





















































































*Emtricitabine*: Emtricitabine-resistant viruses with the M184V or I substitution were cross-resistant to lamivudine, but retained sensitivity to didanosine, stavudine, tenofovir, and zidovudine.

*Tenofovir Alafenamide*: Tenofovir resistance-associated substitutions K65R and K70E result in reduced susceptibility to abacavir, didanosine, emtricitabine, lamivudine, and tenofovir. HIV-1 with multiple thymidine analog substitutions (M41L, D67N, K70R, L210W, T215F/Y, K219Q/E/N/R) or multinucleoside resistant HIV-1 with a T69S double insertion mutation or with a Q151M substitution complex including K65R, showed reduced susceptibility to TAF in cell culture.

### **13. NONCLINICAL TOXICOLOGY**

#### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

*Darunavir*: Darunavir was evaluated for carcinogenic potential by oral gavage administration to mice and rats up to 104 weeks. Daily doses of 150, 450, and 1000 mg/kg were administered to mice and doses of 50, 150, and 500 mg/kg were administered to rats. A dose-related increase in the incidence of hepatocellular adenomas and carcinomas was observed in males and females of both species and an increase in thyroid follicular cell adenomas was observed in male rats. The observed hepatocellular findings in rodents are considered to be of limited relevance to humans. Repeated administration of darunavir to rats caused hepatic microsomal enzyme induction and increased thyroid hormone elimination, which predispose rats but not humans to thyroid neoplasms. At the highest tested doses, the systemic exposures to darunavir (based on AUC) were between 0.5- and 0.6-fold (mice) and was 0.9-fold (rats) of exposures observed in humans at the recommended therapeutic dose of darunavir in SYMTUZA. Darunavir was not mutagenic or genotoxic in a battery of *in vitro* and *in vivo* assays including bacterial reverse mutation (Ames), chromosomal aberration in human lymphocytes, and *in vivo* micronucleus test in mice.

*Cobicistat*: In a long-term carcinogenicity study in mice, no drug-related increases in tumor incidence were observed at doses up to 50 and 100 mg/kg/day in males and females, respectively. Cobicistat exposures at these doses were approximately 8.6 (male) and 20 (females) times, respectively, the human systemic exposure at the therapeutic daily dose of cobicistat in SYMTUZA. In a long-term carcinogenicity study of cobicistat in rats, an increased incidence of follicular cell adenomas and/or carcinomas in the thyroid gland was observed at doses of 25 and 50 mg/kg/day in males, and at 30 mg/kg/day in females. The follicular cell findings are considered to be rat-specific, secondary to hepatic microsomal enzyme induction and thyroid hormone imbalance, and are not relevant for humans. At the highest doses tested in the rat carcinogenicity study, systemic exposures were approximately 2 times the human systemic exposure at the therapeutic daily dose of cobicistat in SYMTUZA. Cobicistat was not genotoxic in the reverse mutation bacterial test (Ames test), mouse lymphoma, or rat micronucleus assays.

*Emtricitabine*: In long-term carcinogenicity studies of emtricitabine, no drug-related increases in tumor incidence were found in mice at doses up to 750 mg per kg per day (26 times the human systemic exposure at the recommended dose of emtricitabine in SYMTUZA) or in rats at doses up to 600 mg per kg per day (31 times the human systemic exposure at the recommended dose). Emtricitabine was not genotoxic in the reverse mutation bacterial test (Ames test), mouse lymphoma, or mouse micronucleus assays. Emtricitabine did not affect fertility in male rats at

approximately 107 times or in male and female mice at approximately 88 times higher exposures (AUC) than in humans given the recommended 200 mg daily dose in SYMTUZA. Fertility was normal in the offspring of mice exposed daily from before birth (*in utero*) through sexual maturity at daily exposures (AUC) of approximately 88 times higher than human exposures at the recommended 200 mg daily dose.

