

# LUPIN LIMITED

## SAFETY DATA SHEET

### Section 1: Identification

#### Section 1, Identification

<b>Material</b>	Abacavir Sulfate, Lamivudine and Zidovudine Tablets 300 mg, 150 mg and 300 mg
<b>Manufacturer</b>	<b>Lupin Limited</b> Pithampur (M.P) – 454 775 INDIA.
<b>Distributor</b>	Lupin Pharmaceuticals, Inc. 111 South Calvert Street, Harborplace Tower, 21st Floor, Baltimore, Maryland 21202 United States Tel. 001-410-576-2000 Fax. 001-410-576-2221

### Section 2: Hazard(s) Identification

#### Section 2, Hazard(s) identification

<b>Fire and Explosion</b>	Expected to be non-combustible.
<b>Health</b>	Abacavir Sulfate, Lamivudine and Zidovudine Tablets are contraindicated in patients with: <ul style="list-style-type: none"><li>previously demonstrated hypersensitivity to abacavir or any other component of the product. NEVER restart abacavir sulfate, lamivudine and zidovudine tablets or any other abacavir-containing product following a hypersensitivity reaction to abacavir, regardless of HLA-B*5701 status.</li><li>hepatic impairment.</li></ul>
<b>Environment</b>	No information is available about the potential of this product to produce adverse environmental effects.

### Section 3: Composition/Information on Ingredients

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Ingredients	CAS
Abacavir Sulfate USP	188062-50-2
Lamivudine USP	134678-17-4
Zidovudine USP	30516-87-1

## Section 4: First-Aid Measures

### Section 4, First-aid measures

#### Ingestion

If conscious, give water to drink and induce vomiting. Do not attempt to give any solid or liquid by mouth if the exposed subject is unconscious or semi-conscious. Wash out the mouth with water. Obtain medical attention.

#### Inhalation

Move individual to fresh air. Obtain medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance.

#### Skin Contact

Remove contaminated clothing and flush exposed area with large amounts of water. Wash all exposed areas of skin with plenty of soap and water. Obtain medical attention if skin reaction occurs.

#### Eye Contact

Flush eyes with plenty of water. Get medical attention.

### NOTES TO HEALTH PROFESSIONALS

#### Medical Treatment

Treat according to locally accepted protocols. For additional guidance, refer to the current prescribing information or to the local poison control information center. Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc.

#### OVERDOSAGE

##### Abacavir

There is no known antidote for abacavir. It is not known whether abacavir can be removed by peritoneal dialysis or hemodialysis.

##### Lamivudine

One case of an adult ingesting 6 grams of lamivudine was reported; there were no clinical signs or symptoms noted and hematologic tests remained normal. It is not known whether lamivudine can be removed by peritoneal dialysis or hemodialysis.

##### Zidovudine

Acute overdoses of zidovudine have been reported in pediatric patients and adults. These involved exposures up to 50 grams. The only consistent findings were nausea and vomiting. Other reported occurrences included headache, dizziness, drowsiness, lethargy, and confusion. Hematologic changes were transient. All patients recovered. Hemodialysis and peritoneal dialysis appear to have a negligible effect on the removal of zidovudine, while elimination of its primary metabolite, 3'-azido-3'-deoxy-5'-O- $\beta$ -D-glucopyranuronosylthymidine (GZDV), is enhanced.

## Section 5: Fire-Fighting Measures

### Section 5, Fire-fighting measures

#### Fire and Explosion Hazards

Assume that this product is capable of sustaining combustion.

<b>Extinguishing Media</b>	Water spray, carbon dioxide, dry chemical powder or appropriate foam.
<b>Special Firefighting Procedures</b>	For single units (packages): No special requirements needed.  For larger amounts (multiple packages/pallets) of product: Since toxic, corrosive or flammable vapors might be evolved from fires involving this product and associated packaging, self-contained breathing apparatus and full protective equipment are recommended for firefighters.
<b>Hazardous Combustion Products</b>	Hazardous combustion or decomposition products are expected when the product is exposed to fire.

