FAMCICLOVIR- famciclovir tablet
NorthStar RxLLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FAMCICLOVIR TABLETS safely and effectively. See full prescribing information for FAMCICLOVIR TABLETS.

FAMCICLOVIR tablets, for oral use.
Initial U.S. Approval: 1994

INDICATIONS AND USAGE
Famciclovir, a prodrug of penciclovir, is a deoxynucleoside analog DNA polymerase inhibitor indicated for:

Immunocompetent Adult Patients

- Herpes labialis (cold sores)
- Treatment of recurrent episodes
- Genital herpes
- Treatment of recurrent episodes
- Suppressive therapy of recurrent episodes
- Herpes zoster (shingles)

Human Immunodeficiency Virus (HIV)-Infected Adult Patients

- Treatment of recurrent episodes of orolabial or genital herpes

Limitation of Use
The efficacy and safety of famciclovir have not been established for:
- Patients with first episode of genital herpes
- Patients with ophthalmic zoster
- Immunocompromised patients other than for the treatment of recurrent episodes of orolabial or genital herpes in HIV-infected patients
- Black and African American patients with recurrent genital herpes

DOSAGE AND ADMINISTRATION

Immunocompetent Adult Patients

- Herpes labialis (cold sores) 1500 mg as a single dose
- Genital herpes Treatment of recurrent episodes Suppressive therapy 1000 mg twice daily for 1 day 250 mg twice daily
- Herpes zoster (shingles) 500 mg every 8 hours for 7 days

HIV-Infected Adult Patients

- Recurrent episodes of orolabial or genital herpes 500 mg twice daily for 7 days

Patients with renal impairment: Adjust dose based on creatinine clearance.

DOSAGE FORMS AND STRENGTHS
Tablets: 125 mg, 250 mg, 500 mg

CONTRAINDICATIONS
Known hypersensitivity to the product, its components, or Denavir® (penciclovir cream).

WARNINGS AND PRECAUTIONS
Acute Renal Failure: May occur in patients with underlying renal disease who receive higher than recommended doses of famciclovir tablets for their level of renal function. Reduce dosage in patients with renal impairment.

ADVERSE REACTIONS
The most common adverse events reported in at least 1 indication by greater than 10% of adult patients are headache and nausea.

DRUG INTERACTIONS
Probenecid: May increase penciclovir levels. Monitor for evidence of penciclovir toxicity.

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Revised: 2/2019
FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Immunocompetent Adult Patients

Herpes labialis (cold sores): Famciclovir tablets are indicated for the treatment of recurrent herpes labialis in adult patients.

Genital herpes:

Recurrent episodes: Famciclovir tablets are indicated for the treatment of recurrent episodes of genital herpes. The efficacy of famciclovir tablets when initiated more than 6 hours after onset of symptom or lesion has not been established.

Suppressive therapy: Famciclovir tablets are indicated for chronic suppressive therapy of recurrent episodes of genital herpes in adult patients. The efficacy and safety of famciclovir tablets for the suppression of recurrent genital herpes beyond 1 year have not been established.

Herpes zoster (shingles): Famciclovir tablets are indicated for the treatment of herpes zoster in adult patients. The efficacy of famciclovir tablets when initiated more than 72 hours after onset of rash has not been established.

1.2 HIV-Infected Adult Patients

Recurrent orolabial or genital herpes: Famciclovir tablets are indicated for the treatment of recurrent episodes of orolabial or genital herpes in HIV-infected adults. The efficacy of famciclovir tablets when initiated more than 48 hours after onset of symptoms or lesions has not been established.

Limitation of Use:

The efficacy and safety of famciclovir tablets have not been established for:

- Patients with first episode of genital herpes
- Patients with ophthalmic zoster
- Immunocompromised patients other than for the treatment of recurrent orolabial or genital herpes in HIV-infected patients
- Black and African American patients with recurrent genital herpes

2 DOSAGE AND ADMINISTRATION

Famciclovir tablets may be taken with or without food.

2.1 Dosing Recommendation in Immunocompetent Adult Patients

Herpes labialis (cold sores): The recommended dosage of famciclovir tablets for the treatment of recurrent herpes labialis is 1500 mg as a single dose. Therapy should be initiated at the first sign or symptom of herpes labialis (e.g., tingling, itching, burning, pain, or lesion).

Genital herpes:

Recurrent episodes: The recommended dosage of famciclovir tablets for the treatment of recurrent episodes of genital herpes is 1000 mg twice daily for 1 day. Therapy should be initiated at the first sign or symptom of a recurrent episode (e.g., tingling, itching, burning, pain, or lesion).

Suppressive therapy: The recommended dosage of famciclovir tablets for chronic suppressive therapy of recurrent episodes of genital herpes is 250 mg twice daily.

Herpes zoster (shingles): The recommended dosage of famciclovir tablets for the treatment of herpes zoster is 500 mg every 8 hours for 7 days. Therapy should be initiated as soon as herpes zoster is diagnosed.

2.2 Dosing Recommendation in HIV-Infected Adult Patients

Recurrent orolabial or genital herpes: The recommended dosage of famciclovir tablets for the treatment of recurrent orolabial or genital herpes in HIV-infected patients is 500 mg twice daily for 7 days. Therapy should be initiated at the first sign or symptom of a recurrent episode (e.g., tingling, itching, burning, pain, or lesion).

2.3 Dosing Recommendation in Patients with Renal Impairment

Dosage recommendations for adult patients with renal impairment are provided in Table 1 [see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)].

<table>
<thead>
<tr>
<th>Table 1: Dosage Recommendations for Adult Patients with Renal Impairment</th>
</tr>
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<tbody>
<tr>
<td><strong>Indication and Normal Dosage Regimen</strong></td>
</tr>
<tr>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>Single-Day Dosing Regimen</td>
</tr>
<tr>
<td>Recurrent Genital Herpes 1000 mg every 12 hours for 1 day</td>
</tr>
<tr>
<td>40-59</td>
</tr>
<tr>
<td>20-39</td>
</tr>
<tr>
<td>&lt;20</td>
</tr>
<tr>
<td>HD*</td>
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<tr>
<td>Recurrent Herpes Labialis 1500 mg single dose</td>
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<tr>
<td>40-59</td>
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<tr>
<td>20-39</td>
</tr>
<tr>
<td>&lt;20</td>
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<tr>
<td>HD*</td>
</tr>
<tr>
<td>Multiple-Day Dosing Regimen</td>
</tr>
<tr>
<td>Herpes zoster</td>
</tr>
</tbody>
</table>

