ABAMUNE Tablets (Abacavir sulfate)

Black Box Warning

Hypersensitivity Reactions
Serious and sometimes fatal hypersensitivity reactions, with multiple organ involvement, have occurred with abacavir.
Patients who carry the HLA-B*5701 allele are at higher risk of a hypersensitivity reaction to abacavir; although, hypersensitivity reactions have occurred in patients who do not carry the HLA-B*5701 allele (See warnings and precautions).
Abacavir is contraindicated in patients with a prior hypersensitivity reaction to abacavir and in HLA-B*5701-positive patients (see contraindications, warnings and precautions). All patients should be screened for the HLA-B*5701 allele prior to initiating therapy with abacavir or reinitiation of therapy with abacavir, unless patients have a previously documented HLA-B*5701 allele assessment. discontinue abacavir immediately if a hypersensitivity reaction is suspected, regardless of HLA-B*5701 status and even when other diagnoses are possible (see contraindications, warnings and precautions)
Following a hypersensitivity reaction to abacavir, never restart abacavir or any other abacavir-containing product because more severe symptoms, including death can occur within hours. Similar severe reactions have also occurred rarely following the reintroduction of abacavir-containing products in patients who have no history of abacavir hypersensitivity (see warnings and precautions).

Composition

ABAMUNE

Each film-coated tablet contains:

Abacavir sulfate …… 300 mg

Dosage Form

Oral tablet

Pharmacology

Pharmacodynamics

Abacavir is a carbocyclic synthetic nucleoside analogue. Abacavir is converted by cellular enzymes to the active metabolite, carbovir triphosphate (CBV-TP), an analogue of deoxyguanosine-5--triphosphate (dGTP). CBV-TP inhibits the activity of HIV-1 reverse transcriptase (RT) both by competing with the natural substrate dGTP and by its incorporation into viral DNA.

Pharmacokinetics

Pharmacokinetics in Adults

The pharmacokinetic properties of abacavir were independent of dose over the range of 300 to 1,200 mgperday.

Absorption and Bioavailability*:* Following oral administration, Abacavir is rapidly and extensively absorbed after oral administration. The geometric mean absolute bioavailability of the tablet is 83%. After oral administration of 300 mg twice daily in 20 patients, the steady-state peak serum abacavir concentration (C_{max}) was 3.0 ± 0.89 mcg/mL (mean ± SD) and $AUC_{(0–12\ hr)}$ was 6.02 ± 1.73 mcg·hr/mL. After oral administration of a single dose of 600 mg of abacavir in 20 patients, C_{max} was 4.26 ± 1.19 mcg/mL (mean ± SD) and AUC_{∞} was 11.95 ± 2.51 mcg•hr/mL.

Effect of Food: Bioavailability of abacavir tablets was assessed in the fasting and fed states with no significant difference in systemic exposure (AUC∞); therefore, abacavir tablets may be administered with or without food. Systemic exposure to abacavir was comparable after administration of abacavir oral solution and abacavir tablets. Therefore, these products may be used interchangeably.

Distribution: The apparent volume of distribution after IV administration of abacavir was 0.86 ± 0.15 L per kg, suggesting that abacavir distributes into extravascular space. In 3 subjects, the CSF $AUC_{(0–6\ h)}$ to plasma abacavir $AUC_{(0–6\ hr)}$ ratio ranged from 27% to 33%.

Binding of abacavir to human plasma proteins is approximately 50%. Binding of abacavir to plasma proteins was independent of concentration. Total blood and plasma drug-related radioactivity concentrations are identical, demonstrating that abacavir readily distributes into the erythrocytes.

Elimination: In single-dose trials, the observed elimination half-life (t½) was 1.54 0.63 hours. After intravenous administration, total clearance was 0.80±0.24 L per hour per kg (mean±SD).

Metabolism: In humans, abacavir is not significantly metabolized by cytochrome P450 enzymes. The primary routes of elimination of abacavir are metabolism by alcohol dehydrogenase (to form the 5'-carboxylic acid) and glucuronyl transferase (to form the 5'-glucuronide). The metabolites do not have antiviral activity. *In vitro* experiments reveal that abacavir does not inhibit human CYP3A4, CYP2D6, or CYP2C9 activity at clinically relevant concentrations.

Excretion: Elimination of abacavir was quantified in a mass balance trial following administration of a 600-mg dose of ^{14}C-abacavir: 99% of the radioactivity was recovered, 1.2% was excreted in the urine as abacavir, 30% as the 5′-carboxylic acid metabolite, 36% as the 5′-glucuronide metabolite, and 15% as unidentified minor metabolites in the urine. Fecal elimination accounted for 16% of the dose.

