Safety Data Sheet
Acyclovir Tablets, USP

Strength: 400 mg, 800 mg. **Pack Size:** 30/90/100/500/1000 Tablets per bottle **Revision No.:** 03
Unit dose blisters of 10X10 Tablet

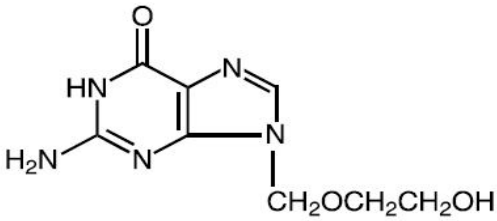
EMERGENCY OVERVIEW

Each Acyclovir Tablet intended for oral administration contains Acyclovir and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

Section 1. Identification

Identification of the product

Product name:	Acyclovir Tablet
Formula:	$C_8H_{11}N_5O_3$
Chemical Name:	2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]-6*H*-purin-6-one



Acyclovir

Manufacturer / supplier identification

Company:	**Cadila Healthcare Ltd. Ahmedabad, India**
Address:	Sarkhej – Bavla. N.H. 8A, Moraiya. Tal. Sanand. Dist. Ahmedabad – 382210. State: Gujarat. India
Contact for information:	Tel.: +91 79 6868100 Fax: +91 79 3750319
Emergency Telephone No.	Tel.: +91 79 6868100
Recommended use / Therapeutic Category	Synthetic nucleoside analogue
Restriction on Use / Contraindications:	Acyclovir capsules are contraindicated for patients who develop hypersensitivity to acyclovir or valacyclovir.

Section 2. Hazard(s) Identification

Dose and Administration

Acute Treatment of Herpes Zoster: 800 mg every 4 hours orally, 5 times daily for 7 to 10 days.
Genital Herpes: Treatment of Initial Genital Herpes: 200 mg every 4 hours, 5 times daily for 10 days.
Chronic Suppressive Therapy for Recurrent Disease: 400 mg 2 times daily for up to 12 months, followed by re-evaluation. Alternative regimens have included doses ranging from 200 mg 3 times daily to 200 mg 5 times daily.
The frequency and severity of episodes of untreated genital herpes may change over time. After 1 year of therapy, the frequency and severity of the patient's genital herpes infection should be re-evaluated to assess the need for continuation of therapy with acyclovir.
Intermittent Therapy: 200 mg every 4 hours, 5 times daily for 5 days. Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.
Treatment of Chickenpox: Children (2 years of age and older): 20 mg/kg per dose orally 4 times daily (80 mg/kg/day) for 5 days. Children over 40 kg should receive the adult dose for chickenpox.
Adults and Children over 40 kg: 800 mg 4 times daily for 5 days.
Intravenous acyclovir is indicated for the treatment of varicella-zoster infections in immunocompromised patients.
When therapy is indicated, it should be initiated at the earliest sign or symptom of chickenpox. There is no information about the efficacy of therapy initiated more than 24 hours after onset of signs and symptoms.
Patients With Acute or Chronic Renal Impairment: In patients with renal impairment, the dose of Acyclovir Tablets should be modified.
Hemodialysis: For patients who require hemodialysis, the mean plasma half-life of acyclovir during hemodialysis is approximately 5 hours. This results in a 60% decrease in plasma concentrations following a 6-hour dialysis period. Therefore, the patient's dosing schedule should be adjusted so that an additional dose is administered after each dialysis.
Peritoneal Dialysis: No supplemental dose appears to be necessary after adjustment of the dosing interval.

Adverse Effects

Herpes Simplex: Short-Term Administration: The most frequent adverse events reported during clinical trials of treatment of genital herpes with acyclovir 200 mg administered orally 5 times daily every 4 hours for 10 days were nausea and/or vomiting in 8 of 298 patient treatments (2.7%). Nausea and/or vomiting occurred in 2 of 287 (0.7%) patients who received placebo.