*Tenofovir alafenamide*: Since TAF is rapidly converted to tenofovir and a lower tenofovir exposure in rats and mice was observed after TAF administration compared to TDF administration, carcinogenicity studies were conducted only with TDF. Long-term oral carcinogenicity studies of TDF in mice and rats were carried out at exposures up to approximately 10 times (mice) and 4 times (rats) those observed in humans at the 300 mg therapeutic dose of TDF for HIV-1 infection. The tenofovir exposure in these studies was approximately 167 times (mice) and 55 times (rat) those observed in humans after administration of the daily recommended dose of TAF. At the high dose in female mice, liver adenomas were increased at tenofovir exposures approximately 10 times (300 mg TDF) and 167 times (10 mg TAF) the exposure observed in humans. In rats, the study was negative for carcinogenic findings.

TAF was not genotoxic in the reverse mutation bacterial test (Ames test), mouse lymphoma, or rat micronucleus assays. There were no effects on fertility, mating performance, or early embryonic development when TAF was administered to male rats at a dose equivalent to 155 times the human dose based on body surface area comparisons for 28 days prior to mating and to female rats for 14 days prior to mating through Day 7 of gestation.

## **13.2 Animal Toxicology and/or Pharmacology**

Minimal to slight infiltration of mononuclear cells in the posterior uvea was observed in dogs with similar severity after 3 and 9 month administration of tenofovir alafenamide; reversibility was seen after a 3-month recovery period. No eye toxicity was observed in the dog at systemic exposures of 3.5 (TAF) and 0.62 (tenofovir) times the exposure seen in humans with the recommended daily dose of TAF in SYMTUZA.

## **14. CLINICAL STUDIES**

### **14.1 Clinical Trial Results in Subjects with HIV-1 Infection with no Prior Antiretroviral Treatment History**

The efficacy of SYMTUZA in HIV-1 subjects with no prior antiretroviral treatment history was evaluated in the Phase 3 trial TMC114FD2HTX3001 [NCT02431247, (AMBER)] in which subjects were randomized in a 1:1 ratio to receive either SYMTUZA (N=362) or a combination of PREZCOBIX and FTC/TDF (N=363) once daily. The median age was 34.0 years (range 18-71), 88.3% were male, 83% White, 11% Black, and 2% Asian. The mean baseline plasma HIV-1 RNA was 4.5 log<sub>10</sub> copies/mL (range 1.3-6.7), and 18% had a baseline viral load ≥100,000 copies/mL. The median baseline CD4+ cell count was 453 cells/mm<sup>3</sup> (range 38 to 1456 cells/mm<sup>3</sup>).

Virologic outcomes at 48 weeks of treatment are presented in Table 11.



**Table 11: Virologic Outcomes in AMBER at Week 48 in HIV-1 Subjects with No Prior Antiretroviral Treatment History**

	<b>SYMTUZA N=362</b>	<b>PREZCOBIX + FTC/TDF N=363</b>
<b>Virologic Response</b>		
HIV-1 RNA <50 copies/mL	91%	88%
Treatment difference <sup>a</sup>	2.7 (95% CI: -1.6; 7.1)	
Virologic Failure <sup>b</sup>	4%	3%
No virologic data at Week 48 window <sup>c</sup>	4%	8%
Reasons		
Discontinued trial due to adverse event or death	2%	4%
Discontinued trial for other reasons <sup>d</sup>	1%	3%
Missing data during window but on trial	1%	1%

<sup>a</sup> Based on stratum adjusted MH test where stratification factors are HIV-1 RNA level ( $\leq 100,000$  or  $> 100,000$  copies/mL) and CD4+ cell count ( $< 200$  or  $\geq 200$  cells/ $\mu$ L).

<sup>b</sup> Included subjects who had  $\geq 50$  copies/mL in the Week 48 window; subjects who discontinued early due to lack or loss of efficacy; subjects who discontinued for reasons other than an adverse event (AE), death, or lack or loss of efficacy and at the time of discontinuation had a viral value of  $\geq 50$  copies/mL.

