SYMTUZA® (darunavir, cobicistat, emtricitabine, and tenofovir alafenamide)
SYMTUZA - Drug Interactions

SUMMARY

- No drug interaction studies have been performed using the fixed-dose combination product SYMTUZA. Interactions that may occur with SYMTUZA are determined by interactions that have been identified with any of its components.[1]
- SYMTUZA can cause and/or is subject to drug interactions which may be life-threatening or result in lack of efficacy.[1] Please see local prescribing information for a list of contraindicated drugs.
- SYMTUZA should not be administered concomitantly with medicinal products requiring pharmacokinetic enhancing with ritonavir (RTV) or cobicistat (COBI). SYMTUZA should also not be administered concomitantly with medicinal products containing tenofovir disoproxil fumarate (TDF), lamivudine (3TC), or adefovir dipivoxil used for the treatment of HBV infection.[1]
- Darunavir (DRV) is an inhibitor of CYP3A, a weak inhibitor of CYP2D6, and an inhibitor or P-glycoprotein (P-gp).[1]
- COBI is an inhibitor of CYP3A and CYP2D6. COBI inhibits the transporters P-gp, BCRP, MATE1, OATP1B1 and OATP1B3. COBI is not expected to inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9 or CYP2C19. COBI is not expected to induce CYP1A2, CYP3A4, CYP2C9, CYP2C19, uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1), or multidrug resistance protein 1 (MDR1).[1]
- Co-administration of SYMTUZA with medicinal products primarily metabolized by CYP3A and/or CYP2D6 may result in increased plasma concentrations of such medicinal products, which could increase or prolong their therapeutic effect and can be associated with serious and/or life-threatening adverse events. Co-administration of SYMTUZA with drugs that have active metabolite(s) formed by CYP3A may result in reduced plasma concentrations of these active metabolite(s), potentially leading to loss of their therapeutic effect.[1]
- DRV and COBI are metabolized by CYP3A. Drugs that induce CYP3A activity are expected to lower plasma concentrations of DRV and COBI which may lead to loss of efficacy of DRV and development of resistance. Co-administration of SYMTUZA and other medicinal products that inhibit CYP3A may increase plasma concentrations of DRV and COBI.[1]
- Emtricitabine (FTC) is not an inhibitor of human CYP450 enzymes. *In vitro* and clinical drug interaction studies have shown that the potential for CYP-mediated interactions involving FTC with other medicinal products is low.[1]
- FTC is primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion. No drug interactions due to competition for renal excretion have been observed; however, co-administration of FTC with drugs that are eliminated by active tubular secretion may increase concentrations of FTC and/or the co-administered drug. Drugs that decrease renal function may increase concentrations of FTC.[1]
- Tenofovir alafenamide (TAF) is not an inhibitor of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2D6 *in vitro*. It is not an inhibitor or inducer of CYP3A *in vivo*.[1]
- TAF is a substrate of the efflux transporter P-gp. Drugs that induce P-gp activity are expected to decrease the absorption of TAF, resulting in decreased plasma concentrations of TAF, which may lead to loss of therapeutic effect of SYMTUZA and development of resistance. Co-administration of SYMTUZA with drugs that inhibit P-gp may increase the absorption and plasma concentration of TAF.[1]
- Please see local prescribing information for expected or predicted interactions.
    - Expected interactions between SYMTUZA with potential concomitant drugs are based on studies conducted with the components of SYMTUZA, as individual agents or in combination, or are predicted interactions. It should be noted that the interaction profile of DRV depends on whether RTV or COBI was used as pharmacokinetic enhancer; refer to the prescribing information for DRV for further information.[1]

    - SYMTUZA is a complete antiretroviral treatment regimen. Therefore, information regarding drug interactions with other antiretroviral products is not provided.[1]
- The label of each drug that is co-administered with SYMTUZA should be consulted for information related to the route of metabolism, interaction pathways, potential risks, and specific actions to be taken with regards to co-administration.[1]

LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, and DERWENT® (and/or other resources, including internal/external databases) conducted on 25 October 2023 did not identify any relevant literature pertaining to this topic.

REFERENCES

1. Data on File. Darunavir/Cobicistat/Emtricitabine/Tenofovir alafenamide. Company Core Data Sheet. Janssen Research & Development, LLC. EDMS-ERI-119231875; December 2021.