ORAL ANTIRETROVIRAL/HCV DAA ADMINISTRATION: INFORMATION ON CRUSHING AND LIQUID DRUG FORMULATIONS

Drug	Oral Liquid Preparation			Case Reports/Clinical Compounding	Information on Crushing or Splitting Tablets
	Commercial Oral Liquid Available?	Formulation	Stability		
Combination Products:					
Atripla® (efavirenz/ emtricitabine/ tenofovir DF)	no	Consider use of Truvada® tabs and efavirenz caps as alternate formulations (see separate entries)		Atripla® tablet was **crushed, dissolved in 5 mL of water and diluted to 20 mL with Ora-Sweet** oral vehicle. The solution was prepared within 24 hours of administration to ensure drug stability in solution. Bioequivalence of Atripla® tablet and compounded oral liquid formulation (above) in HIV-negative volunteers was **not** demonstrated. The 90% CI for FTC Cmax and AUC fell within the range of 0.8-1.25 thus, bioequivalence was met, but the 90% CI for efavirenz Cmax fell below the range of bioequivalence while efavirenz AUC∞ fell slightly above the range and tenofovir Cmax and AUC∞ fell above the range. Tenofovir Cmax and AUC∞ were approximately 40% and 20% higher, respectively with the liquid formulation. The clinical implications of these data are unknown, however the authors state that crushed Atripla® may be a viable option in certain patients and risks vs.	See information on crushing Atripla® in the Case Reports section. Although Truvada® tablets may be split, splitting Atripla® tablets has not been studied. There are no studies evaluating the pharmacokinetics of a split tablet vs. a whole tablet. Efavirenz is not water soluble.

		benefits should be carefully considered. (King et al. JAIDS 2011;56(5):e131-2.)	
Biktarvy® (bictegravir/ emtricitabine/ tenofovir alafenamide)	no	In a single-centre, retrospective review of 19 patients who received either crushed/dissolved B/F/TAF via enteral tube for at least 1 week (median 19 days), 17 (89%) remained/achieved viral suppression within 1 year of follow-up; 2 participants who did not meet the endpoint were either lost to care or deceased. (Mercure et al. OFID 2025;12(10):ofaf588.) Case reports of dissolving B/F/TAF: A virally suppressed, 52 year old female was switched to bictegravir/emtricitabine/tenofovir alafenamide. The patient self-administered by **dissolving each Biktarvy® tablet in a tablespoon of orange juice for 10 minutes, then swallowing** the mixture. At one year follow-up, viral load suppression was maintained. (Sanchez-Rubio Ferrandez et al. Ann Pharmacother 2021;55:556-7). Case reports of crushing B/F/TAF: A 78 year old male with pancreatic cancer, virally suppressed on RPV/F/TDF was switched to B/F/TAF to avoid PPI interactions. Due to	**Dissolving tablet in water is preferred over crushing the tablet**. In a phase 1 bioequivalence study in adult participants, the bioavailability of B/F/TAF when dissolved in water or crushed in applesauce compared to the solid tablet. Dissolving B/F/TAF fulfilled all but one (lower bound of 90% CI of TAF Cmax) criteria for bioequivalence, whereas the crushed tablet did not, primarily due to reducted F/TAF bioavailability. (Hocqueloux et al. J Antimicrob Chemother 2022;78:161-8). By visual inspection, when a Biktarvy tablet was submerged in orange juice (pH 4), the film coating disappeared after 4 minutes, and the tablet was easily disintegrated after 14 minutes without agitation. (Sanchez-Rubio Ferrandez et al. Ann Pharmacother 2021;55:556-7).

		dysphagia, B/F/TAF was crushed, diluted in 30-60 mL water and administered via PEG tube. Viral suppression was maintained. (Roa & Bazzi. Int J STD AIDS 2022;33:97-8.) A 64 year-old male with HIV suppressed on dolutegravir/abacavir/ lamivudine was diagnosed with esophageal cancer and significant dysphagia. Therapy was changed to crushed Biktarvy® tablets for a smaller tablet size. The patient opted to **crush the tablet and dilute in 30-60 mL of water, then administer via the PEG tube**, immediately followed by 240 mL of enteral formula (Jevity 1.2). The viral load remained undetectable during 10 months of cancer therapy. The patient was able to resume oral therapy after. (Fulco PP et al. Am J Health-Syst Pharm 2020;77(7):509-10.) A 39 year-old woman who was antiretroviral experienced and lost to follow-up presented with cerebral toxoplasmosis and was undergoing treatment. Biktarvy® was started with an adequate 4-week virologic response (decreased from 1,023,292 to 1,084 copies/mL). After 2 months, the patient`s condition progressed with acute neurologic deterioration, right hemiparesis and dysphagia due	