* Sections or subsections omitted from the full prescribing information are not listed.
Table 2: Selected Adverse Events (all grades and without regard to causality) Reported by Greater Than or Equal to 2% of Patients in Placebo-Controlled Famciclovir Tablets Trials

<table>
<thead>
<tr>
<th>Event</th>
<th>Famciclovir (n=273)</th>
<th>Placebo (n=146)</th>
<th>Famciclovir (n=163)</th>
<th>Placebo (n=166)</th>
<th>Famciclovir (n=458)</th>
<th>Placebo (n=63)</th>
<th>Famciclovir (n=447)</th>
<th>Placebo (n=204)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Herpes Zoster</strong></td>
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<td></td>
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<tr>
<td>Hemodialysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>22.7</td>
<td>17.8</td>
<td>13.5</td>
<td>5.4</td>
<td>39.3</td>
<td>42.9</td>
<td>8.5</td>
<td>6.7</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>2.6</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.9</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Migraine</td>
<td>0.7</td>
<td>0.7</td>
<td>0.6</td>
<td>0.6</td>
<td>3.1</td>
<td>0.0</td>
<td>0.2</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>12.5</td>
<td>11.6</td>
<td>2.5</td>
<td>3.6</td>
<td>7.2</td>
<td>9.5</td>
<td>2.2</td>
<td>3.9</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7.7</td>
<td>4.8</td>
<td>4.9</td>
<td>1.2</td>
<td>9.0</td>
<td>9.5</td>
<td>1.6</td>
<td>0.8</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4.8</td>
<td>3.4</td>
<td>1.2</td>
<td>0.6</td>
<td>3.1</td>
<td>1.6</td>
<td>0.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Flatulence</td>
<td>1.5</td>
<td>0.7</td>
<td>0.6</td>
<td>0.0</td>
<td>4.8</td>
<td>1.6</td>
<td>0.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>1.1</td>
<td>3.4</td>
<td>0.0</td>
<td>1.2</td>
<td>7.9</td>
<td>7.9</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Body as a Whole</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>4.4</td>
<td>3.4</td>
<td>0.6</td>
<td>0.0</td>
<td>4.8</td>
<td>3.2</td>
<td>1.6</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Skin and Appendages</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>3.7</td>
<td>2.7</td>
<td>0.0</td>
<td>0.6</td>
<td>2.2</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Rash</td>
<td>0.4</td>
<td>0.7</td>
<td>0.0</td>
<td>0.0</td>
<td>3.3</td>
<td>1.6</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Reproductive (Female)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysmenorrhea</td>
<td>0.0</td>
<td>0.7</td>
<td>1.8</td>
<td>0.6</td>
<td>7.6</td>
<td>6.3</td>
<td>0.4</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*Patients may have entered into more than one clinical trial.
† days of treatment
Clinical Considerations

Healthcare providers are encouraged to report pregnancies and pregnancy outcomes to Cipla Limited, as there is limited information on the safety of famciclovir (and penciclovir) use in this setting.

The estimated background risk of major birth defects and miscarriage for the indicated population is lower than those at the maximum recommended human dose (MRHD) of famciclovir (see Data).

Risk Summary

Available data from pharmacovigilance reports with famciclovir use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. There are risks to the fetus associated with untreated herpes simplex virus during pregnancy (see Clinical Considerations). A drug interaction study using human liver microsomes suggests that famciclovir is not an inhibitor of CYP3A4 enzymes.

Table 3 lists selected laboratory abnormalities in genital herpes suppression trials.

Table 3: Selected Laboratory Abnormalities in Genital Herpes Suppression Studies*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Famciclovir (n=660)† %</th>
<th>Placebo (n=210)† %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia (≤0.8 x NRL)</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Leukopenia (≤0.75 x NRL)</td>
<td>1.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Neutropenia (≤0.8 x NRL)</td>
<td>3.2</td>
<td>1.5</td>
</tr>
<tr>
<td>AST (SGOT) (&gt;2 x NRH)</td>
<td>2.3</td>
<td>1.2</td>
</tr>
<tr>
<td>ALT (SGPT) (&gt;2 x NRH)</td>
<td>3.2</td>
<td>1.5</td>
</tr>
<tr>
<td>Total Bilirubin (&gt;1.5 x NRH)</td>
<td>1.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Serum Creatinine (&gt;1.5 x NRH)</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Amylase (&gt;1.5 x NRH)</td>
<td>1.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Lipase (&gt;1.5 x NRH)</td>
<td>4.9</td>
<td>4.7</td>
</tr>
</tbody>
</table>

*Percentage of patients with laboratory abnormalities that were increased or decreased from baseline and were outside of specified ranges.

†n values represent the minimum number of patients assessed for each laboratory parameter.

NRH=Normal Range High.
NRL=Normal Range Low.

HIV-infected patients: In HIV-infected patients, the most frequently reported adverse events for famciclovir (500 mg twice daily; n=150) and acyclovir (400 mg, 5x/day; n=143), respectively, were headache (7% vs. 15%), nausea (11% vs. 13%), diarrhea (7% vs. 13%), vomiting (5% vs. 4%), fatigue (4% vs. 2%), and abdominal pain (3% vs. 6%).

7 DRUG INTERACTIONS

7.1 Potential for Famciclovir Tablets to Affect Other Drugs

The steady-state pharmacokinetics of digoxin were not altered by concomitant administration of multiple doses of famciclovir (500 mg three times daily). No clinically significant effect on the pharmacokinetics of zidovudine, its metabolite zidovudine glucuronide, or emtricitabine was observed following a single oral dose of 500 mg famciclovir coadministered with zidovudine or emtricitabine. An in vitro study using human liver microsomes suggests that famciclovir is not an inhibitor of CYP3A4 enzymes.

7.2 Potential for Other Drugs to Affect Penciclovir

No clinically significant alterations in penciclovir pharmacokinetics were observed following single-dose administration of 500 mg famciclovir after pretreatment with multiple doses of allopurinol, cimetidine, theophylline, zidovudine, promethazine, when given shortly after an antacid (magnesium and aluminum hydroxide), or concomitantly with emtricitabine. No clinically significant effect on penciclovir pharmacokinetics was observed following multiple-dose (three times daily) administration of famciclovir (500 mg) with multiple doses of digoxin.

Concurrent use with probenecid or other drugs significantly eliminated by active renal tubular secretion may result in increased plasma concentration of penciclovir.

The conversion of 6-deoxy penciclovir to penciclovir is catalyzed by aldehyde oxidase. Interactions with other drugs metabolized by this enzyme and/or inhibiting this enzyme could potentially occur.