<sup>c</sup> Day 295 – Day 378

<sup>d</sup> Other includes reasons such as withdrew consent, loss to follow-up, and non-compliance.

The mean increase from baseline in CD4+ cell count at Week 48 was 189 and 174 cells/mm<sup>3</sup> in the SYMTUZA and PREZCOBIX + FTC/TDF groups, respectively.

#### **14.2 Clinical Trial Results in Virologically-Suppressed Subjects with HIV-1 Infection Who Switched to SYMTUZA**

Phase 3 trial TMC114IFD3013 [NCT02269917, (EMERALD)] evaluated the efficacy of SYMTUZA in virologically-suppressed (HIV-1 RNA less than 50 copies/mL) subjects with HIV-1 infection. Subjects were virologically suppressed for at least 2 months and no more than once had a viral load elevation above 50 HIV-1 RNA copies/mL during the year prior to enrollment. Subjects were on a stable antiretroviral regimen (for at least 6 months), consisting of a bPI [either darunavir once daily or atazanavir (both boosted with ritonavir or cobicistat), or lopinavir with ritonavir] combined with emtricitabine and TDF. Subjects had no history of failure on darunavir treatment and no known or suspected darunavir resistance-associated substitutions. Emtricitabine or tenofovir resistance-associated substitutions were not specifically excluded by the protocol. They either switched to SYMTUZA (N=763) or continued their treatment regimen (N=378) (randomized 2:1). Subjects had a median age of 46 years (range 19-78), 82% were male, 75% White, 21% Black, and 2% Asian. The median baseline CD4+ cell count was 628 cells/mm<sup>3</sup> (range 111-1921 cells/mm<sup>3</sup>). Overall, 15% (N=169) of subjects had prior virologic failure. Five subjects had archived tenofovir resistance-associated substitutions and 53 subjects had archived emtricitabine resistance-associated substitutions, mainly at RT position M184. All of these subjects with emtricitabine resistance-associated substitutions had HIV-1 RNA <50 copies/mL at Week 48 (N=50) or at the last on-treatment viral load (N=3). Virologic outcomes are presented in Table 12. Prior virologic failure did not impact treatment outcomes.

**Table 12: Virologic Outcomes in EMERALD at Week 48 in HIV-1 Virologically-Suppressed Subjects Who Switched to SYMTUZA**

	<b>SYMTUZA N=763</b>	<b>bPI+FTC/TDF N=378</b>
<b>Virologic Failure<sup>a</sup></b>	1%	1%
Treatment difference <sup>b</sup>	0.3 (95% CI: -0.7; 1.2)	
HIV-1 RNA <50 copies/mL	95%	94%
No virologic data at Week 48 window <sup>c</sup>	4%	6%
Reasons		
Discontinued trial due to adverse event or death	1%	1%
Discontinued trial for other reasons <sup>d</sup>	3%	4%
Missing data during window <sup>c</sup> but on trial	<1%	1%

<sup>a</sup> Included subjects who had  $\geq 50$  copies/mL in the Week 48 window; subjects who discontinued early due to lack or loss of efficacy; subjects who discontinued for reasons other than an adverse event (AE), death, or lack or loss of efficacy and at the time of discontinuation had a viral value  $\geq 50$  copies/mL.

<sup>b</sup> Based on MH test adjusting for bPI at screening (ATV with rtv or COBI, DRV with rtv or COBI, LPV with rtv).

<sup>c</sup> Day 295 – Day 378

<sup>d</sup> Other includes reasons such as withdrew consent, loss to follow-up, and non-compliance

The mean increase from baseline in CD4+ cell count at Week 48 was 20 cells/mm<sup>3</sup> in subjects who switched to SYMTUZA and 8 cells/mm<sup>3</sup> in subjects who stayed on their baseline PI + FTC/TDF.