			to progressive multifocal leukoencephalopathy. The patient received nasogastric (NG) feeds and **Biktarvy® was crushed and administered as a solution via the NG tube** x 6 weeks. After 12 weeks of starting Biktarvy® therapy, the viral load was 10,232 copies/mL and resistance testing showed several mutations (M184V,L74I and R263K). Therapy was switched to tenofovir alafenamide, emtricitabine and darunavir/ritonavir with only partial response (viral load 204 copies/mL). It is unknown whether Biktarvy® failure was due to past exposure with possible failure to other ARVs (lopinavir/ritonavir, tenofovir DF, emtricitabine, abacavir, raltegravir) vs. NG administration of crushed tablets. (Lozano AB et al. Antiviral Res 2020 Jan 23 [Epub ahead of print].)	
Combivir® (lamivudine/ zidovudine)	yes (individual components)	Use lamivudine & zidovudine liquid products		No data, but likely OK to crush tablets (film-coated); crush immediately before ingestion. May have bitter taste. Tablets can be crushed and added to small amount of liquid or semi-solid food; consume immediately. (Duggan et al. Am J Health-Syst Pharm. 2015; 72:1555-65.)

Complera® (tenofovir DF/ emtricitabine/ rilpivirine)	no			Splitting or crushing Complera® tablets into a liquid medium has not been studied and is not recommended. Rilpivirine hydrochloride is insoluble in water over a wide pH range. (Email communication, Gilead July 2012).
Descovy® (tenofovir AF emtricitabine)	no		Case report of successful administration of **crushed** tenofovir AF/emtricitabine and dolutegravir tablets, **mixed with water and injection via catheter syringe into percutaneous endoscopic gastrotomy (PEG) tube, immediately followed by a can of enteral nutrition (Ensure).** (Fulco & Higginson, AJHP 2018;75:594-5.)	Crushing or splitting Descovy® tablets has not been studied and is not recommended. TAF is soluble in water. However, it has a bitter and burnt aromatic flavor profile. Emtricitabine is soluble in water. (Email communication, Gilead January 2017; updated April 2020).
Delstrigo® (doravirine/ lamivudine/ tenofovir DF)	yes	Only lamivudine liquid available		Crushing or splitting Delstrigo® has not been studied and is not recommended. The product should be swallowed whole. The tablets are film-coated (e-mail communication Merck Canada Inc, September 2018).
Dovato® (dolutegravir/ lamivudine)	yes	Only lamivudine liquid available		The manufacturer recommends swallowing the tablet whole. The tablets are film-coated. For patients who cannot swallow the tablet who, in theory, the tablet may be split in halves or crushed and added to a small amount of semi-solid food or liquid and the full contents consumed immediately (e-mail communication, ViiV Healthcare, Med US, March 2019).

Evotaz® (atazanavir/ cobicistat)	no		The manufacturer recommends swallowing the tablet whole; do not crush or chew tablets (Evotaz Product Monograph, Sept 2015).
Genvoya® (elvitegravir/ cobicistat/ tenofovir AF/ emtricitabine)	no	A cancer patient received Genvoya® via a percutaneous gastrostomy tube. The tablet was **crushed (pulverized), mixed with 30 mL of tap water, and administered via a syringe followed by 2 x 250 mL cans of enteral feeds (Diabetisource AC).** At week 14, the viral load was < 20 copies/mL. The patient died of metastatic cancer within 15 weeks of starting crushed Genvoya®. (Kaplun et al. Am J Health-Syst Pharm 2019;76(16):1180-81.) See case reports for Stribild®.	In 12 healthy volunteers who took E/C/F/TAF as a single whole dose and dissolved E/C/F/TAF in 120 mL tap water, bioequivalence was established for FTC. EVG Cmax and AUC were higher by 18% and 12%, respectively, TAF and tenofovir AUC and Cmax were 5-8% lower with dissolved vs intact tablet. These differences are not considered clinically relevant. E/C/F/TAF dissolved rapidly in water and had no unpleasant taste. Dissolving E/C/F/TAF in water may be suitable for those with difficulty swallowing pills.(Andrade et al. AIDS Res Hum Retr 2023;39:38-43.).
Juluca® (dolutegravir/ rilpivirine)	no		The efficacy, safety and pharmacokinetics of crushing dolutegravir/rilpivirine have not been evaluated. The tablet should be swallowed whole and taken with a meal to ensure administration of the entire dose. The tablets are film-coated. Based on clinical judgment if the Juluca® tablet requires splitting, it should be split in half and both halves ingested immediately with a meal. If the

