SYMTUZA® 800 mg/150 mg/200 mg/10 mg film-coated tablets PRESCRIBING INFORMATION

ACTIVE INGREDIENT(S): darunavir, cobicistat, emtricitabine, tenofovir alafenamide.

Please refer to Summary of Product Characteristics (SmPC) before prescribing. **INDICATION(S):** Treatment of human immunodeficiency virus type 1 (HIV 1) infection in adults and adolescents (aged 12 years and older with body weight at least 40 kg). Genotypic testing should guide the use of SYMTUZA.

DOSAGE & ADMINISTRATION: Initiate by physician experienced in management of HIV 1 infection. **Adults and adolescents aged ≥ 12 years weighing ≥ 40 kg:** one tablet daily with food in *Antiretroviral Therapy* (ART-naïve patients). *ARTexperienced patients:* one tablet daily with food if no darunavir resistance associated mutations (DRV-RAMs) and plasma HIV-1 RNA < 100,000 copies/ml and CD4+ cell count ≥ 100 cells x 10^6/l.
If dose > 12 hours late, do not take missed dose and resume usual dosing schedule. If patient vomits ≤ 1 hour after taking tablet, take another dose with food as soon as possible; if > 1 hour, take next dose at regularly scheduled time.
Children: Not established in children aged 3-11 years, or weighing < 40 kg. No data available. Should not be used below 3 years of age. **Elderly:** Limited information; use with caution in patients > 65 years of age. **Renal impairment:** $eGFR_{CG}$ ≥ 30 mL/min: no dose adjustment. $eGFR_{CG}$ < 30 mL/min: do not start/discontinue treatment as no data. **Hepatic impairment:** mild (Child-Pugh Class A)/moderate (Child-Pugh Class B) hepatic impairment: no dose adjustment; use with caution. Severe hepatic impairment (Child-Pugh Class C): not studied; do not use.

CONTRAINDICATIONS: Hypersensitivity to active substances/excipients. Severe (Child-Pugh Class C) hepatic impairment. Co-administration with carbamazepine, phenobarbital, phenytoin, rifampicin, lopinavir/ritonavir, St. John's Wort (*Hypericum perforatum*), alfuzosin, amiodarone, dronedarone, ivabradine, quinidine, ranolazine, colchicine (with renal and/or hepatic impairment), ergot derivatives (e.g. dihydroergotamine, ergometrine, ergotamine, methylergonovine), dapoxetine, domperidone, naloxegol, pimozide, quetiapine, sertindole, lurasidone, elbasvir/grazoprevir, triazolam, midazolam administered orally, sildenafil (for treatment of pulmonary arterial hypertension), avanafil, simvastatin, lovastatin, lomitapide, ticagrelor.

SPECIAL WARNINGS & PRECAUTIONS: ***ART-experienced patients:*** not for treatment-experienced patients with one or more DRV-RAMs or with HIV-1 RNA ≥ 100,000 copies/ml or CD4+ cell count < 100 cells x 10^6/l. ***Pregnancy:*** Darunavir and cobicistat levels decreased when administered during pregnancy. May result in virological failure and increased risk of mother to child HIV transmission (see 'Pregnancy' below). ***Co-infection with hepatitis B/C virus:*** increased risk for severe, potentially fatal hepatic adverse reactions. Safety/efficacy not established when co-infection with HIV-1 and hepatitis C virus (HCV). Tenofovir alafenamide active against HBV. Discontinuation of Symtuza may result in severe acute exacerbations of hepatitis if co-infection with HBV; monitor closely (clinical/laboratory follow-up for at least several months after stopping Symtuza). With advanced liver disease or cirrhosis, discontinuation not recommended; post-treatment exacerbation of hepatitis may lead to hepatic decompensation. Do not use concomitantly with medicinal products containing tenofovir disoproxil (e.g. fumarate, phosphate, succinate), lamivudine, or adefovir dipivoxil (for HBV). ***Mitochondrial dysfunction:*** mitochondrial dysfunction reported in HIV negative infants exposed *in utero* and/or postnatally to nucleoside analogues. Main adverse reactions (often transitory) are haematological disorders (anaemia, neutropenia) and metabolic disorders