### 14.3 Clinical Trial Results in Pediatric Subjects with HIV-1 Infection

The pharmacokinetic profile, safety, and antiviral activity of the components of SYMTUZA were evaluated in open-label clinical trials in pediatric subjects with HIV-1 infection aged 12 to less than 18 years: GS-US-216-0128 (N=7) and GS-US-292-0106 (N=50).

In the Phase 2/3 trial GS-US-216-0128, darunavir 800 mg and cobicistat 150 mg once daily with 2 NRTIs were evaluated in 7 virologically suppressed pediatric subjects aged 12 to less than 18 years and weighing at least 40 kg. Subjects had a median (range) age of 14 (12-16) years and a median (range) weight of 57 (45-78) kg. At baseline, plasma HIV-1 RNA was <50 copies/mL in all subjects, and the median (range) CD4+ cell count was 1,117 (658-2,416) cells/mm<sup>3</sup>. At Week 48, the proportion of subjects who maintained HIV-1 RNA <50 copies/mL was 86%, and the median change in CD4+ cell count from baseline was -342 cells/mm<sup>3</sup> (range -1,389 to 210 cells/mm<sup>3</sup>). All 6 subjects with available data had CD4+ cell counts above 800 cells/mm<sup>3</sup> at Week 48.

In the Phase 2/3 trial GS-US-292-0106, cobicistat 150 mg, emtricitabine 200 mg, and tenofovir alafenamide 10 mg, as part of a fixed-dose combination regimen together with elvitegravir 150 mg, were evaluated in 50 treatment-naïve pediatric subjects with HIV-1 aged 12 to less than 18 years and weighing at least 35 kg. Subjects had a median (range) age of 15 (12-17) years. At baseline, median (range) plasma HIV-1 RNA was 4.7 (3.3-6.5) log<sub>10</sub> copies/mL, median (range) CD4+ cell count was 456 (95-1,110) cells/mm<sup>3</sup>, and 22% had baseline plasma HIV-1 RNA >100,000 copies/mL. At Week 48, the proportion of subjects who had HIV-1 RNA <50 copies/mL was 92%, and the median increase in CD4+ cell count from baseline was 220 cells/mm<sup>3</sup>.

The use of SYMTUZA in pediatric patients weighing less than 40 kg has not been established [*see Use in Specific Populations (8.4)*].

## 16. HOW SUPPLIED/STORAGE AND HANDLING

SYMTUZA<sup>®</sup> (darunavir, cobicistat, emtricitabine, and tenofovir alafenamide) tablets are supplied as yellow to yellowish-brown, capsule-shaped, film-coated tablets debossed with “8121” on one side and “JG” on the other side.

SYMTUZA is packaged in bottles of 30 tablets (NDC 59676-800-30), with a silica gel desiccant and child-resistant closure.

### Storage

- Store at 20°C-25°C (between 68°F-77°F); with excursions permitted to 15°C-30°C (59°F-86°F).
- Dispense only in the original container. Keep container tightly closed with desiccant inside to protect from moisture.
- Keep SYMTUZA out of reach of children.

## 17. PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

### Instructions for Use

Advise patients to take SYMTUZA with food every day on a regular dosing schedule, as missed doses can result in development of resistance. Inform patients not to alter the dose of SYMTUZA or discontinue therapy with SYMTUZA without consulting their physician. For patients who are unable to swallow tablets whole, SYMTUZA may be split using a tablet-cutter, and the entire dose should be consumed immediately after splitting [*see Dosage and Administration (2.2)*].

### Post-treatment Acute Exacerbation of Hepatitis B in Patients with HBV Co-Infection

Severe acute exacerbations of hepatitis B have been reported in patients who are coinfecting with HBV and HIV-1 and have discontinued products containing emtricitabine and/or TDF, and may likewise occur with discontinuation of SYMTUZA [*see Warnings and Precautions (5.1)*]. Advise the patient to not discontinue SYMTUZA without first informing their healthcare provider.