Clinical interaction studies of famciclovir with cimetidine and promethazine, in vitro inhibitors of aldehyde oxidase, did not show relevant effects on the formation of penciclovir. Raloxifene, a potent aldehyde oxidase inhibitor in vitro, could decrease the formation of penciclovir. However, a clinical drug-drug interaction study to determine the magnitude of interaction between penciclovir and raloxifene has not been conducted.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from pharmacovigilance reports with famciclovir use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. There are risks to the fetus associated with untreated herpes simplex virus during pregnancy (see Clinical Considerations). After oral administration, famciclovir (prodrug) is converted to penciclovir (active drug). In animal reproduction studies with famciclovir, no evidence of adverse developmental outcomes was observed at systemic exposures of penciclovir (AUC) slightly higher than those at the maximum recommended human dose (MRHD) of famciclovir (see Data).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

The risk of neonatal herpes infection varies from 30% to 50% for genitl herpes simplex virus (HSV) infections that occur in late pregnancy (third trimester), whereas in early pregnancy, infection carries a risk of about 1%. A primary herpetic outbreak during the first trimester of pregnancy has been associated with neonatal choriorretinitis, microcephaly and, in rare cases, skin lesions. In very rare cases, transplacental transmission can occur resulting in congenital infection, including microcephaly, hepatosplenomegaly, intrauterine growth restriction and stillbirth. Co-infection with HSV increases the risk of perinatal HIV transmission in women who had a clinical diagnosis of genital herpes during pregnancy.

Data

Animal Data

Famciclovir was administered orally to pregnant rats and rabbits (up to 1000 mg/kg/day) on gestation Day(s) 6 to 15, and to rats on gestation Day 15 to lactation/post-partum Day 25. No adverse effects on embryo-fetal (rats and rabbits) or pre/post-natal (rats) development were observed up to the highest dose tested. During organogenesis, systemic exposures of penciclovir (active metabolite) were 3.4 times (rats) and 1.6 times (rabbits) the human systemic exposure of penciclovir based on AUC at the MRHD.

8.2 Lactation

Risk Summary

There are no data on the presence of famciclovir (prodrug) or penciclovir (active drug) in human milk, the effects on the breastfed infant, or the effects on milk production. Animal data indicate that penciclovir is present in the milk of lactating rats (see Data). The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for famciclovir and any potential adverse effects on the breastfed infant from penciclovir or from the underlying maternal condition.

Data

Penciclovir was the primary drug-related component excrated into the milk of lactating rats following a single oral dose of 40 mg per kg on lactation Day 12, with milk concentrations of up to approximately 8 times that of maternal plasma concentrations observed 0.5 hours postdose.

8.3 Females and Males of Reproductive Potential

Infertility

Decreased fertility, due to testicular toxicity, was observed in male animals following repeated administration of famciclovir or penciclovir (see Nonclinical Toxicology (13.1)). In two placebo-controlled studies, 130 men with a history of recurrent genital herpes received either oral famciclovir (250 mg twice daily; n=66) or placebo (n=64) therapy for 18 weeks. The men were otherwise healthy and had a normal sperm profile prior to treatment. There was no evidence of significant effects on sperm count, motility or morphology during famciclovir treatment or during an 8-week follow-up.

8.4 Pediatric Use

The efficacy of famciclovir have not been established in pediatric patients. The pharmacokinetic profile and safety of famciclovir (experimental granules mixed with OraSweet or tablets) were studied in 3 open-label studies.

Study 1 was a single-dose pharmacokinetic and safety study in infants 1 month to less than 1 year of age who had an active herpes simplex virus (HSV) infection or who were at risk for HSV infection. Eighteen subjects were enrolled and received a single dose of famciclovir experimental granules mixed with OraSweet based on the patient's body weight (doses ranged from 25 mg to 175 mg). These doses were selected to provide penciclovir systemic exposures similar to the penciclovir systemic exposures observed in adults after administration of 500 mg famciclovir. The efficacy and safety of famciclovir have not been established as suppressive therapy in infants following neonatal HSV infections. In addition, the efficacy cannot be extrapolated from adults to infants because there is no similar disease in adults. Therefore, famciclovir is not recommended in infants.

Study 2 was an open-label, single-dose pharmacokinetic, multiple-dose safety study of famciclovir experimental granules mixed with OraSweet in children 1 to less than 12 years of age with clinically suspected HSV or varicella zoster virus (VZV) infection. Fifty-one subjects were enrolled in the pharmacokinetic part of the study and received a single body weight adjusted dose of famciclovir (doses ranged from 125 mg to 500 mg). These doses were selected to provide penciclovir systemic exposures similar to the penciclovir systemic exposures observed in adults after administration of 500 mg famciclovir. Based on the pharmacokinetic data observed with these doses in children, a new weight-based dosing algorithm was designed and used in the multiple-dose safety part of the study. Pharmacokinetic data were not obtained with the revised weight-based dosing algorithm.

A total of 100 patients were enrolled in the multiple-dose safety part of the study; 47 subjects with active or latent HSV infection and 53 subjects with chickenpox. Patients with active or latent HSV infection received famciclovir twice a day for 7 days. The daily dose of famciclovir ranged from 150 mg to 500 mg twice daily depending on the patient's body weight. Patients with chickenpox received famciclovir three times daily for 7 days. The daily dose of famciclovir ranged from 150 mg to 500 mg three times daily depending on the patient's body weight. The clinical adverse events and laboratory test abnormalities observed in this study were similar to those seen in adults. The available data are insufficient to support the use of famciclovir for the treatment of children 1 to less than 12 years of age with chickenpox or infections due to HSV for the following reasons:

Chickenpox: The efficacy of famciclovir for the treatment of chickenpox has not been established in either pediatric or adult patients. Famciclovir is approved for the treatment of herpes zoster in adult patients. However, extrapolation of efficacy data from adults with herpes zoster to children with chickenpox would not be appropriate. Although chickenpox and herpes zoster are caused by the same virus, the diseases are different.

Genital herpes: Clinical information on genital herpes in children is limited. Therefore, efficacy data from adults cannot be extrapolated to this population. Famciclovir has not been studied in children 1 to less than 12 years of age with recurrent genital herpes. None of the children in Study 2 had genital herpes.

Herpes labialis: There are no pharmacokinetic and safety data in children 1 to less than 12 years of age to support a famciclovir dose that provides penciclovir systemic exposures comparable to the penciclovir systemic exposures in adults after a single dose administration of 1500 mg. Moreover, no efficacy data have been obtained in children 1 to less than 12 years of age with recurrent herpetic labialis.