Long-Term Administration: The most frequent adverse events reported in a clinical trial for the prevention of recurrences with continuous administration of 400 mg (two 200-mg capsules) 2 times daily for 1 year in 586 patients treated with acyclovir were nausea (4.8%) and diarrhea (2.4%). The 589 control patients receiving intermittent treatment of recurrences with acyclovir

for 1 year reported diarrhea (2.7%), nausea (2.4%), and headache (2.2%).

Herpes Zoster: The most frequent adverse event reported during 3 clinical trials of treatment of herpes zoster (shingles) with 800 mg of oral acyclovir 5 times daily for 7 to 10 days in 323 patients was malaise (11.5%). The 323 placebo recipients reported malaise (11.1%).

Chickenpox: The most frequent adverse event reported during 3 clinical trials of treatment of chickenpox with oral acyclovir at doses of 10 to 20 mg/kg 4 times daily for 5 to 7 days or 800 mg 4 times daily for 5 days in 495 patients was diarrhea (3.2%). The 498 patients receiving placebo reported diarrhea (2.2%).

Observed During Clinical Practice: In addition to adverse events reported from clinical trials, the following events have been identified during post-approval use of acyclovir. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to eithertheir seriousness, frequency of reporting, potential causal connection to acyclovir, or a combination of these factors.

General: Anaphylaxis, angioedema, fever, headache, pain, peripheral edema.
Nervous: Aggressive behavior, agitation, ataxia, coma, confusion, decreased consciousness, delirium, dizziness, dysarthria, encephalopathy, hallucinations, paresthesia, psychosis, seizure, somnolence, tremors. These symptoms may be marked, particularly in older adults or in patients with renal impairment .
Digestive: Diarrhea, gastrointestinal distress, nausea.
Hematologic and Lymphatic: Anemia, leukocytoclastic vasculitis, leukopenia, lymphadenopathy, thrombocytopenia.
Hepatobiliary Tract and Pancreas: Elevated liver function tests, hepatitis, hyperbilirubinemia, jaundice.
Musculoskeletal: Myalgia.
Skin: Alopecia, erythema multiforme, photosensitive rash, pruritus, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria.
Special Senses: Visual abnormalities.
Urogenital: Renal failure, renal pain (may be associated with renal failure), elevated blood urea nitrogen, elevated creatinine, hematuria .

Over Dose Effect

Overdoses involving ingestion of up to 100 capsules (20 g) have been reported. Adverse events that have been reported in association with overdosage include agitation, coma, seizures, and lethargy. Precipitation of acyclovir in renal tubules may occur when the solubility (2.5 mg/mL) is exceeded in the intratubular fluid. Overdosage has been reported following bolus injections or inappropriately high doses and in patients whose fluid and electrolyte balance were not properly monitored. This has resulted in elevated

BUN and serum creatinine and subsequent renal failure. In the event of acute renal failure and anuria, the patient may benefit from hemodialysis until renal function is restored .

Medical Conditions

Patients are instructed to consult with their physician if they experience severe or troublesome adverse reactions, they become pregnant or intend to become pregnant, they intend to breastfeed while taking orally administered acyclovir, or they have any other questions.

Patients should be advised to maintain adequate hydration.

Contraindications

Acyclovir tablets are contraindicated for patients who develop hypersensitivity to acyclovir or valacyclovir.

Pregnancy Comments

There are no adequate and well-controlled studies in pregnant women.Acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Pregnancy Category **B**

Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component:		
Acyclovir 400, 800mg	Not Found	59277-89-3
Inactive Ingredients :		
Colloidal silicon dioxide	Not Found	7631-86-9
Magnesium stearate	Not Found	577-04-0
Microcrystalline cellulose	Not Found	9004-34-6
Pregelatinized starch	Not Found	9005-25-8
Sodium starch glycolate	Not Found	9063-38-1

Section 4. First aid measures

General

Inhalation:
Remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen. Seek medical attention.