### Hepatotoxicity

Inform patients that drug-induced hepatitis (e.g., acute hepatitis, cytolytic hepatitis) and liver injury, including some fatalities, could potentially occur with SYMTUZA. Advise patients to contact their healthcare provider immediately if signs and symptoms of liver problems develop [*see Warnings and Precautions (5.2)*].

### Severe Skin Reactions

Inform patients that skin reactions ranging from mild to severe, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, could potentially occur with SYMTUZA. Advise patients to contact their healthcare provider

immediately if signs or symptoms of severe skin reactions develop, including but not limited to severe rash or rash accompanied with fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, and/or conjunctivitis [see *Warnings and Precautions (5.3)*].

### Pregnancy

Advise patients that SYMTUZA is not recommended during pregnancy and to alert their healthcare provider if they get pregnant while taking SYMTUZA. Inform patients that there is an antiretroviral pregnancy registry to monitor fetal outcomes of pregnant individuals exposed to SYMTUZA [see *Use in Specific Populations (8.1)*].

### Lactation

Instruct individuals with HIV-1 infection not to breastfeed because HIV-1 can be passed to the baby in breast milk [see *Use in Specific Populations (8.2)*].

### Drug Interactions

SYMTUZA may interact with many drugs; therefore, inform patients of the potential serious drug interactions with SYMTUZA, and that some drugs are contraindicated with SYMTUZA and other drugs may require dosage adjustment. Advise patients to report to their healthcare provider the use of any other prescription or nonprescription medication or herbal products, including St. John's wort [see *Contraindications (4), Warnings and Precautions (5.4), and Drug Interactions (7)*].

### Immune Reconstitution Syndrome

Advise patients to inform their healthcare provider immediately of any symptoms of infection, as in some patients with advanced HIV infection (AIDS), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started [see *Warnings and Precautions (5.5)*].

### Renal Impairment

Advise patients to avoid taking SYMTUZA with concurrent or recent use of nephrotoxic agents. Renal impairment, including cases of acute renal failure, has been reported in association with the use of tenofovir prodrugs [see *Warnings and Precautions (5.6)*].

### Lactic Acidosis and Severe Hepatomegaly

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with use of drugs similar to SYMTUZA. Advise patients that they should stop SYMTUZA if they develop clinical symptoms suggestive of lactic acidosis or pronounced hepatotoxicity [see *Warnings and Precautions (5.8)*].

### Fat Redistribution

Inform patients that redistribution or accumulation of body fat may occur in patients receiving antiretroviral therapy, including SYMTUZA, and that the cause and long-term health effects of these conditions are not known at this time [see *Warnings and Precautions (5.10)*].

Manufactured for:  
Janssen Products, LP, Horsham PA 19044, USA

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**PATIENT INFORMATION**  
**SYMTUZA® (sim toó zah)**  
**(darunavir, cobicistat, emtricitabine, and tenofovir alafenamide)**  
**tablets**

**What is the most important information I should know about SYMTUZA?**

**SYMTUZA can cause serious side effects, including:**

- **Worsening of Hepatitis B virus infection (HBV).** Your healthcare provider will test you for HBV before starting treatment with SYMTUZA. If you have HBV infection and take SYMTUZA, your HBV may get worse (flare-up) if you stop taking SYMTUZA. A “flare-up” is when your HBV infection suddenly returns in a worse way than before.
  - Do not stop taking SYMTUZA without first talking to your healthcare provider.
  - Do not run out of SYMTUZA. Refill your prescription or talk to your healthcare provider before your SYMTUZA is all gone.
  - If you stop taking SYMTUZA, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your HBV infection, or give you a medicine to treat your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking SYMTUZA.
- **Change in liver enzymes.** People with a history of hepatitis B or C virus infection or who have certain liver enzyme changes may have an increased risk of developing new or worsening liver problems during treatment with SYMTUZA. Liver problems can also happen during treatment with SYMTUZA in people without a history of liver disease. Your healthcare provider may need to do tests to check your liver enzymes before and during treatment with SYMTUZA.
- **Severe liver problems.** In rare cases, severe liver problems can happen that can lead to death. **Tell your healthcare provider right away if you get these symptoms:** skin or the white part of your eyes turns yellow, dark “tea-colored” urine, light-colored stools, loss of appetite for several days or longer, nausea, vomiting, or stomach-area pain.