Special populations

Patients with Renal impairment

The pharmacokinetic properties of abacavir have not been determined in patients with impaired renal function. Renal excretion of unchanged abacavir is a minor route of elimination in humans.

Patients Hepatic Impairment

The pharmacokinetics of abacavir has been studied in subjects with mild hepatic impairment (Child-Pugh Class A). Results showed that there was a mean increase of 89% in the abacavir AUC, and an

increase of 58% in the half-life of abacavir after a single dose of 600 mg of abacavir. The AUCs of the metabolites were not modified by mild liver disease; however, the rates of formation and elimination of the metabolites were decreased **(**see **CONTRAINDICATIONS).**

Pregnant Women

Abacavir: Abacavir pharmacokinetics were studied in 25 pregnant women during the last trimester of pregnancy receiving abacavir 300 mg twice daily. Abacavir exposure (AUC) during pregnancy was similar to those in postpartum and in HIV-infected non-pregnant historical controls. Consistent with passive diffusion of abacavir across the placenta, abacavir concentrations in neonatal plasma cord samples at birth were essentially equal to those in maternal plasma at delivery.

Geriatric Patients

The pharmacokinetics of abacavir has not been studied in subjects over 65 years of age.

Male and Female Patient

A population pharmacokinetic analysis in HIV-1-infected male (n = 304) and female (n = 67) subjects showed no gender differences in abacavir AUC normalized for lean body weight.

Race

There are no significant differences between blacks and whites in abacavir pharmacokinetics.

Indications

ABAMUNE Tablet, is indicated for the treatment of human immunodeficiency virus (HIV-1) infection in combination with other antiretroviral agents.

Dosage and Administration

Screening for HLA-B*5701 Allele Prior To Starting ABAMUNE

Screen for the HLA-B*5701 allele prior to initiating therapy with abacavir **(**see **BOXED WARNING, WARNINGS AND PRECAUTIONS).**

Recommended Dosage for Adult Patients

The recommended dosage of **ABAMUNE** for adults is 600 mg daily, administered orally as either 300 mg twice daily or 600 mg once daily in combination with other antiretroviral agents.

Recommended Dosage for Patients with Hepatic Impairment

The recommended dose of **ABAMUNE** in patients with mild hepatic impairment (Child-Pugh Class A) is 200 mg twice daily. The safety, efficacy, and pharmacokinetic properties of abacavir have not been established in patients with moderate to severe hepatic impairment and, therefore, **ABAMUNE** is contraindicated in these patients.

Contraindications

ABAMUNE is contraindicated in patients:

- who have the HLA-B*5701 allele **(**see **WARNINGS AND PRECAUTIONS)**.
- with prior hypersensitivity reaction to abacavir **(**see **WARNINGS AND PRECAUTIONS)**.
- with moderate or severe hepatic impairment. **(**see **WARNINGS AND PRECAUTIONS)**.

Warnings and Precautions

Drug Interactions

Methadone

In a trial of 11 HIV-1-infected subjects receiving methadone-maintenance therapy with 600 mg of abacavir twice daily (twice the currently recommended dose), oral methadone clearance increased. This alteration will not result in a methadone dose modification in the majority of patients; however, an increased methadone dose may be required in a small number of patients.

Hypersensitivity Reactions

Serious and sometimes fatal hypersensitivity reactions have occurred with abacavir. These hypersensitivity reactions have included multi-organ failure and anaphylaxis and typically occurred within the first 6 weeks of treatment with abacavir (median time to onset was 9 days); although abacavir hypersensitivity reactions have occurred any time during treatment **(**see **UNDESIRABLE EFFECTS).** Patients who carry the HLA-B*5701 allele are at a higher risk of abacavir hypersensitivity reactions; although, patients who do not carry the HLA-B*5701 allele have developed hypersensitivity reactions. Hypersensitivity to abacavir was reported in approximately 206 (8%) of 2,670 patients in 9 clinical trials with abacavir-containing products where HLA-B*5701 screening was not performed. The incidence of suspected abacavir hypersensitivity reactions in clinical trials was 1% when subjects carrying the HLA-B*5701 allele were excluded. In any patient treated with abacavir, the clinical diagnosis of hypersensitivity reaction must remain the basis of clinical decision making.