				Juluca® tablet requires crushing, it should be crushed and added to a small amount of liquid or semi-solid food and the full tablet content consumed immediately with a meal. (Data on File, ViiV Healthcare, May 2018)
Kivexa® (abacavir/ lamivudine)	yes (individual components)	Use abacavir & lamivudine liquid products		Film-coated immediate release tablet; however, no studies regarding stability of split or crushed tablets. (Email communication, GlaxoSmithKline, May 2008) Tablet may be split or crushed and added to a small amount of food or water. (European Medicines Agency, EPAR summary for the public, Ziagen updated 05-2010)
Odefsey® (tenofovir AF/ emtricitabine/ rilpivirine)	no			Crushing or splitting Odefsey® tablets has not been studied and is not recommended. TAF is soluble in water. However, it has a bitter and burnt aromatic flavour profile. Rilpivirine hydrochloride is insoluble in water over a wide pH range. (Email communication, Gilead January 2017).
Prezcobix® (darunavir/ cobicistat)	no	See darunavir and ritonavir for other liquid options (substitution of cobicistat with ritonavir may be required)	The chemical stability of crushed Prezcobix (2 tablets crushed and suspended in 20 mL Syrspend® and 1% w/v CMC solution) was evaluated. Darunavir and cobicistat remained within ±20% of the initial value for 7 days when stored at 4C and at room temperature (~25C).(Zanon et al. Data Brief 2020	Splitting Prezcobix® film-coated tablets has not been studied. Tablets should be swallowed whole without breaking or crushing to ensure administration of the entire dose. (Prezcobix® Product Monograph, 2014) Tablets are immediate-release formulation; no anticipated absorption issues if the tablets

		Jun;30:105552).	are chewed, split or crushed. (Huesgen et al. Pharmacother 2016;36(11):1145-65.)
Stribild® (elvitegravir/ cobicistat/ emtricitabine/ tenofovir)	no	Case report describing successful virological suppression with **crushed Stribild® in juice** (Fulco et al. AJHP 2014;71(10);784-6.)	Pharmacokinetics of crushed Stribild® tablets were studied in healthy volunteers. Whole tablets with breakfast were compared to: I. Crushed and suspended with breakfast II. Crushed and suspended with enteral nutrition (Nutrison®). The groups were shown to be bioequivalent for elvitegravir, tenofovir and emtricitabine. Elvitegravir Cmax failed to fall within bioequivalence range (100-120%), but this difference is unlikely to be clinically significant. Cobicistat AUC was reduced by 10% for intervention I only. (Jongbloed-de Hoon et al. JAIDS. 2017;74(5):571-574.)
Symtuza® (darunavir/ cobicistat/ emtricitabine/ tenofovir alafenamide)			Symtuza® should be swallowed whole. The manufacturer does not recommend breaking or crushing Symtuza® to ensure administration of the entire dose. Film-coated tablets. The relative bioavailability of darunavir/cobicistat/ emtricitabine/tenofovir alafenamide (D/C/F/TAF) single tablet regimen was compared with the tablet administered whole, split or crushed. In the split group there was an 11% decrease in TAF Cmax only (not clinically relevant). In the