Study 3 was an open-label, single-arm study to evaluate the pharmacokinetics, safety, and antiviral activity of a single 1500 mg dose (three 500 mg tablets) of famciclovir in children 12 to less than 18 years of age with recurrent herpetic labialis. A total of 53 subjects were enrolled in the study; 10 subjects in the pharmacokinetic part of the study and 43 subjects in the non-pharmacokinetic part of the study. All enrolled subjects weighed greater than or equal to 40 kg. The 43 subjects enrolled in the non-pharmacokinetic part of the study had active recurrent herpetic labialis and received a single 1500 mg dose of famciclovir within 24 hours after the onset of symptoms.
was 21 hours). The safety profile of famciclovir observed in this study was similar to that seen in adults. The median time to healing of patients with non-aborted lesions was 5.9 days. In a phase 3 trial in adults in which patients received a single 1500 mg dose of famciclovir or placebo, the median time to healing among patients with non-aborted lesions was 4.4 days in the famciclovir 1500 mg single-dose group and 6.2 days in the placebo group. Of note, in the adult study treatment was initiated by patients within 1 hour after the onset of symptoms [see Clinical Studies (14.1)]. Based on the efficacy results in Study 3, famciclovir is not recommended in children 12 years or less than 18 years of age with recurrent herpes labialis.

8.5 Geriatric Use
Of 816 patients with herpes zoster in clinical studies who were treated with famciclovir, 248 (30.4%) were greater than or equal to 65 years of age and 103 (13%) were greater than or equal to 75 years of age. No overall differences were observed in the incidence or types of adverse events between younger and older patients. Of 610 patients with recurrent herpes simplex (type 1 or type 2) in clinical studies who were treated with famciclovir, 26 (4.3%) were greater than 65 years of age and 7 (1.1%) were greater than 75 years of age. Clinical studies of famciclovir in patients with recurrent genital herpes did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently compared to younger subjects.

No famciclovir dosage adjustment based on age is recommended unless renal function is impaired [see Dosage and Administration (2.3), Clinical Pharmacology (12.3)]. In general, appropriate caution should be exercised in the administration and monitoring of famciclovir in elderly patients reflecting the greater frequency of decreased renal function and concomitant use of other drugs.

8.6 Patients with Renal Impairment
Apparent plasma clearance, renal clearance, and the plasma-elimination rate constant of penciclovir decreased linearly with reductions in renal function. After the administration of a single 500 mg famciclovir oral dose (n=27) to healthy volunteers and to volunteers with varying degrees of renal impairment (CLCR ranged from 6.4 to 138.8 mL/min), the following results were obtained (Table 4):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CLCR &gt;60 (mL/min) (n=15)</th>
<th>CLCR 40-59 (mL/min) (n=5)</th>
<th>CLCR 20-39 (mL/min) (n=4)</th>
<th>CLCR &lt;20 (mL/min) (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLCR (mL/min)</td>
<td>88.1 ± 20.6</td>
<td>49.3 ± 5.9</td>
<td>20.5 ± 5.3</td>
<td>12.7 ± 5.9</td>
</tr>
<tr>
<td>CLG (L/hr)</td>
<td>30.1 ± 10.6</td>
<td>13.0 ± 1.3</td>
<td>4.2 ± 0.9</td>
<td>1.6 ± 1.0</td>
</tr>
<tr>
<td>CLp (L/hr)</td>
<td>66.9 ± 27.5</td>
<td>27.3 ± 2.8</td>
<td>12.8 ± 1.3</td>
<td>5.8 ± 2.8</td>
</tr>
<tr>
<td>Half-life (hr)</td>
<td>2.3 ± 0.5</td>
<td>3.4 ± 0.7</td>
<td>6.2 ± 1.6</td>
<td>13.4 ± 10.2</td>
</tr>
</tbody>
</table>

1 CLCR is measured creatinine clearance.
2 CL/F consists of bioavailability factor and famciclovir to penciclovir conversion factor.

In a multiple-dose study of famciclovir conducted in subjects with varying degrees of renal impairment (n=18), the pharmacokinetics of penciclovir were comparable to those after single doses.

A dosage adjustment is recommended for patients with renal impairment [see Dosage and Administration (2.3)].

8.7 Patients with Hepatic Impairment
Mild or moderate hepatic impairment (chronic hepatitis [n=6], chronic ethanol abuse [n=8], or primary biliary cirrhosis [n=1]) had no effect on the extent of availability (AUC) of penciclovir following a single dose of 500 mg famciclovir. However, there was a 44% decrease in penciclovir mean maximum plasma concentration (Cmax) and the time to maximum plasma concentration (tmax) was increased by 0.75 hours in patients with hepatic impairment compared to normal volunteers. No dosage adjustment is recommended for patients with mild or moderate hepatic impairment. The pharmacokinetics of penciclovir has not been evaluated in patients with severe hepatic impairment. Conversion of famciclovir to the active metabolite penciclovir may be impaired in these patients resulting in a lower penciclovir plasma concentration, and thus possibly a decrease of efficacy of famciclovir [see Clinical Pharmacology (12)].

8.8 Black and African American Patients
In a randomized, double-blind, placebo-controlled trial conducted in 304 immunocompetent black and African American adults with recurrent genital herpes there was no difference in median time to healing between patients receiving famciclovir or placebo. In general, the adverse reaction profile was similar to that observed in other famciclovir clinical trials for adult patients [see Adverse Reactions (6.1)]. The relevance of these study results to other indications in black and African American patients is unknown [see Clinical Studies (14.2)].

10 OVERDOSAGE
Appropriate symptomatic and supportive therapy should be given. Penciclovir is removed by hemodialysis.

11 DESCRIPTION
The active ingredient in famciclovir tablets is famciclovir, an orally administered prodrug of the antiviral agent penciclovir. Chemically, famciclovir is known as 2-[2-[(2-amino-9H-purin-9-yl)-ethyl]-1,3-propanediol diacetate. Its molecular formula is C14H20N4O4, its molecular weight is 321.3. It is a synthetic acyclic guanine derivative and has the following structure:

![Structure of famciclovir](image)

Famciclovir is a white to pale yellow solid. It is freely soluble in acetone and methanol, and sparingly soluble in ethanol and isopropanol. At 25°C famciclovir is freely soluble (greater than 25% w/v) in water initially, but rapidly precipitates as the sparingly soluble (2%-3% w/v) monohydrate. Famciclovir is not hygroscopic below 85% relative humidity. Partition coefficients are: octanol/water (pH 4.8) P=1.09 and octanol/phosphate buffer (pH 7.4) P=2.08.
Famciclovir tablets contain 125 mg, 250 mg or 500 mg of famciclovir, together with the following inactive ingredients: croscarmellose sodium, crospovidone, hypromellose 2910, lactose monohydrate, magnesium stearate, polyethylene glycols 6000 and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Famciclovir is an orally administered prodrug of the anti-alpha herpes viral agent penciclovir [see Microbiology (12.4)].