**SYMTUZA may cause severe or life-threatening skin reactions or rash.** Sometimes these skin reactions and skin rashes can become severe and require treatment in a hospital. Call your healthcare provider right away if you develop a rash. **Stop taking SYMTUZA** and call your healthcare provider right away if you develop any skin changes with symptoms below:

- |                        |   |
|------------------------|---|
| • fever                | • blisters or skin lesions                                  |
| • tiredness            | • mouth sores or ulcers                                     |
| • muscle or joint pain | • red or inflamed eyes, like “pink eye”<br>(conjunctivitis) |

**See “What are the possible side effects of SYMTUZA?”** for more information about side effects.

**What is SYMTUZA?**

SYMTUZA is a prescription medicine that is used without other antiretroviral medicines to treat Human Immunodeficiency Virus-1 (HIV-1) infection in adults and in children who weigh at least 88 pounds (40 kg) who:

- have not received anti-HIV-1 medicines in the past, **or**
- when their healthcare provider determines that they meet certain requirements.

HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS).

SYMTUZA contains the prescription medicines darunavir, cobicistat, emtricitabine, and tenofovir alafenamide.

It is not known if SYMTUZA is safe and effective in children weighing less than 88 pounds (40 kg).

**Who should not take SYMTUZA?**

Do not take SYMTUZA with any of the following medicines:

- alfuzosin
- carbamazepine
- colchicine, if you have liver or kidney problems
- dronedarone
- elbasvir and grazoprevir
- ergot-containing medicines, such as:
  - dihydroergotamine
  - ergotamine tartrate
  - methylergonovine
- ivabradine
- lomitapide
- lovastatin or a product that contains lovastatin
- lurasidone
- midazolam, when taken by mouth
- naloxegol
- phenobarbital
- phenytoin
- pimozide
- ranolazine
- rifampin
- sildenafil, when used for the treatment of pulmonary arterial hypertension (PAH)
- simvastatin or a product that contains simvastatin
- St. John's wort (*Hypericum perforatum*), or a product that contains St. John's wort
- triazolam

Serious problems can happen if you take any of these medicines with SYMTUZA. This is not a complete list of medicines. Therefore, tell your healthcare provider about all medicines you take.

**Before taking SYMTUZA, tell your healthcare provider about all of your medical conditions, including if you:**

- have liver problems, including hepatitis B or hepatitis C
  - have kidney problems
  - are allergic to sulfa (sulfonamide)
  - have diabetes
  - have hemophilia
  - are pregnant or plan to become pregnant.
    - It is not known if SYMTUZA will harm your unborn baby.
    - SYMTUZA should not be used during pregnancy because you may not have enough SYMTUZA in your body during pregnancy.
    - Tell your healthcare provider if you become pregnant while taking SYMTUZA. Your healthcare provider will prescribe different medicines if you become pregnant while taking SYMTUZA.
- Pregnancy Registry:** There is a pregnancy registry for those who take antiretroviral medicines during pregnancy. The purpose of the registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. Do not breastfeed if you take SYMTUZA.
    - You should not breastfeed if you have HIV-1 because of the risk of passing HIV to your baby.
    - One of the medicines in SYMTUZA called emtricitabine can pass into your breast milk. It is not known if the other medicines in SYMTUZA can pass into your breast milk.
    - Talk to your healthcare provider about the best way to feed your baby.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, topical creams, vitamins, and herbal supplements. Some medicines interact with SYMTUZA. Keep a list of your medicines to show your healthcare provider and pharmacist.