## Section 6: Accidental Release Measures

### Section 6, Accidental release measures

<b>Personal Precautions</b>	Wear protective clothing and equipment consistent with the degree of hazard.
<b>Environmental Precautions</b>	For large spills, take precautions to prevent entry into waterways sewers, or surface drainage systems.
<b>Clean-up Methods</b>	Collect and place it in a suitable, properly labeled container for recovery or disposal.

## Section 7: Handling and Storage

### Section 7, Handling and storage

<b>Handling</b>	No special control measures required for the normal handling of this product.
<b>Storage</b>	Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

## Section 8: Exposure Controls/Personal Protection

### Section 8, Exposure controls/personal protection

Wear appropriate clothing to avoid skin contact. Wash hands and arms thoroughly after handling.

## Section 9: Physical and Chemical Properties

### Section 9, Physical and chemical properties

<b>Physical Form</b>	Abacavir sulfate, lamivudine and zidovudine is available as tablets. Each tablet contains 300 mg of abacavir as abacavir sulfate, 150 mg of lamivudine, and 300 mg of zidovudine. The tablets are blue-green colored, oval shaped, biconvex, film-coated, debossed with "LU" on one side and "N51" on the other side. They are packaged as follows:
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Bottles of 60 Tablets NDC 68180-286-07  
Bottles of 100 Tablets NDC 68180-286-01  
Bottles of 500 Tablets NDC 68180-286-02

## Section 10: Stability and Reactivity

### Section 10, Stability and reactivity

Stable under recommended storage conditions.

## Section 11: Toxicological Information

### Section 11, Toxicological information

#### Carcinogenesis, Mutagenesis, Impairment of Fertility

##### Carcinogenicity

**Abacavir:** Abacavir was administered orally at 3 dosage levels to separate groups of mice and rats in 2-year carcinogenicity studies. Results showed an increase in the incidence of malignant and non-malignant tumors. Malignant tumors occurred in the preputial gland of males and the clitoral gland of females of both species, and in the liver of female rats. In addition, non-malignant tumors also occurred in the liver and thyroid gland of female rats. These observations were made at systemic exposures in the range of 6 to 32 times the human exposure at the recommended dose. It is not known how predictive the results of rodent carcinogenicity studies may be for humans.

**Lamivudine:** Long-term carcinogenicity studies with lamivudine in mice and rats showed no evidence of carcinogenic potential at exposures up to 10 times (mice) and 58 times (rats) those observed in humans at the recommended therapeutic dose for HIV-1 infection.

**Zidovudine:** Zidovudine was administered orally at 3 dosage levels to separate groups of mice and rats (60 females and 60 males in each group). Initial single daily doses were 30, 60, and 120 mg/kg/day in mice and 80, 220, and 600 mg/kg/day in rats. The doses in mice were reduced to 20, 30, and 40 mg/kg/day after day 90 because of treatment-related anemia, whereas in rats only the high dose was reduced to 450 mg/kg per day on day 91 and then to 300 mg/kg/day on day 279.

In mice, 7 late-appearing (after 19 months) vaginal neoplasms (5 nonmetastasizing squamous cell carcinomas, 1 squamous cell papilloma, and 1 squamous polyp) occurred in animals given the highest dose. One late-appearing squamous cell papilloma occurred in the vagina of a middle-dose animal. No vaginal tumors were found at the lowest dose.

In rats, 2 late-appearing (after 20 months), nonmetastasizing vaginal squamous cell carcinomas occurred in animals given the highest dose. No vaginal tumors occurred at the low or middle dose in rats. No other drug-related tumors were observed in either sex of either species.

At doses that produced tumors in mice and rats, the estimated drug exposure (as measured by AUC) was approximately 3 times (mouse) and 24 times (rat) the estimated human exposure at the recommended therapeutic dose of 100 mg every 4 hours.