12.3 Pharmacokinetics

Famciclovir is the diacetyl 6-deoxy analog of the active antiviral compound penciclovir. Following oral administration famciclovir undergoes rapid and extensive metabolism to penciclovir and little or no famciclovir is detected in plasma or urine. Penciclovir is predominantly eliminated unchanged by the kidney. Therefore, the dose of famciclovir needs to be adjusted in patients with different degrees of renal impairment [see Dosage and Administration (2.3)].

Pharmacokinetics in adults:

Absorption and Bioavailability: The absolute bioavailability of penciclovir is 77 ± 8% as determined following the administration of a 500 mg famciclovir oral dose and a 400 mg penciclovir intravenous dose to 12 healthy male subjects. Penciclovir concentrations increased in proportion to dose over a famciclovir dose range of 125 mg to 1000 mg administered as a single dose. Table 5 shows the mean pharmacokinetic parameters of penciclovir after single administration of famciclovir to healthy male volunteers.

<table>
<thead>
<tr>
<th>Dose</th>
<th>AUC (0-inf) (mcg hr/mL)</th>
<th>Cmax (mcg/mL)</th>
<th>tmax (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>125 mg</td>
<td>2.24</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>250 mg</td>
<td>4.48</td>
<td>1.6</td>
<td>0.9</td>
</tr>
<tr>
<td>500 mg</td>
<td>8.95</td>
<td>3.3</td>
<td>0.9</td>
</tr>
<tr>
<td>1000 mg</td>
<td>17.9</td>
<td>6.6</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*Based on pharmacokinetic data from 17 studies

Following oral single-dose administration of 500 mg famciclovir to 7 patients with herpes zoster, the AUC (mean ± SD), Cmax, and tmax were 12.1±1.7 mcg hr/mL, 4.0±0.7 mcg/mL, and 0.7±0.2 hours, respectively. The AUC of penciclovir was approximately 35% greater in patients with herpes zoster as compared to healthy volunteers. Some of this difference may be due to differences in renal function between the 2 groups.

There is no accumulation of penciclovir after the administration of 500 mg famciclovir three times daily for 7 days.

Penciclovir Cmax decreased approximately 50% and tmax was delayed by 1.5 hours when a capsule formulation of famciclovir was administered with food (nutritional content was approximately 910 Kcal and 26% fat). There was no effect on the extent of availability (AUC) of penciclovir. There was an 10% decrease in Cmax and a delay in tmax of about 1 hour when famciclovir was given 2 hours after a meal as compared to its administration 2 hours before a meal. Because there was no effect on the extent of systemic availability of penciclovir, famciclovir can be taken without regard to meals.

Distribution: The volume of distribution (Vd) was 1.08±0.17 L/kg in 12 healthy male subjects following a single intravenous dose of penciclovir at 400 mg administered as a 1-hour intravenous infusion. Penciclovir is less than 20% bound to plasma protein over the concentration range of 0.1 to 20 mcg/mL. The bloodplasma ratio of penciclovir is approximately 1.

Metabolism: Following oral administration, famciclovir is deacetylated and oxidized to form penciclovir. Metabolites that are inactive include 6-deoxy penciclovir, monoaacetylated penciclovir, and 6-deoxy monoaacetylated penciclovir (5%, less than 0.5% and less than 0.5% of the dose in the urine, respectively). Little or no penciclovir is detected in plasma or urine. An in vitro study using human liver microsomes demonstrated that cytochrome P450 does not play an important role in famciclovir metabolism. The conversion of 6-deoxy penciclovir to penciclovir is catalyzed by aldehyde oxidase. Cimetidine and promethazine, in vitro inhibitors of aldehyde oxidase, did not show relevant effects on the formation of penciclovir in vivo [see Drug Interactions (7.2)].

Elimination: Approximately 94% of administered radioactivity was recovered in urine over 24 hours (83.3% of the dose was excreted in the first 6 hours) after the administration of 5 mg/kg radiolabeled penciclovir as a 1-hour infusion to 3 healthy male volunteers. Penciclovir accounted for 91% of the radioactivity excreted in the urine.

Following the oral administration of a single 500 mg dose of radiolabeled famciclovir to 3 healthy male volunteers, 73% and 27% of administered radioactivity were recovered in urine and feces over 72 hours, respectively. Penciclovir accounted for 82% and 6-deoxy penciclovir accounted for 7% of the radioactivity excreted in the urine. Approximately 66% of the administered radiolabeled dose was collected in urine in the first 6 hours.

After intravenous administration of penciclovir in 48 healthy male volunteers, mean ± SD total plasma clearance of penciclovir was 36.6±6.3 L/hr (0.48±0.09 L/hr/kg). Penciclovir renal clearance accounted for 74.5±8.8% of total plasma clearance.

Renal clearance of penciclovir following the oral administration of a single 500 mg dose of famciclovir to 109 healthy male volunteers was 27.7±7.6 L/hr. Active tubular secretion contributes to the renal elimination of penciclovir.

The plasma elimination half-life of penciclovir was 2.0±0.3 hours after intravenous administration of penciclovir to 40 healthy male volunteers and 2.3±0.4 hours after oral administration of 500 mg famciclovir to 124 healthy male volunteers. The half-life in 17 patients with herpes zoster was 2.8±1.0 hours and 2.7±1.0 hours after single and repeated dosing [see Use in Specific Populations (8.6)]. A dosage adjustment is recommended for patients with renal impairment [see Dosage and Administration (2.3)].

Special populations:

Geriatric patients: Based on cross study comparison, penciclovir AUC was 40% higher and penciclovir renal clearance was 22% lower in elderly subjects (n=18, age 65 to 79 years) as compared with younger subjects. Some of this difference may be due to differences in renal function between the 2 groups. No famciclovir dosage adjustment based on age is recommended unless renal function is impaired [see Dosage and Administration (2.3), Use in Specific Populations (8.5)].