Due to the potential for severe, serious, and possibly fatal hypersensitivity reactions with abacavir:

- All patients should be screened for the HLA-B*5701 allele prior to initiating therapy with abacavir or reinitiation of therapy with abacavir, unless patients have a previously documented HLA-B*5701 allele assessment.
- Abacavir is contraindicated in patients with a prior hypersensitivity reaction to abacavir and in HLA-B*5701-positive patients.
- Before starting abacavir, review medical history for prior exposure to any abacavir containing product. NEVER restart abacavir or any other abacavir-containing product following a hypersensitivity reaction to abacavir, regardless of HLA-B*5701 status.
- To reduce the risk of a life-threatening hypersensitivity reaction, regardless of HLA-B*5701 status, discontinue abacavir immediately if a hypersensitivity reaction is suspected, even when other diagnoses are possible (e.g., acute onset respiratory diseases such as pneumonia, bronchitis, pharyngitis, or influenza; gastroenteritis; or reactions to other medications).
- If a hypersensitivity reaction cannot be ruled out, do not restart abacavir or any other abacavir-containing products because more severe symptoms which may include life-threatening hypotension and death, can occur within hours.
- If a hypersensitivity reaction is ruled out, patients may restart abacavir. Rarely, patients who have stopped abacavir for reasons other than symptoms of hypersensitivity have also experienced life-threatening reactions within hours of reinitiating abacavir therapy. Therefore, reintroduction of abacavir or any other abacavir-containing product is recommended only if medical care can be

readily accessed.

Lactic Acidosis/ Severe Hepatomegaly with Steatosis

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues, including abacavir. A majority of these cases have been in women.. Female sex and obesity may be risk factors for the development of lactic acidosis and severe hepatomegaly with steatosis in patients treated with antiretroviral nucleoside analogues. Treatment with abacavir should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

Immune Reconstitution Syndrome

Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including abacavir. During the initial phase of combination antiretroviral treatment, patients whose immune systems respond may develop an inflammatory response to indolent or residual opportunistic infections (such as *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jirovecii* pneumonia [PCP], or tuberculosis), which may necessitate further evaluation and treatment.

Autoimmune disorders (such as Graves' disease, polymyositis, and Guillain-Barré syndrome) have also been reported to occur in the setting of immune reconstitution, however, the time to onset is more variable, and can occur many months after initiation of treatment.

Myocardial Infarction

Several prospective, observational, epidemiological studies have reported an association with the use of abacavir and the risk of myocardial infarction (MI). Meta-analyses of randomized, controlled, clinical trials have observed no excess risk of MI in abacavir-treated subjects as compared with control subjects. To date, there is no established biological mechanism to explain a potential increase in risk. In totality, the available data from the observational studies and from controlled clinical trials show inconsistency; therefore, evidence for a causal relationship between abacavir treatment and the risk of MI is inconclusive.

As a precaution, the underlying risk of coronary heart disease should be considered when prescribing antiretroviral therapies, including abacavir, and action taken to minimize all modifiable risk factors (e.g., hypertension, hyperlipidemia, diabetes mellitus, and smoking).

Pregnancy

Risk Summary

Available data from the Antiretroviral Pregnancy Registry show no difference in the overall risk of birth defects for abacavir compared with the background rate for birth defects of 2.7% in the US reference population of the Metropolitan Atlanta Congenital Defects Program (MACDP) reference population. The APR uses the MACDP as the U.S. reference population for birth defects in the general population. The MACDP evaluates women and infants from a limited geographic area and does not include outcomes for births that occurred at less than 20 weeks gestation. The rate of miscarriage is not reported in the APR. The estimated background rate of miscarriage in clinically recognized pregnancies in the U.S. general population is 15% to 20%. The background risk for major birth defects and miscarriage for the indicated population is unknown.

In animal reproduction studies, oral administration of abacavir to pregnant rats during organogenesis resulted in fetal malformations and other embryonic and fetal toxicities at exposures 35 times the human exposure (AUC) at the recommended clinical daily dose. However, no adverse developmental effects were observed following oral administration of abacavir to pregnant rabbits during organogenesis, at exposures approximately 9 times the human exposure (AUC) at the recommended clinical dose.

