of a hepatic metabolic enzyme in monkeys. NOAELs in rats and monkeys were 300 and 1000 mg/kg/day, respectively. No adverse effects were reported in rats at oral doses of up to 300 mg/kg/day GS- 9883-01 for up to 26 weeks. The NOAEL in rats was considered to be the high dose of 300 mg/kg/day.

Thirteen-week repeated dose toxicity studies were conducted in monkeys administered oral doses of up to 1000 mg/kg/day GS-9883-01. The NOAEL was the highest dose of 1000 mg/kg/day. In a 39-week toxicity study in monkeys, hepatobiliary toxicity was observed at the highest dose of 1000 mg/kg/day GS-9883-01, and the NOEL in monkeys was considered to be 200 mg/kg/day.

STOT-repeated exposure/Repeat-dose toxicity …continued

Administration of FTC alone, at a dose of 20 mg/kg/day, was well tolerated by dogs for four weeks. Based on the clinical and anatomical pathology findings, the NOAEL was 20 mg/kg/day for FTC alone.

There were no target organs identified in repeat-dose studies with emtricitabine. The only significant effect of emtricitabine identified at dose levels significantly higher than the human equivalent dose was a minor anemia. 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 organ: kidney). 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.

Reproductive toxicity

No adverse effects on fertility were observed in rats administered oral doses of GS- 9883-01 of up to 300 mg/kg/day during organogenesis (the highest dose was considered to be the NOEL).

No effects on fertility were observed in mice and rats administered oral doses of emtricitabine of 1000 and 3000 mg/kg/day, respectively.

In a TAF monofumarate oral rat fertility study, the NOAEL for reproductive and early embryonic toxicity was 160 mg/kg/day.

Developmental toxicity

No adverse effects on embryofetal development were observed in rats administered oral doses of GS-9883-01 of up to 300 mg/kg/day during organogenesis (the highest dose was considered to be the developmental NOEL).

In a rabbit developmental study, maternal effects (*e.g.*, decreased body weight and food consumption) occurred at oral doses of 1000 mg/kg/day GS-9883-01 administered during organogenesis and these were associated with decreased fetal body weights and fetal loss. The maternal and developmental NOELs in rabbits were both considered to be 300 mg/kg/day.

The incidence of fetal variations/malformations was not increased in the offspring of mice or rabbits treated orally with emtricitabine at doses 60- and 120-fold higher, respectively, than those used in humans (based on exposure levels).

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 embryofetal development studies was 100 mg/kg/day. TDF is not considered to be

Developmental toxicity …continued	a developmental toxicant based on studies conducted in laboratory animals at doses ≥450 mg/kg/day.
Genotoxicity	GS-9883 (free acid) was negative for genotoxicity when tested *in vitro,* with or without metabolic activation, in a bacterial reverse mutation (Ames) assay and in a chromosomal aberration assay in cultured human lymphocytes. It was also negative in an *in vivo* rat bone marrow micronucleus test. 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. TAF monofumarate was negative for genotoxic effects in an *in vitro* mouse lymphoma assay, in an *in vitro* bacterial mutagenicity test (Ames test), and in an *in vivo* mouse micronucleus assay.
Carcinogenicity	Daily administration of GS-9883-01 at oral doses of up to 300 mg/kg/day in rats for a minimum of 104 weeks did not impact survival or result in any increased incidence of neoplasms. Daily administration of GS-9883-01 for at least 26 weeks to rasH2 hemizygous mice at oral doses of up to 100 and 300 mg/kg/day in males and females, respectively, resulted in no carcinogenic effects. 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 studies conducted for TAF fumarate or TAF monofumarate. Long-term oral carcinogenicity studies of TDF 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
Bictegravir	NOEC (32-day early life cycle; post-hatch survival)	Pimephales promelas (fathead minnow)	1.2 mg/L
	NOEC (21-day reproduction)	Daphnia magna (water flea)	0.17 mg/L
	NOEC (72h) (population growth and yield)	Pseudokirchneriella subcapitata (algae)	0.066 mg/L
	NOEL (3 hour, respiration)	Soil microorganisms	26 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)
Magnesium Stearate	--	--	--
Titanium dioxide	LC_{50}/48h	Leuciscus idus	>1000 mg/L

Additional toxicity information

EC_{50}s of 940 and >1000 mg a.i./L were identified for tenofovir disoproxil fumarate and emtricitabine, respectively, 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 led to the following conclusions:

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;

Additional toxicity information …continued

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

Bictegravir (GS-9883-01) is a sodium salt, is not lipophilic and is unlikely to bioaccumulate. In a ready biodegradability test (OECD 301B "Modified Sturm test"), the mean % biodegradation after 28 days was 5%. Bictegravir was not readily biodegradable under the conditions of this test.