- You can ask your healthcare provider or pharmacist for a list of medicines that interact with SYMTUZA.
- **Do not start taking a new medicine without telling your healthcare provider.** Your healthcare provider can tell you if it is safe to take SYMTUZA with other medicines.

**How should I take SYMTUZA?**

- Take SYMTUZA exactly as your healthcare provider tells you.
- Do not change your dose or stop taking SYMTUZA without talking to your healthcare provider.
- Take SYMTUZA 1 time a day with food.
- If you have difficulty swallowing, the tablet may be split using a tablet-cutter. After splitting the tablet, the entire dose (both halves) should then be taken right away.
- Do not miss a dose of SYMTUZA.
- When your SYMTUZA supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to SYMTUZA and become harder to treat.
- If you take too much SYMTUZA, call your healthcare provider or go to the nearest hospital emergency room right away.



### What are the possible side effects of SYMTUZA?

SYMTUZA may cause serious side effects, including:

- See **“What is the most important information I should know about SYMTUZA?”**
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having new symptoms after starting your HIV-1 medicine.
- **New or worse kidney problems, including kidney failure.** Your healthcare provider should do blood and urine tests to check your kidneys before you start and while you are taking SYMTUZA. Your healthcare provider may tell you to stop taking SYMTUZA if you develop new or worse kidney problems.
- **Too much lactic acid in your blood (lactic acidosis).** Too much lactic acid is a serious but rare medical emergency that can lead to death. **Tell your healthcare provider right away if you get these symptoms:** weakness or being more tired than usual, unusual muscle pain, being short of breath or fast breathing, stomach pain with nausea and vomiting, cold or blue hands and feet, feel dizzy or lightheaded, or a fast or abnormal heartbeat.
- **Diabetes and high blood sugar (hyperglycemia).** Some people who take protease inhibitors including SYMTUZA can get high blood sugar, develop diabetes, or your diabetes can get worse. Tell your healthcare provider if you notice an increase in thirst or if you start urinating more often while taking SYMTUZA.
- **Changes in body fat** can happen in people who take HIV-1 medicines. The changes may include an increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the middle of your body (trunk). Loss of fat from the legs, arms, and face may also happen. The exact cause and long-term health effects of these conditions are not known.
- **Increased bleeding for hemophiliacs.** Some people with hemophilia have increased bleeding with protease inhibitors.

#### The most common side effects of SYMTUZA, include:

- |            |                    |
|------------|--------------------|
| ○ diarrhea | ○ headache         |
| ○ rash     | ○ stomach problems |
| ○ nausea   | ○ gas              |
| ○ fatigue  |                    |

These are not all of the possible side effects of SYMTUZA.

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 SYMTUZA?

- Store SYMTUZA tablets at room temperature between 68°F to 77°F (20°C to 25°C).
- The SYMTUZA bottle contains a desiccant and has a child-resistant cap.
- Keep the SYMTUZA container tightly closed with the desiccant inside of it to protect SYMTUZA from moisture.

**Keep SYMTUZA out of reach of children.**

**General information about the safe and effective use of SYMTUZA.**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use SYMTUZA for a condition for which it was not prescribed. Do not give SYMTUZA to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your healthcare provider or pharmacist for information about SYMTUZA that is written for health professionals.

**What are the ingredients in SYMTUZA?**

**Active ingredient:** darunavir, cobicistat, emtricitabine, and tenofovir alafenamide

**Inactive ingredients:** colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, and microcrystalline cellulose. The tablets are film-coated with a coating material containing polyethylene glycol (macrogol), polyvinyl alcohol (partially hydrolyzed), talc, titanium dioxide, and yellow ferric oxide.

Manufactured for: Janssen Products, LP, Horsham PA 19044, USA

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For more information call 1-800-526-7736.

This Patient Information has been approved by the U.S. Food and Drug Administration.

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