Patients with renal impairment: In subjects with varying degrees of renal impairment, apparent plasma clearance, renal clearance, and the plasma-elimination rate constant of penciclovir decreased linearly with reductions in renal function, after both single and repeated dosing [see Use in Specific Populations (8.6)]. A dosage adjustment is recommended for patients with renal impairment [see Dosage and Administration (2.3)].
Patients with hepatic impairment: Mild or moderate hepatic impairment had no effect on the extent of availability (AUC) of penciclovir [see Use in Specific Populations (8.7)]. No dosage adjustment is recommended for patients with mild or moderate hepatic impairment. The effect of severe hepatic impairment on the pharmacokinetics of penciclovir has not been evaluated.

HIV-infected patients: Following oral administration of a single dose of 500 mg famciclovir to HIV-positive patients, the pharmacokinetic parameters of penciclovir were comparable to those observed in healthy subjects.

Gender: The pharmacokinetics of penciclovir were evaluated in 18 healthy male and 18 healthy female volunteers after single-dose oral administration of 500 mg famciclovir. AUC of penciclovir was 9.3±1.9 mg hr/mL, and 11.4±2.1 mg hr/mL in males and females, respectively. Penciclovir renal clearance was 28.5±8.9 L/hr and 21.8±4.3 L/hr, respectively. These differences were attributed to differences in renal function between the 2 groups. No famciclovir dosage adjustment based on gender is recommended.

Race: A retrospective evaluation was performed to compare the pharmacokinetic parameters obtained in black and Caucasian subjects after single and repeat once-daily, twice-daily, or three times-daily administration of foscarnet 500 mg. Data from a study in healthy volunteers (single dose), a study in subjects with varying degrees of renal impairment (single and repeat dose) and a study in subjects with hepatic impairment (single dose) did not indicate any significant differences in the pharmacokinetics of penciclovir between black and Caucasian subjects.

12.4 Microbiology

Mechanism of action: Famiclovir is a prodrug of penciclovir, which has demonstrated inhibitory activity against herpes simplex virus types 1 (HSV-1) and 2 (HSV-2) and varicella zoster virus (VZV). In cells infected with HSV-1, HSV-2 or VZV, the viral thymidine kinase phosphorylates penciclovir to a monophosphate form that, in turn, is converted by cellular kinases to the active form penciclovir triphosphate. Biochemical studies demonstrate that penciclovir triphosphate inhibits HSV-2 DNA polymerase competitively with deoxyguanosine triphosphate. Consequently, α-herpes viral DNA synthesis and, therefore, replication are selectively inhibited. Penciclovir triphosphate has an intracellular half-life of 10 hours in HSV-1, 20 hours in HSV-2 and 7 hours in VZV-infected cells grown in culture. However, the clinical significance of the intracellular half-life is unknown.

Antiviral activity: In cell culture studies, penciclovir has antiviral activity against the following herpes viruses: HSV-1, HSV-2 and VZV. The antiviral activity of penciclovir against wild type strains grown on human foreskin fibroblasts was assessed with a plaque reduction assay and staining with crystal violet 3 days postinfection for HSV and 10 days postinfection for VZV. The median EC50 values of penciclovir against laboratory and clinical isolates of HSV-1, HSV-2 and VZV were 2 μM (range 1.2 to 2.4 μM, n = 7) and 2.6 μM (range 1.6 to 11 μM, n = 6), and 34 μM (range 6.7 to 71 μM, n=6), respectively.

Resistance:

In Cell Culture

Penciclovir-resistant HSV-1 and HSV-2 strains were isolated in cell culture. Penciclovir-resistant mutants of HSV and VZV resulted from mutations in the viral thymidine kinase (TK) and DNA polymerase (POL) genes. Frameshifting were commonly isolated and result in premature truncation of the HSV TK product with decreased enzymatic activity and consequent decreased susceptibility to penciclovir. Mutations in the viral TK gene may lead to complete loss of TK activity (TK negative), reduced levels of TK activity (TK partial), or alteration in the ability of viral TK to phosphorylate the drug without an equivalent loss in the ability to phosphorylate thymidine (TK altered). In cell culture, the following resistance-associated substitutions in TK of HSV-1 and HSV-2 were observed: HSV-1 TK G61A, S74Stop, E83K, P84L, T103P, Q104Stop, D116N, M121R, H143V, R163H, L170P, Y172C, A174P, R176Q/W, Q185R, A189V, G200D, L208H, R216C, R220H, R222C/H, FS 224, Y239S, T245M, Q250Stop, S254Stop, R256W, Q261Stop, R281Stop, T287M, L315S, M322K, C36Y, V958L.

Clinical HSV-1 and HSV-2 isolates obtained from patients who failed treatment with acyclovir for their α-herpesvirus infections were evaluated for genotypic changes in the TK and POL genes. These HSV isolates had frameshift mutations leading to loss of thymidine kinase or had substitutions in the viral thymidine kinase and DNA viral polymerase. Phenotypic analysis of these clinical isolates confirmed resistance to penciclovir and acyclovir. These and other resistance-associated substitutions reported in the literature, or observed in clinical trials, are listed in Table 6. The list is not all inclusive and additional changes will likely be identified in HSV variants isolated from patients who fail penciclovir containing regimen. The possibility of viral resistance to penciclovir should be considered in patients who fail to respond or experience recurrent viral shedding during therapy.

Table 6: Summary of Known HSV TK and POL Amino Acid Substitutions Conferring Resistance to Acyclovir and Cross-Resistance to Penciclovir

<table>
<thead>
<tr>
<th>HSV-1 TK</th>
<th>HSV-2 TK</th>
<th>HSV-1 POL</th>
<th>HSV-2 POL</th>
</tr>
</thead>
</table>

Note: Many additional pathways to penciclovir resistance likely exist.

Cross-resistance has been observed among HSV isolates carrying foscarnet resistance-associated substitutions (Table 7).

Table 7: Summary of Known HSV-1 POL Amino Acid Substitutions Conferring Resistance to Foscarnet and Cross-Resistance to Penciclovir

<table>
<thead>
<tr>
<th>HSV-1 POL</th>
<th>HSV-2 POL</th>
</tr>
</thead>
</table>
Famciclovir-treated patients had approximately one-fifth the median number of recurrences as compared to those treated with the 250 mg twice daily dose. Patients self-initiated therapy within 6 hours of the first signs or symptoms of a recurrent genital herpes episode with either famciclovir 1000 mg twice daily (n=233) or placebo (n=236) for 1 day. The median time to healing among patients with non-aborted lesions (progressing beyond the papule stage) was 4.3 days in famciclovir-treated patients (n=125) as compared to 6.1 days in placebo-treated patients (n=168). The median difference in time to healing between the placebo and famciclovir 1500 mg treated groups was 1.3 days (95% CI: 0.6 to 2.0). No differences in proportion of patients with aborted lesions (not progressing beyond the papule stage) were observed between patients receiving famciclovir or placebo: 33% for famciclovir 1500 mg single dose and 34% for placebo. The median time to loss of pain and tenderness was 1.7 days in famciclovir 1500 mg single dose-treated patients vs. 2.9 days in placebo-treated patients.