(hyperlactataemia, hyperlipasaemia). Late-onset neurological disorders have been reported (hypertonia, convulsion, abnormal behaviour); not known if transient or permanent. Follow up/investigate any child exposed *in utero*. Follow current national recommendations for pregnant women. ***Hepatotoxicity:*** Hepatitis reported with darunavir/ritonavir. Increased if pre-existing liver dysfunction, including severe/potentially fatal hepatic adverse reactions. If concomitant antiviral therapy for hepatitis B or C, refer to relevant SmPCs. Conduct laboratory tests prior to initiating therapy; monitor during treatment. Consider increased AST/ALT monitoring with underlying chronic hepatitis, cirrhosis, pre-treatment transaminase elevations, especially during first months. Consider prompt interruption/discontinuation of Symtuza if evidence of new/worsening liver dysfunction. ***Nephrotoxicity:*** acute renal failure and proximal renal tubulopathy have been reported with tenofovir alafenamide-containing products, potential risk from chronic exposure to low levels of tenofovir alafenamide, Assess renal function before initiating therapy with Symtuza, monitor during therapy as clinically appropriate. Consider discontinuation in patients who develop clinically significant decreases in renal function or evidence of proximal renal tubulopathy**.** ***Renal impairment:*** Cobicistat decreases estimated creatinine clearance. ***Haemophilia:*** reports of increased bleeding. ***Severe skin reactions:*** Discontinue Symtuza immediately if signs/symptoms of severe skin reactions. Drug Rash with Eosinophilia and Systemic Symptoms (DRESS), StevensJohnson Syndrome (SJS), toxic epidermal necrolysis (TEN) and acute generalised exanthematous pustulosis reported with darunavir/ritonavir. ***Sulphonamide allergy:*** caution; contains sulphonamide moiety. ***Immune reconstitution inflammatory syndrome (IRIS):*** Inflammatory response to asymptomatic or residual opportunistic pathogens may arise in patients with severe immune deficiency at start of combination antiretroviral therapy (CART); evaluate symptoms when necessary. Herpes simplex/zoster reactivation observed with darunavir/ritonavir. Autoimmune disorders reported. ***Opportunistic infections:*** can develop; close clinical observation required. ***Other:*** Increase in weight, levels of blood lipids and glucose may occur, monitor blood lipids and glucose; refer to HIV treatment guidelines. Do not use Symtuza in combination with another antiretroviral requiring pharmaco-enhancement, with ritonavir, cobicistat, tenofovir disoproxil (as fumarate, phosphate or succinate), lamivudine or adefovir dipivoxil.

SIDE EFFECTS: Very common: headache, diarrhoea, rash (including macular, maculopapular, papular, erythematous, pruritic rash, generalised rash, and allergic dermatitis). **Common:** anaemia, drug hypersensitivity, diabetes mellitus, anorexia, hypercholesterolaemia, low density lipoprotein increased, hypertriglyceridaemia, hyperlipidaemia, dyslipidaemia, abnormal dreams, dizziness, vomiting, nausea, abdominal pain, abdominal distension, dyspepsia, flatulence, hepatic enzyme increased, pruritus, urticaria, arthralgia, myalgia, asthenia, fatigue, increased blood creatinine. **Other side effects:** IRIS, pancreatitis acute, acute hepatitis, cytolytic hepatitis, angioedema, DRESS, SJS, TEN, acute generalised exanthematous pustulosis, osteonecrosis, crystal nephropathy.
Refer to SmPC for other side effects.

PREGNANCY: Symtuza should not be initiated during pregnancy. Switch to alternative regimen (e.g. darunavir/ low dose ritonavir) if Symtuza therapy started before pregnancy.
LACTATION: In order to avoid transmission of HIV to the infant it is recommended that women living with HIV do not breast-feed.

INTERACTIONS: Symtuza not studied; interactions identified in studies with individual components. Refer to the SmPC for full details before initiating therapy. See contraindications above. ***Do not use:*** voriconazole (unless positive benefit risk ratio).

Not recommended: rifabutin, rifapentine, oxcarbazepine, efavirenz, bosentan, apixaban, rivaroxaban, irinotecan, everolimus, betamethasone, budesonide, fluticasone, mometasone, prednisone, triamcinolone, glecaprevir/pibrentasvir, salmeterol, tadalafil (for pulmonary arterial hypertension), clopidogrel. ***Use with caution:*** systemic dexamethasone, clarithromycin, artemether/lumefantrine, dasatinib, nilotinib, vinblastine, vincristine, sildenafil, vardenafil, tadalafil (erectile dysfunction). ***Therapeutic drug monitoring advised:*** disopyramide, flecainide, mexiletine, propafenone, systemic lidocaine, ciclosporin, sirolimus, tacrolimus. ***Clinical monitoring recommended &/or dose adjustment:*** dabigatran etexilate, edoxaban, alfentanil, digoxin, warfarin (monitor INR), clonazepam, paroxetine, sertraline, amitriptyline, desipramine, imipramine, nortriptyline, trazodone, metformin, clotrimazole, fluconazole, itraconazole, isavuconazole, posaconazole, colchicine (patients with normal renal/hepatic function), fesoterodine, solifenacin, perphenazine, risperidone, thioridazine, carvedilol, metoprolol, timolol, amlodipine, diltiazem, felodipine, nicardipine, nifedipine, verapamil, prednisone, atorvastatin, fluvastatin, pitavastatin, pravastatin, rosuvastatin, methadone, buprenorphine/naloxone, fentanyl, oxycodone, tramadol, buspirone, clorazepate, diazepam, estazolam, flurazepam, parenteral midazolam, zolpidem, hormone replacement therapy (with oestrogen), drospirenone-containing product. ***No dosing recommendations:*** oral contraceptives - alternative or additional contraceptive measures required.
Refer to SmPC for full details of interactions.

LEGAL CATEGORY: POM

PRESENTATIONS, PACK SIZES, MARKETING AUTHORISATION NUMBER(S) & BASIC NHS COSTS

PRESENTATIONS	PACK SIZES	MARKETING AUTHORISATION NUMBER(S)	BASIC NHS COSTS
Bottle	30 tablets	PLGB 00242/0664	£ 672.97

MARKETING AUTHORISATION HOLDER:
Janssen-Cilag Ltd, 50-100 Holmers Farm Way, High Wycombe, Buckinghamshire, HP12 4EG, UK

FURTHER INFORMATION IS AVAILABLE FROM: Janssen-Cilag Limited, 50-100 Holmers Farm Way, High Wycombe, Buckinghamshire, HP12 4EG UK.

Prescribing information last revised: March 2025.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Limited on 01494 567447 or at dsafety@its.jnj.com.