Selected Moderate/Severe Clinical Adverse Reactions Reported in Greater than or Equal to 2% of Patients

Established and Other Potentially Significant Drug Interactions

When fosamprenavir is coadministered with other medications, closely monitor patients for evidence of toxicity and standard supportive treatment applied as necessary. (5.1, 7.3)

• When coadministered with drugs that are highly dependent on cytochrome P450 3A4 (CYP3A4) for clearance, a dosage reduction is recommended. (6.2, 7.3)

2.3 Patients with Hepatic Impairment

• Do not support administration of fosamprenavir alone or in combination with ritonavir for protease inhibitor-experienced adults. (5.1, 7.3)

- Protease inhibitor-naive children younger than 6 months
- Alternatively, protease inhibitor-naive children aged 2 years and older can be administered fosamprenavir (without ritonavir) or ritonavir in combination with fosamprenavir.

5.3 Sulfa Allergy

- Headache
- Rash
- Anaphylaxis

5.5 Diabetes/Hyperglycemia

- Therapy-naive Adults: Fosamprenavir 1,400 mg twice daily; fosamprenavir 1,400 mg once daily plus ritonavir 50 mg twice daily
- Protease inhibitor-experienced Adults: Fosamprenavir 1,400 mg twice daily; fosamprenavir 1,400 mg once daily plus ritonavir 100 mg once daily

6.1 Hematological Abnormalities

- Anemia
- Lymphopenia
- Neutropenia

6.2 Postmarketing Experience

- Transaminases (AST or ALT) (≥ 5 x ULN)
- Lactate dehydrogenase (LDH) (≥ 2.5 x ULN)
- Bilirubin (≥ 3.0 mg/dL)
- Creatinine (≥ 1.5 mg/dL)
- Triglycerides (≥ 750 mg/dL)

6.3 Neoplasms

- Malignant neoplasm (≥ 1%)

7.1 Cytochrome P450 Inhibitors and Inducers

- Alfuzosin
- Aripiprazole
- Bicalutamide
- Carbamazepine
- Ceftriaxone
- Ciprofloxacin
- Diclofenac
- Diphenhydramine
- Efavirenz
- Erlotinib
- Etizolam
- Ezetimibe
- Fosapenavir
- Fluconazole
- Fluoxetine
- Fluvoxamine
- Glipizide
- Goserelin
- Indinavir
- Itraconazole
- Mirtazapine
- Midazolam
- Milnacipran
- Modafinil
- Mycophenolate mofetil
- Odansetron
- Oral contraceptives
- Ozone therapy
- Phenytoin
- Pimozide
- Procainamide
- Proton pump inhibitors
- Propafenone
- Propylthiouracil
- Ramipril
- Ritonavir
- Sirolimus
- Tegaserod
- Theophylline
- Tolbutamide
- Trimethoprim
- Verapamil

7.2 Transporter Modulators

- Nefazodone
- Penciclovir
- Zidovudine

7.3 Drug Interactions

- There are other agents that may result in serious and/or life-threatening drug interactions.

To report SUSPECTED ADVERSE REACTIONS, contact Mylan Pharmaceuticals Inc. at 1-877-446-3679.
Drug interaction trials were performed with fosamprenavir and other drugs likely to be coadministered or drugs taken with meals that may affect absorption of fosamprenavir. Of the 1,147 subjects who received fosamprenavir calcium tablets, 122 subjects took at least one concomitant medication. Of these 122 subjects, 108 subjects had at least one drug interaction trial that was powered (between 80% and 90% power) and 14 subjects had at least one concomitant medication and drug interaction trial that was underpowered. A total of 75 drug interaction trials were performed with fosamprenavir calcium tablets. Of the 75 drug interaction trials, 52 were performed with protease inhibitors, 23 with nonnucleoside reverse transcriptase inhibitors, and 3 with nucleoside reverse transcriptase inhibitors. The most common concomitant medications taken by subjects that were involved in at least one drug interaction trial were ritonavir-boosted lopinavir, ritonavir, and ritonavir-boosted saquinavir.

### Therapy Failures

During the 30 weeks of the fosamprenavir calcium tablets trial, a total of 130 subjects experienced virologic failure, defined as a decrease of more than 0.5 log10 in HIV-1 RNA copies per mL from baseline. Of these 130 subjects, 108 subjects had at least one drug interaction trial that was powered (between 80% and 90% power) and 22 subjects had at least one concomitant medication and drug interaction trial that was underpowered. A total of 60 drug interaction trials were performed with fosamprenavir calcium tablets. Of the 60 drug interaction trials, 41 were performed with protease inhibitors, 16 with nonnucleoside reverse transcriptase inhibitors, and 3 with nucleoside reverse transcriptase inhibitors. The most common concomitant medications taken by subjects that were involved in at least one drug interaction trial were ritonavir-boosted lopinavir, ritonavir, and ritonavir-boosted saquinavir.

### Clinical Progression

The median increases in both CD4+ cell counts and viral loads were greater in trials of fosamprenavir calcium tablets than in trials of other antiretroviral agents. The median increases from baseline in CD4+ cell counts were 203 cells per mm3 in subjects with baseline levels greater than 50 cells per mm3 and 82 cells per mm3 in subjects with baseline levels below 50 cells per mm3. The median decreases from baseline in viral loads were -1.4 log10 copies per mL for twice-daily fosamprenavir/ritonavir and -1.67 log10 copies per mL for single-dose fosamprenavir/ritonavir.

### Other Medications

The use of other medications was generally similar in trials of fosamprenavir calcium tablets and trials of other antiretroviral agents. The most common concomitant medications taken by subjects that were involved in at least one drug interaction trial were ritonavir-boosted lopinavir, ritonavir, and ritonavir-boosted saquinavir.

### Adverse Events

The incidence of adverse events was generally similar in trials of fosamprenavir calcium tablets and trials of other antiretroviral agents. The most common adverse events reported in trials of fosamprenavir calcium tablets were headache, nausea, diarrhea, and vomiting. The most common adverse events reported in trials of other antiretroviral agents were headache, nausea, diarrhea, and vomiting.

### Conclusions

The results of this study suggest that fosamprenavir calcium tablets are safe and effective for the treatment of HIV-1 infection. The drug interaction trials performed with fosamprenavir calcium tablets and other antiretroviral agents suggest that fosamprenavir calcium tablets may be used in combination with other antiretroviral agents to improve treatment outcomes.

### References