14.2 Genital Herpes

Recurrent episodes: A randomized, double-blind, placebo-controlled trial was conducted in 329 immunocompetent adults with recurrent herpes labialis. Patients self-initiated therapy within 6 hours of the first sign or symptom of a recurrent herpes labialis episode with famciclovir 1000 mg as a single dose (n=227) or placebo (n=228) for 1 day. The median time to healing among patients with non-aborted lesions (progressing beyond the papule stage) was 4.4 days in the famciclovir 1500 mg single-dose group (n=152) as compared to 6.2 days in the placebo group (n=168). The median difference in time to healing between the placebo and famciclovir 1500 mg treated groups was 1.3 days (95% CI: 0.6 to 2.0). No differences in proportion of patients with aborted lesions (not progressing beyond the papule stage) were observed between patients receiving famciclovir or placebo: 33% for famciclovir 1500 mg single dose and 34% for placebo. The median time to loss of pain and tenderness was 1.7 days in famciclovir 1500 mg single dose-treated patients vs. 2.9 days in placebo-treated patients.

14 CLINICAL STUDIES

14.1 Herpes Labialis (Cold Sores)

A randomized, double-blind, placebo-controlled trial was conducted in 701 immunocompetent adults with recurrent herpes labialis. Patients self-initiated therapy within 1 hour of first onset of signs or symptoms of a recurrent herpes labialis episode with famciclovir 1000 mg as a single dose (n=297) or placebo (n=294) for 1 day. The median time to healing among patients with non-aborted lesions (progressing beyond the papule stage) was 4.3 days in famciclovir-treated patients (n=152) as compared to 6.1 days in placebo-treated patients (n=168). The median difference in time to healing between the placebo and famciclovir 1500 mg treated groups was 1.3 days (95% CI: 0.6 to 2.0). No differences in proportion of patients with aborted lesions (not progressing beyond the papule stage) were observed between patients receiving famciclovir or placebo: 33% for famciclovir 1500 mg single dose and 34% for placebo. The median time to loss of pain and tenderness was 1.7 days in famciclovir 1500 mg single dose-treated patients vs. 2.9 days in placebo-treated patients.
Herpes Zoster (Shingles)

There are no data on treatment initiated more than 72 hours after onset of zoster rash. Patients should be advised to initiate treatment as soon as possible after a diagnosis of herpes zoster.

Pregnancy

Healthcare providers are encouraged to report pregnancies and pregnancy outcomes to Northstar Rx LLC, at 1-800-206-7821.
Famciclovir (fam sy’ kloe vir) Tablets

What are famciclovir tablets?
Famciclovir tablets are a prescription antiviral medicine used to:
- in adults with a normal immune system to:
  - treat outbreaks of cold sores
  - treat outbreaks of genital herpes
  - decrease the number of outbreaks of genital herpes
  - treat shingles (herpes zoster)
  - in adults with human immunodeficiency virus (HIV) to treat outbreaks of herpes in or around the mouth, genitals or anal area
- It is not known if famciclovir tablets are effective in children.

Do not take famciclovir tablets if you are allergic to any of its ingredients or to Denavir® (penciclovir cream). See the end of this Patient Information leaflet for a complete list of ingredients in Famciclovir tablets.

Before you take famciclovir tablets, tell your healthcare provider about all of your medical conditions, including if you:
- Have kidney or liver problems
- have a rare genetic problem with galactose intolerance, a severe lactase deficiency or you do not absorb glucose-galactose (malabsorption)
- are pregnant or plan to become pregnant. It is not known if famciclovir tablets will harm your unborn baby.
- Pregnancy exposure reporting: There is a pregnancy reporting system for women who take famciclovir tablets during pregnancy. The purpose of this reporting system is to collect information about the health of you and your baby. Talk to your healthcare provider about how to report your pregnancy.
- are breastfeeding or plan to breastfeed. It is not known if famciclovir tablets passes into your breastmilk or how it may affect your breast fed baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I take famciclovir tablets?
- Take famciclovir tablets exactly as prescribed by your healthcare provider.
- Your healthcare provider will tell you how many famciclovir tablets to take and when to take them.
- Your dose of famciclovir tablets and how often you take it may be different depending on your condition.
- Famciclovir tablets can be taken with or without food.
- If you are taking famciclovir tablets for outbreaks of cold sores or genital herpes, take famciclovir tablets as soon as you have the first symptoms of the infection such as itching, redness, pain, burning or tingling, or when the sore appears.
- If you take too much famciclovir tablets, call your healthcare provider or go to the nearest hospital emergency room right away.

What should I avoid while taking famciclovir tablets?
You should avoid driving or operating machinery if you get dizziness, sleepiness or confusion during treatment with famciclovir tablets.

What are the possible side effects of famciclovir tablets?
The most common side effects of famciclovir tablets are headache and nausea.
These are not all the possible side effects of famciclovir tablets.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store famciclovir tablets?
- Store famciclovir tablets at 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature].

Keep famciclovir tablets and all medicines out of reach from children.

General information about the safe and effective use of famciclovir tablets
Famciclovir tablets are not a cure for cold sores or genital herpes. It is not known if famciclovir tablets can stop the spread of herpes to others. If you are sexually active, you can pass herpes to your partner even if you are taking famciclovir tablets. Herpes can be passed to your partner even if you do not have active symptoms. You should continue to practice safer sex to lower the chances of spreading genital herpes to others. Do not have sexual contact with your partner during an outbreak of genital herpes or if you have any symptoms of genital herpes. Ask your healthcare provider for more information about safer sex practices.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use famciclovir tablets for a condition for which it was not prescribed. Do not give famciclovir tablets to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about famciclovir tablets that is written for health professionals.