Two transplacental carcinogenicity studies were conducted in mice. One study administered zidovudine at doses of 20 mg/kg/day or 40 mg/kg/day from gestation day 10 through parturition and lactation with dosing

continuing in offspring for 24 months postnatally. At these doses, exposures were approximately 3 times the estimated human exposure at the recommended doses. After 24 months at the 40-mg/kg/day dose, an increase in incidence of vaginal tumors was noted with no increase in tumors in the liver or lung or any other organ in either gender. These findings are consistent with results of the standard oral carcinogenicity study in mice, as described earlier. A second study administered zidovudine at maximum tolerated doses of 12.5 mg/day or 25 mg/day (~1,000 mg/kg nonpregnant body weight or ~450 mg/kg of term body weight) to pregnant mice from days 12 through 18 of gestation. There was an increase in the number of tumors in the lung, liver, and female reproductive tracts in the offspring of mice receiving the higher dose level of zidovudine.

It is not known how predictive the results of rodent carcinogenicity studies may be for humans.

#### **Mutagenicity**

**Abacavir:** Abacavir induced chromosomal aberrations both in the presence and absence of metabolic activation in an *in vitro* cytogenetic study in human lymphocytes. Abacavir was mutagenic in the absence of metabolic activation, although it was not mutagenic in the presence of metabolic activation in an L5178Y/TK+/- mouse lymphoma assay. Abacavir was clastogenic in males and not clastogenic in females in an *in vivo* mouse bone marrow micronucleus assay. Abacavir was not mutagenic in bacterial mutagenicity assays in the presence and absence of metabolic activation.

**Lamivudine:** Lamivudine was mutagenic in an L5178Y/TK+/- mouse lymphoma assay and clastogenic in a cytogenetic assay using cultured human lymphocytes. Lamivudine was negative in a microbial mutagenicity assay, in an *in vitro* cell transformation assay, in a rat micronucleus test, in a rat bone marrow cytogenetic assay, and in an assay for unscheduled DNA synthesis in rat liver.

**Zidovudine:** Zidovudine was mutagenic in an L5178Y/TK+/- mouse lymphoma assay, positive in an *in vitro* cell transformation assay, clastogenic in a cytogenetic assay using cultured human lymphocytes, and positive in mouse and rat micronucleus tests after repeated doses. It was negative in a cytogenetic study in rats given a single dose.

#### **Impairment of Fertility**

**Abacavir:** Abacavir had no adverse effects on the mating performance or fertility of male and female rats at a dose approximately 8 times the human exposure at the recommended dose based on body surface area comparisons.

**Lamivudine:** In a study of reproductive performance, lamivudine, administered to male and female rats at doses up to 130 times the usual adult dose based on body surface area considerations, revealed no evidence of impaired fertility judged by conception rates and no effect on the survival, growth, and development to weaning of the offspring.

**Zidovudine:** Zidovudine, administered to male and female rats at doses up to 7 times the usual adult dose based on body surface area considerations, had no effect on fertility judged by conception rates.

## **Section 12: Ecological Information**

No relevant studies identified.

## Section 13: Disposal Considerations

Incinerate in an approved facility. Follow all federal state and local environmental regulations.

## Section 14: Transport Information

### IATA/ICAO - Not Regulated

IATA Proper shipping Name	:	N/A
IATA UN/ID No	:	N/A
IATA Hazard Class	:	N/A
IATA Packaging Group	:	N/A
IATA Label	:	N/A

### IMDG - Not Regulated

IMDG Proper shipping Name	:	N/A
IMDG UN/ID No	:	N/A
IMDG Hazard Class	:	N/A
IMDG Flash Point	:	N/A
IMDG Label	:	N/A

### DOT - Not Regulated

DOT Proper shipping Name	:	N/A
DOT UN/ID No	:	N/A
DOT Hazard Class	:	N/A
DOT Flash Point	:	N/A
DOT Packing Group	:	N/A
DOT Label	:	N/A

## Section 15: Regulatory Information

This Section Contains Information relevant to compliance with other Federal and/or state laws.

## Section 16: Other Information

### Section 16, Other information

The above information is believed to be correct but does not purport to be all-inclusive and shall be used only as a guide. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose.

**Lupin** shall not be held liable for any damage resulting from handling or from contact with the above product. Lupin reserves the right to revise this MSDS.