Data

Human Data*:* Based on prospective reports to the Antiretroviral Pregnancy Registry of over 2,000 exposures to abacavir during pregnancy resulting in live births (including over 1000 exposed in the first trimester), there was no difference between the overall risk of birth defects for abacavir compared with the background birth defect rate of 2.7% in the U.S reference population of the MACDP. The prevalence of defects in live births was 2.9% (95% CI: 2.0% to 4.1%) following first trimester exposure to abacavir-containing regimens and 2.7% (95% CI: 1.9% to 3.7%) following second/third trimester exposure to abacavir-containing regimens.

Abacavir has been shown to cross the placenta and concentrations in neonatal plasma at birth were essentially equal to those in maternal plasma at delivery.

Animal Data*:* Abacavir was administered orally to pregnant rats (at 100, 300, and 1,000 mg per kg per day) and rabbits (at 125, 350, or 700 mg per kg per day) during organogenesis (on gestation Days 6 through 17 and 6 through 20, respectively). Fetal malformations (increased incidences of fetal anasarca and skeletal malformations) and developmental toxicity (decreasedfetal body weight and crown-rump length) were observed in rats at a doses up to 1,000 mg per kg per day, resulting in exposures approximately 35 times the human exposure(AUC) at the recommended daily dose. No developmental effects were observed in rats at 100 mg per kg per day, resulting in exposures (AUC) 3.5 times the human exposure at the recommended daily dose. In a fertility and early embryo-fetal development study conducted in rats (at 60, 160, or 500 mg per kg per day), embryonic and fetal toxicities (increased resorptions, decreased fetal body weights) or toxicities to the offspring (increased incidence of stillbirth and lower body weights) occurred at doses up to 500 mg per kg per day. No developmental effects were observed in rats at 60 mg per kg per day, resulting in exposures (AUC) approximately 4 times the human exposure at the recommended daily dose. Studies in pregnant rats showed that abacavir is transferred to the fetus through the placenta. In pregnant rabbits, no developmental toxicities and no increases in fetal malformations occurred at up to the highest dose evaluated, resulting in exposures (AUC) approximately 9 times the human exposure at the recommended dose.

Lactation

Risk Summary

The Centers for Disease Control and Prevention recommend that HIV-1-infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV-1 infection. Abacavir is present in human milk. There is no information on the effects of abacavir on the breastfed infant or the effects of the drug on milk production. Because of the potential for (1) HIV-1 transmission (in HIV-negative infants), (2) developing viral resistance (in HIV positive infants), and (3) adverse reactions in a breastfed infant, instruct mothers not to breastfeed if they are receiving abacavir.

Pediatric Use

The safety and effectiveness of abacavir have been established in pediatric patients aged 3 months

and older. Use of abacavir sulfate is supported by pharmacokinetic trials and evidence from adequate and well-controlled trials of abacavir sulfate in adults and pediatric subjects **(**see **PHARMACOLOGY, UNDESIRABLE EFFECTS)**.

Geriatric Use

Clinical trials of abacavir did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, caution should be exercised in the administration of abacavir in elderly patients reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Patients with Impaired Hepatic Function

A dose reduction is required for patients with mild hepatic impairment (Child-Pugh Class A) **(**see **DOSAGE AND ADMINISTRATION)**. The safety, efficacy, and pharmacokinetic properties of abacavir have not been established in patients with moderate or severe hepatic impairment; therefore, abacavir is contraindicated in these patients **(**see **CONTRAINDICATIONS, PHARMACOLOGY).**

Undesirable effects

The following are the adverse reactions are discussed in other sections of the labelling

- Serious and sometimes fatal hypersensitivity reactions. **(**see **BOXED WARNING, WARNINGS AND PRECAUTIONS)**.
- Lactic acidosis and severe hepatomegaly with steatosis **(**see **BOXED WARNING, WARNINGS AND PRECAUTIONS)**.
- Immune reconstitution syndrome **(**see **WARNINGS AND PRECAUTIONS**).
- Myocardial infarction **(**see **WARNINGS AND PRECAUTIONS)**.

Clinical Trials Experience in Adult Subjects

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Serious and Fatal Abacavir-associated Hypersensitivity Reactions

In clinical trials, serious and sometimes fatal hypersensitivity reactions have occurred with abacavir **(**see **BOXED WARNING, WARNINGS AND PRECAUTIONS)**. These reactions have been characterized by 2 or more of the following signs or symptoms: (1) fever; (2) rash; (3) gastrointestinal symptoms (including nausea, vomiting, diarrhea, or abdominal pain); (4) constitutional symptoms (including generalized malaise, fatigue, or achiness); (5) respiratory symptoms (including dyspnea, cough, or pharyngitis). Almost all abacavir hypersensitivity reactions include fever and/or rash as part of the syndrome.