	Contact with skin: Immediately wash skin with soap and copious amounts of water for at least 15 minutes. If irritation persists, seek medical attention. Ingestion: If swallowed, wash out mouth with water, provided person is concious. Seek medical advice Remove and wash/dispose of contaminated clothing promptly.
Overdose Treatment	NA

Section 5. Fire -fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature:	Not Found	**Lower Flammable Limit:**	Not Found
Extinguishing Media	Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material.	**Fire and Explosion Hazard**	Not Found

Fire Fighting Procedure	As with all fires, evacuate personnel to a safe area. Fire fighter should use self- contained breathing equipment and protective clothing.

Section 6. Accidental Release Measures

Spill Response	Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site.

Section 7. Handling and Storage

Storage	Store at 20° to 25°C (68° to 77°F) **.** Protect from light and moisture. Dispense in a tight, light-resistant container .
Incompatibilities:	Reacting with oxidizing substance.

Section 8. Exposure controls and personal protection

Respiratory Protection	Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate.
Skin Protection	Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling.
Eye protection	Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.

Section 9. Physical and chemical properties

Appearance	Acyclovir Tablets USP, 400 mg are white to off-white colored, round shaped, biconvex, uncoated tablets, debossed with "791" on one side and plain on the other side. Acyclovir Tablets USP, 800 mg are white to off-white colored, oval shaped, biconvex, uncoated tablets, debossed with "792" on one side and plain on the other side.		
Solubility	Soluble in diluted Hcl, slightly soluble in water, insoluble in alcohol.	**Odour**	Not available.
Boiling point	Not available.	**Melting Point**	Not available.
Evaporation rate	Not available.	**Vapour density**	Not available.
Reactivity in water	Not available.	**Vapour pressure**	Not available.
Percentage Volatile by volume	Not available.	**Specific gravity**	Not available.
Vapour pressure	Not available.		
Other information	Acyclovir is a white or almost white, crystalline powder with the molecular formula $C_8H_{11}N_5O_3$ and a molecular weight of 225.20. It is soluble in diluted hydrochloric acid; slightly soluble in water and insoluble in alcohol. The pka's of acyclovir are 2.27 and 9.25.		

Section 10. Stability and Reactivity

Condition to avoid	Avoid exposure to extreme heat, light and moisture.	**Stable**	Product is stable.
Decomposition Products	Reacting with oxidizing substance.	**Hazardous Reaction**	No data available.
Incompatibilities:	Reacting with oxidizing substance.		

Section 11. Toxicological information

General

Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.

Target organ

Eye contact, Skin contact and inhalation is not great risk as this product is tablet.

Other

Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of up to 450 mg/kg administered by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. Maximum plasma concentrations were 3 to 6 times human levels in the mouse bioassay and 1 to 2 times human levels in the rat bioassay.

Acyclovir was tested in 16 in vitro and in vivo genetic toxicity assays. Acyclovir was positive in 5 of the assays.

Acyclovir did not impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). In the mouse study, plasma levels were 9 to 18 times human levels, while in the rat study, they were 8 to 15 times human levels. At higher doses (50 mg/kg/day, s.c.) in rats and rabbits (11 to 22 and 16 to 31 times human levels, respectively) implantation efficacy, but not litter size, was decreased. In a rat peri- and post-natal study at 50 mg/kg/day, s.c., there was a statistically significant decrease in group mean numbers of corpora lutea, total implantation sites and live fetuses.

No testicular abnormalities were seen in dogs given 50 mg/kg/day, IV for 1 month (21 to 41 times human levels) or in dogs given 60 mg/kg/day orally for 1 year (6 to 12 times human levels). Testicular atrophy and aspermatogenesis were observed in rats and dogs at higher dose levels.

Section 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil

Section 13. Disposal Consideration

Disposal Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. Transport Information

The product is not hazardous when shipping via air (IATA), ground(DOT), or sea(IMDG).

Section 15. Regulatory Information

Generic Medicine. Approved by USFDA & the ANDA Number is 204314

Section 16. Other information

None

Date of issue: 28/05/2015 **Supersedes edition of:** 02

The information contained herein is based on the state of our knowledge. It Characterises the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.