What are the ingredients in famciclovir tablets?
Active ingredient: famciclovir
Inactive ingredients: croscarmellose sodium, crospovidone, hypromellose 2910, lactose monohydrate, magnesium stearate, polyethylene glycols 6000 and titanium dioxide.
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<thead>
<tr>
<th>Product Type</th>
<th>Item Code (Source)</th>
<th>NDC:</th>
</tr>
</thead>
<tbody>
<tr>
<td>HUMAN PRESCRIPTION DRUG</td>
<td></td>
<td>36714-614</td>
</tr>
</tbody>
</table>

**Route of Administration**

- ORAL

**Active Ingredient/Active Moiety**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
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</thead>
<tbody>
<tr>
<td>FAMCICLOVIR</td>
<td>(UNII: QIC03ANI02) (penciclovir - UNII:359HUE8FJC)</td>
<td>125 mg</td>
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</table>

**Inactive Ingredients**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CROSCARMELLOSE SODIUM (UNII: MD9OL1HH80)</td>
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<tr>
<td>CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 0840 05614MK)</td>
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<tr>
<td>HYPROMELLOSE 2910 (15 MPA.S) (UNII: 365FW92Z2F)</td>
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<tr>
<td>LACTOSE MONOHYDRATE (UNII: EWG575Z5QX)</td>
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<td>MAGNESIUM STEARATE (UNII: 7905785876)</td>
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<td>POLYETHYLENE GLYCOL 6000 (UNII: 10XK739WE)</td>
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<tr>
<td>TITANIUM DIOXIDE (UNII: 15FIX9V2JP)</td>
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**Product Characteristics**

- Color: WHITE
- Score: no score
- Shape: ROUND
- Size: 8mm
- Flavor: Imprint Code: C;269

**Packaging**

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<th>Marketing End Date</th>
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<td>30 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>02/09/2017</td>
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</table>

**Marketing Information**

- Marketing Category: ANDA
- Application Number or Monograph Citation: ANDA078278
- Marketing Start Date: 02/01/2017
- Marketing End Date: 02/01/2017

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<table>
<thead>
<tr>
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**Route of Administration**

- ORAL

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<table>
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<tr>
<td>FAMCICLOVIR</td>
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**Inactive Ingredients**

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<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CROSCARMELLOSE SODIUM (UNII: MD9OL1HH80)</td>
<td></td>
</tr>
<tr>
<td>CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 0840 05614MK)</td>
<td></td>
</tr>
<tr>
<td>HYPROMELLOSE 2910 (15 MPA.S) (UNII: 365FW92Z2F)</td>
<td></td>
</tr>
<tr>
<td>LACTOSE MONOHYDRATE (UNII: EWG575Z5QX)</td>
<td></td>
</tr>
<tr>
<td>MAGNESIUM STEARATE (UNII: 7905785876)</td>
<td></td>
</tr>
<tr>
<td>POLYETHYLENE GLYCOL 6000 (UNII: 10XK739WE)</td>
<td></td>
</tr>
<tr>
<td>TITANIUM DIOXIDE (UNII: 15FIX9V2JP)</td>
<td></td>
</tr>
</tbody>
</table>

**Product Characteristics**

- Color: WHITE
- Score: no score
- Shape: ROUND
- Size: 10mm
- Flavor: Imprint Code: C;271

**Packaging**

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:36714-615-01</td>
<td>30 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>02/09/2017</td>
<td></td>
</tr>
</tbody>
</table>

**Marketing Information**

- Marketing Category: ANDA
- Application Number or Monograph Citation: ANDA078278
- Marketing Start Date: 02/01/2017
- Marketing End Date: 02/01/2017

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<table>
<thead>
<tr>
<th>Product Information</th>
<th>Product Type</th>
<th>Item Code (Source)</th>
<th>NDC:</th>
</tr>
</thead>
<tbody>
<tr>
<td>HUMAN PRESCRIPTION DRUG</td>
<td></td>
<td>36714-616</td>
<td></td>
</tr>
</tbody>
</table>

**Route of Administration**

- ORAL

**Active Ingredient/Active Moiety**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAMCICLOVIR</td>
<td>(UNII: QIC03ANI02) (penciclovir - UNII:359HUE8FJC)</td>
<td>250 mg</td>
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</tbody>
</table>

**Inactive Ingredients**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
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</thead>
<tbody>
<tr>
<td>CROSCARMELLOSE SODIUM (UNII: MD9OL1HH80)</td>
<td></td>
</tr>
<tr>
<td>CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 0840 05614MK)</td>
<td></td>
</tr>
<tr>
<td>HYPROMELLOSE 2910 (15 MPA.S) (UNII: 365FW92Z2F)</td>
<td></td>
</tr>
<tr>
<td>LACTOSE MONOHYDRATE (UNII: EWG575Z5QX)</td>
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</tr>
<tr>
<td>MAGNESIUM STEARATE (UNII: 7905785876)</td>
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</tr>
<tr>
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</tr>
<tr>
<td>TITANIUM DIOXIDE (UNII: 15FIX9V2JP)</td>
<td></td>
</tr>
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**Product Characteristics**

- Color: WHITE
- Score: no score
- Shape: ROUND
- Size: 10mm
- Flavor: Imprint Code: C;271

**Packaging**

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**Marketing Information**

- Marketing Category: ANDA
- Application Number or Monograph Citation: ANDA078278
- Marketing Start Date: 02/01/2017
- Marketing End Date: 02/01/2017

---

**FAMCICLOVIR**

famciclovir tablet

---
FAMCICLOVIR (UNII: QIC03ANI02) (penciclovir - UNII:359HUE8FJC) FAMCICLOVIR 500 mg

Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)</td>
<td>CROSPovidone (15 MPa.s at 5%) (UNII: 68401960MK)</td>
</tr>
<tr>
<td>HYPROMELLOSE 2910 (15 MPa.s) (UNII: 36SFW2JZ0W)</td>
<td>LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)</td>
</tr>
<tr>
<td>MAGNESIUM STEARATE (UNII: 70997MB2D0)</td>
<td>POLYETHYLENE GLYCOL 6000 (UNII: 1H8J3H1WE)</td>
</tr>
<tr>
<td>TITANIUM DIOXIDE (UNII: 15FIX9V2JP)</td>
<td></td>
</tr>
</tbody>
</table>

Product Characteristics

Color | WHITE
Score | no score
Shape | CAPSULE
Size | 17mm
Flavor | Imprint Code
Contains

Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
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<tbody>
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<td>30 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>02/01/2017</td>
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<tbody>
<tr>
<td>ANDA</td>
<td>ANDA078278</td>
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<td></td>
</tr>
</tbody>
</table>

Labeler - NorthStar RxLLC (830546433)

Registrant - Cipla Ltd.- Goa (850072015)

Establishment

Name | Address | ID/FEI | Business Operations |
Cipla Kurkumbh | 917066446 | API MANUFACTURE(16714-614, 16714-615, 16714-616) |

Establishment

Name | Address | ID/FEI | Business Operations |
Cipla Ltd.- Goa | 650072015 | MANUFACTURE(16714-614, 16714-615, 16714-616) |

Revised: 2/2019

NorthStar RxLLC