Other signs and symptoms have included lethargy, headache, myalgia, edema, arthralgia, and paresthesia. Anaphylaxis, liver failure, renal failure, hypotension, adult respiratory distress syndrome, respiratory failure, myolysis, and death have occurred in association with these hypersensitivity reactions. Physical findings have included lymphadenopathy, mucous membrane lesions (conjunctivitis and mouth ulcerations), and maculopapular or urticarial rash (although some patients had other types of rashes and others did not have a rash). There were reports of erythema

multiforme. Laboratory abnormalities included elevated liver chemistries, elevated creatine phosphokinase, elevated creatinine, and lymphopenia, and abnormal chest x-ray findings (predominantly infiltrates, which were localized).

Additional Adverse Reaction with Use of Abacavir

Therapy-naive Adults: Treatment-emergent clinical adverse reactions (rated by the investigator as moderate or severe) with a greater than or equal to 5% frequency during therapy with abacavir 300 mg twice daily, lamivudine 150 mg twice daily, and efavirenz 600 mg daily compared with zidovudine 300 mg twice daily, lamivudine 150 mg twice daily, and efavirenz 600 mg daily from CNA30024 are listed in Table 1.

Table 1. Treatment-emergent (all causality) adverse reactions of at least moderate intensity (grades 2-4, greater than or equal to 5% frequency) in therapy-naive adults (CNA30024a) through 48 weeks of treatment

Adverse Reaction	**Abacavir plus Lamivudine plus Efavirenz (n = 324)**	**Zidovudine plus lamivudine plus efavirenz (n = 325)**
Dreams/sleep disorders	10%	10%
Drug hypersensitivity	9%	<1%[b]
Headaches/migraine	7%	11%
Nausea	7%	11%
Fatigue/malaise	7%	10%
Diarrhea	7%	6%
Rashes	6%	12%
Abdominal pain/gastritis/ gastrointestinal signs and symptoms	6%	8%
Depressive disorders	6%	6%
Dizziness	6%	6%
Musculoskeletal pain	6%	5%
Bronchitis	4%	5%
Vomiting	2%	9%

[a] This trial used double-blind ascertainment of suspected hypersensitivity reactions. During the blinded portion of the trial, suspected hypersensitivity to abacavir was reported by investigators in 9% of 324 subjects in the abacavir group and 3% of 325 subjects in the zidovudine group.

[b] Ten (3%) cases of suspected drug hypersensitivity were reclassified as not being due to abacavir following unblinding.

Treatment-emergent clinical adverse reactions (rated by the investigator as moderate or severe) with a greater than or equal to 5% frequency during therapy with abacavir 300 mg twice daily, lamivudine 150 mg twice daily, and zidovudine 300 mg twice daily compared with indinavir 800 mg 3 times daily, lamivudine 150 mg twice daily, and zidovudine 300 mg twice daily from CNA3005 are listed in Table 2.

Table 2. Treatment-emergent (all causality) adverse reactions of at least moderate intensity (grades

2-4, greater than or equal to 5% frequency) in therapy-naive adults (CNA3005) through 48 weeks of treatment

Adverse Reaction	**Abacavir plus Lamivudine/Zidovudine (n = 262)**	**Indinavir plus Lamivudine/Zidovudine (n=264)**
Nausea	19%	17%
Headache	13%	9%
Malaise and fatigue	12%	12%
Nausea and vomiting	10%	10%
Hypersensitivity reaction	8%	2%
Diarrhea	7%	5%
Fever and /or chills	6%	3%
Depressive disorders	6%	4%
Musculoskeletal pain	5%	7%
Skin rashes	5%	4%
Ear/nose/throat infections	5%	4%
Viral respiratory infections	5%	5%
Anxiety	5%	3%
Renal signs/symptoms	<1%	5%
Pain (non-site-specific)	<1%	5%

Five subjects receiving abacavir in CNA3005 experienced worsening of pre-existing depression compared with none in the indinavir arm. The background rates of pre-existing depression were similar in the 2 treatment arms.