Emtricitabine was not readily biodegradable. The results of environmental fate studies indicate that TFV would not be significantly degraded in sewage treatment facilities, or be removed from the aqueous phase *via* sorption to sewage biosolids. The results of a sediment water transformation study indicated that the half-life of TFV was approximately 10-33 days.

Bioaccumulative potential

The log octanol/water distribution coefficient of GS-9883-01 was determined to be 2.2 at pH 7, indicating that it is unlikely to bioaccumulate in aquatic organisms. Emtricitabine is unlikely to bioaccumulate, based on its respective octanol/water partition coefficient. The mean log K_{OW} of TFV was determined to be -3.8 and -4.3, at pH 2 and 7, respectively, suggesting that partitioning to lipids in biota would be insignificant and that it is unlikely to enter the food chain.

Mobility in soil

Emtricitabine did not adsorb significantly to activated sludge. K_{OC} values ranged from 21.1 to 45.6. The data suggest that emtricitabine will partition into the aquatic environment rather than the sediment.

The log K_{OC} for TFV ranges from 14-50 in activated sludge. The adsorption coefficient (expressed as K_f) for sewage sludge is very low, 6 - 21 L.kg-1, which suggests that TFV will not extensively partition to the solid phase in sewage treatment plants and will mostly be discharged to receiving waters. TFV discharged into receiving water, such as rivers, would likely be mainly in solution or associated with suspended or dissolved solids. TFV is expected to be discharged to surface water, where it will likely partition to suspended solids and ultimately be deposited as sediment where it will be slowly degraded.

Bictegravir distributes to sediment with more than 10% of an applied dose associated with sediment after Day 14. Bictegravir is likely to partition to sewage solids with sludge $K_f > 3,700$. Once in municipal sewage-treatment plants, the available data suggest bictegravir will not be rapidly degraded and is likely to bind to sewage solids, which are removed after settling. The adsorption coefficient is sufficiently high to suggest that bictegravir will potentially reach the terrestrial soil environment.

SECTION 12 - ECOLOGICAL INFORMATION …continued

Results of PBT and vPvB assessment	Emtricitabine has not been evaluated for PBT because of low log K_{OW} values. TFV is not considered a PBT or vPvB due to its low log K_{OW} value and toxicity values. Bictegravir is not considered a PBT substance as the log D_{OW} @ pH 7 is 2.2.
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. The hazards of tenofovir alafenamide fumarate are considered to be similar to those of the compounds tenofovir alafenamide monofumarate (GS-7340-02) and tenofovir disoproxil fumarate (TDF).

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 regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
UN number	3077
UN proper shipping name	Environmentally Hazardous Substance, Solid, n.o.s. (contains Bictegravir)
Transport hazard classes and packing group	Hazard Class - 9; Packing Group III (exceptions from Environmentally Hazardous Substance marking exists for certain package sizes)
Environmental hazards	Based on the available data, this substance should be regarded as hazardous to the environment, but it is not listed as a marine pollutant [in accordance with IMDG].

SECTION 14 - TRANSPORT INFORMATION …continued

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	Titanium dioxide (e.g., airborne particles of respirable size) is listed.
Additional information	No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	STOT-RE2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2. H373 - May cause damage to liver, bone or kidneys through prolonged or repeated exposure. CA2 - Chronic Aquatic Toxicity Category 2. H411 - Toxic to aquatic life with long lasting effects. CA1 - Chronic Aquatic Toxicity Category 1. H410 - Very toxic to aquatic life with long lasting effects.
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

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued	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	9 February 2018
Revisions	This is the sixth version of this SDS.
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.