Administration of *Tivicay* via Nasogastric or Gastric Feeding Tubes

Summary

- No pharmacokinetic (PK) or clinical studies have evaluated the administration of *Tivicay* (dolutegravir, [DTG]) film-coated tablets (FCT) or DTG dispersible tablets for oral suspension (DTG PD) via nasogastric or gastric feeding tubes. Additionally, no studies have evaluated adherence of DTG to various types of tubing.
- Based on the physicochemical and PK characteristics of the active ingredient, as well as the *in vitro* dissolution behavior of:[1]
    - DTG FCT in water, DTG FCT may be crushed and added to a small amount of semi-solid food or liquid, all of which should be consumed immediately. Administration of crushed DTG FCT is not expected to have an effect on the absorption of DTG.
    - DTG PD, administration of DTG PD (that has been completely dispersed in water) via nasogastric feeding tube is not expected to have an effect on the absorption of DTG.
- Based on absorption rate analysis modeling, the absorption of DTG is thought to take place predominately in the upper small intestine.[2,3] No PK studies have evaluated the site of absorption of DTG in the gastrointestinal tract.
- DTG can be administered with or without food. Coadministration of DTG with a low-, moderate-, or high-fat meal increased DTG plasma levels (area under the concentration-time curve from 0 to infinity [AUC0–∞]) by 33%, 41%, and 66%, respectively.[4]
- The absorption of DTG is reduced when coadministered with polyvalent cations, including Ca (calcium), Mg (magnesium), Al (aluminum), or Fe (iron).[5] Thus, DTG should be administered 2 hours before or 6 hours after taking medications, enteral nutrition, or antacids containing polyvalent cations. Alternatively, medications, enteral nutrition, or antacids containing polyvalent cations (Ca, Fe, Mg, or Al) can be taken 2 hours after or 6 hours before administration of DTG.
- Important safety information can be found in the Prescribing Information link and can also be accessed at Our HIV Medicines.

To access additional scientific information related to ViiV Healthcare medicines, visit the ViiV US Medical Portal at viivhcmedinfo.com.

The efficacy or safety of crushing DTG FCT or DTG PD prior to oral or nasogastric tube feeding has not been studied. To ensure administration of the entire dose of DTG tablets, the film-coated tablet(s) should ideally be swallowed without crushing. DTG PD should be swallowed whole and should not be chewed, crushed, or cut. DTG PD should be swallowed whole or dispersed in drinking water.

Alternatively, DTG FCT may be crushed and added to a small amount of semi-solid food or liquid, all of which should be consumed immediately.[1] Administration of crushed DTG FCT with a small amount of semi-solid food or liquid is not expected to have an adverse impact on the pharmaceutical quality and would not be expected to alter the clinical effect. Additionally, administration of crushed DTG FCT via nasogastric or gastric tube feeding is not expected to impact the absorption of DTG. These recommendations are based on the physicochemical and PK characteristics of the active ingredient and the *in vitro* dissolution behavior of

DTG tablets in water, assuming that the patient crushes and transfers 100% of the tablets and ingests immediately.

DTG PD should not be chewed, cut, or crushed; these tablets should be swallowed whole or completely dispersed in clean drinking water.[6] Administration of DTG PD that has been dispersed in water is not expected to have an adverse impact on the pharmaceutical quality and would not be expected to alter the clinical effect. Additionally, administration of DTG PD that is completely dispersed in water via nasogastric or gastric tube feeding is not expected to impact the absorption of DTG.[6] These recommendations are based on the physicochemical and PK characteristics of the active ingredient and the *in vitro* dissolution behavior of DTG PD in water.

Based on absorption rate analysis modeling, the absorption of DTG is thought to take place predominately in the upper small intestine.[2,3] Absorption rate analysis was performed using PK data from subjects receiving DTG during bioavailability studies. Absorption rate profiles were calculated from individual plasma time-concentration data.

A two-part, randomized, open-label, crossover, PK study evaluated coadministration of DTG with a low-fat (300 calories, 7% fat), moderate-fat (600 calories, 30% fat), or high-fat (870 calories, 53% fat) meal.[4] Coadministration of DTG with a low-, moderate-, or high-fat meal increased DTG plasma levels ($AUC_{0-\infty}$) by 33%, 41%, and 66%, respectively.

In a randomized, open-label, four-period, crossover, PK study, coadministration of a single dose of DTG with either 1200 mg of calcium carbonate or 324 mg of ferrous fumarate under fasted conditions resulted in a reduction in plasma DTG exposure by approximately 37 to 39% with calcium carbonate, and 54 to 57% with ferrous fumerate, compared to DTG 50 mg alone.[5] Under fed conditions, coadministration of a single dose of DTG with calcium carbonate or ferrous fumarate resulted in plasma exposures comparable to DTG alone under fasted conditions, or DTG given 2 hours prior to calcium or iron in the fasted state.

OTHER RELEVANT STUDIES

Additional case reports have been included in the references section for your review.[7-9]

Some information contained in this response may not be included in the approved Prescribing Information. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labeling. Please note that reports of adverse events in the published literature often lack causality assessments and may contain incomplete information; therefore, conclusions about conclusions about causality generally cannot be drawn.

In order for ViiV Healthcare to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 877–844–8872. Please consult the Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

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