Abacavir Once Daily Versus Abacavir Twice Daily (CNA30021): Treatment-emergent clinical adverse reactions (rated by the investigator as at least moderate) with a greater than or equal to 5% frequency during therapy with abacavir 600 mg once daily or abacavir 300 mg twice daily both in combination with lamivudine 300 mg once daily and efavirenz 600 mg once daily from CNA30021 were similar. For hypersensitivity reactions, subjects receiving abacavir once daily showed a rate of 9% in comparison with a rate of 7% for subjects receiving abacavir twice daily. However, subjects receiving abacavir 600 mg once daily experienced a significantly higher incidence of severe drug hypersensitivity reactions and severe diarrhea compared with subjects who received abacavir 300 mg twice daily. Five percent (5%) of subjects receiving abacavir 600 mg once daily had severe drug hypersensitivity reactions compared with 2% of patients receiving abacavir 300 mg twice daily. Two percent (2%) of subjects receiving abacavir 600 mg once daily had severe diarrhea while none of the subjects receiving abacavir 300 mg twice daily had this event.

Laboratory Abnormalities: Laboratory abnormalities (Grades 3-4) in therapy-naïve adults during therapy with abacavir 300 mg twice daily, lamivudine 150 mg twice daily, and efavirenz 600 mg daily compared with zidovudine 300 mg twice daily, lamivudine 150 mg twice daily, and efavirenz 600 mg daily from CNA30024 are listed in Table 3.

Table 3. Laboratory abnormalities (grades 3-4) in therapy-naive adults (CNA30024) through 48 weeks of treatment

Grade 3/4 Laboratory Abnormalities	Abacavir plus Lamivudine plus Efavirenz (n = 324)	Zidovudine plus Lamivudine plus Efavirenz (n = 325)
Elevated CPK (>4 X ULN)	8%	8%
Elevated ALT (>5 X ULN)	6%	6%
Elevated AST (>5 X ULN)	6%	5%
Hypertriglyceridemia (>750mg/dl)	6%	5%
Hyperamylasemia (>2 X ULN)	4%	5%
Neutropenia (ANC <750/mm^3)	2%	4%
Anemia (Hgb ≤6.9 gm/dl)	<1%	2%
Thrombocytopenia (Platelets <50,000/mm^3)	1%	<1%
Leukopenia (WBC ≤1,500/mm^3)	<1%	2%

ULN = Upper limit of normal.

n = Number of subjects assessed.

Laboratory abnormalities in CNA3005 are listed in Table 4.

Table 4. Treatment-emergent laboratory abnormalities (grades 3-4) in CNA3005

Grade 3/4 Laboratory Abnormalities	Number of Subjects by Treatment Group	
	Abacavir plus Lamivudine/Zidovudine (n = 262)	Indinavir plus Lamivudine/Zidovudine (n = 264)
Elevated CPK (>4 X ULN)	18 (7%)	18 (7%)
ALT (>5 X ULN)	16 (6%)	16 (6%)
Neutropenia (<750/mm^3)	13 (5%)	13 (5%)
Hypertriglyceridemia (>750mg/dl)	5 (2%)	3 (1%)
Hyperamylasemia (>2 X ULN)	5 (2%)	1 (<1%)
Hyperglycemia (>13.9 mmol/L)	2 (<1%)	2 (<1%)
Anemia (Hgb ≤6.9 gm/dl)	0 (0%)	3 (1%)

ULN = Upper limit of normal.

n = Number of subjects assessed.

The frequencies of treatment-emergent laboratory abnormalities were comparable between treatment groups in CNA30021.

Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of abacavir sulfate. Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposures.

Body as a Whole: Redistribution/accumulation of body fat.

Cardiovascular: Myocardial infarction.

Hepatic: Lactic acidosis and hepatic steatosis **(see WARNINGS AND PRECAUTIONS).**

Skin: Suspected Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in patients receiving abacavir primarily in combination with medications known to be associated with SJS and TEN, respectively. Because of the overlap of clinical signs and symptoms between hypersensitivity to abacavir and SJS and TEN, and the possibility of multiple drug sensitivities in some patients, abacavir should be discontinued and not restarted in such cases. There have also been reports of erythema multiforme with abacavir use **(**see **UNDESIRABLE EFFECTS).**

If you experience any side effects, talk to your doctor or pharmacist or write to **drugsafety@cipla.com.** You can also report side effects directly via the national pharmacovigilance program of India by calling on **1800 180 3024**.

By reporting side effects you can help provide more information on the safety of this product.

Overdosage

There is no known specific treatment for overdose with abacavir. If overdose occurs, the patient should be monitored and standard supportive treatment applied as required. It is not known whether abacavir can be removed by peritoneal dialysis or hemodialysis.

Storage and Handling Instructions

Store below 30°C.

Packaging Information

ABAMUNE Tablets ..... Container of 30 tablets

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