				crushed group there was a 17% decrease in the emtricitabine Cmax and TAF Cmax and AUC were decreased by 29% and 18%, respectively (clinical relevance not assessed, but impact expected to be minimal based on wide therapeutic window for TAF). (Brown K et al. Clin Pharmacol Drug Dev 2019;8(4):541-48.)
Triumeq® (abacavir/ lamivudine/ dolutegravir (DTG))	no	Use abacavir & lamivudine liquid products. Dolutegravir tablets may be crushed (see dolutegravir). See Crushing &Splitting section also.	Case report of successful administration of **crushed dolutegravir/abacavir/lamivudine tablet with administration via NG tube**; adequate antiretroviral concentrations confirmed via TDM and patient achieved rapid viral suppression. (Chrdle et al. Int J STD AIDS 2019;30(1):94-8.) Case report of a 44 year-old female who presented for a heart and lung transplant who received **crushed Triumeq® via nasogastric (NG) tube** while on veno-arterial extracorporeal membrane oxygenation (VA ECMO). ARV pharmacokinetics were conducted during and post VA ECMO. The Cmax and AUC were higher for all 3 ARVs during ECMO vs. post-decannulation. ARV dose adjustments were not made and virologic suppression was maintained during 50-day hospitalization. (Blackman et al. Antiviral Ther 2020 Apr 28	Triumeq® is film-coated, non-scored, and non-sustained released formulation. Although not studied, splitting or crushing tablets is not expected to affect the dissolution or absorption. Tablets may be crushed and added to a small amount of semi-solid food or liquid, and consumed immediately. (Data on File, ViiV Healthcare, Oct 2014) **Nasogastric or gastric feeding tubes:** No clinical or pharmacokinetic studies done to evaluate. The administration of crushed Triumeq® tablets should not have an effect on the absorption of the components of Triumeq®. The absorption of Triumeq® is thought to occur in the proximal small intestine (duodenum/jejunum). (Data on File, ViiV Healthcare, March 2017) Pharmacokinetics of crushed Triumeq® tablets were studied in healthy volunteers. Whole tablets in fasting state were compared to:

			[Epub ahead of print].)	I. Crushed and suspended in fasting state II. Crushed and suspended with enteral nutrition taken PO (Nutrison®-250 mL contains elemental calcium 200 mg, iron 4 mg, protein 10 g, carbohydrates 30.8 g, fat 9.8 g). Intervention I showed 26% and 30% increase in DTG AUC and Cmax. Intervention II showed an 18 % and 21 % increase in DTG AUC and Cmax, respectively. Although bio-equivalence was not demonstrated, the increase in DTG exposure was not considered to be clinically relevant. However, caution is warranted if crushed DTG is given once daily or BID with food, as DTG exposure will likely be higher. (Roskam-Kwint et al. JAC 2018;73:2430-4.)
Trizivir® (abacavir/ lamivudine/ zidovudine)	yes (individual components)	Use abacavir, lamivudine & zidovudine liquid products.		Film coated immediate release tablet however no studies regarding stability of split or crushed tablets.
Truvada® (tenofovir/ emtricitabine)	yes (individual components-US only)	See tenofovir & emtricitabine.	The absorption of raltegravir, etravirine, emtricitabine, and tenofovir was not compromised when the drugs were **crushed, dissolved in 60 mL warm water, and administered by gastrostomy tube** to a 52 year old HIV-positive male with ulcerative esophagitis. (Sandkovsky et al. Pharmacother 2012;32(2):142-7.)	May split tablets. May crush and stir into water, grape juice or orange juice. The stability of the mixture is unknown. (Email communication, Gilead, July 2012). Case where patient chewed TDF/FTC tablets (for PrEP) due to swallowing difficulties. Monthly urine samples indicated tenofovir concentrations >1000

		Case report of complex HIV patient with MAC with intractable nausea/vomiting requiring ARVs (tenofovir DF 300 mg/emtricitabine 200 mg as Truvada® and dolutegravir 50 mg daily) via jejunostomy (J)-tube. ARVs were **crushed, mixed with 3-5 mL or water, administered, and flushed with 10 mL of water**. Concentrations of oral and J-tube administration of ARVs were assessed. DTG and TDF exposures were similar between J-tube and oral administration. FTC AUC was 38% lower for J-tube vs. oral. Compared to a reference population, overall AUC was lower for both routes- DTG 75-76% lower and TDF 55-61% lower. However, FTC via J-tube AUC was similar to the reference population and 71% higher when given orally. Reduced drug absorption was the primary cause for decreased drug exposure. TDM is recommended to assess drug concentrations in patients with the potential for impaired absorption (Brooks et al. Pharmacother 2017;37:e82-9.) Case report of an HIV patient with difficulty swallowing pills who preferred ARV formulations that he could crush. Tenofovir DF-emtricitabine (Truvada®) 1 tab daily and dolutegravir 50 mg daily were **crushed using a pill**	ng/mL, indicative of protection from HIV acquisition. (Lalley-Chareczko et al. Antivir Ther 2017;22:639-41.)

		crusher, added to applesauce, and consumed immediately. The 4- week viral load decreased from 10,800 to < 20 copies/mL (Buscemi L. Am J Health-Syst Pharm 2016;73(15):1125-26.) Case report of a 22 year-old male with difficulty swallowing tenofovir DF-emtricitabine (Truvada®) for pre-exposure prophylaxis (PrEP) **chewed the whole tablets**. Monthly urine samples showed tenofovir concentrations > 1000 ng/mL (protective level). Plasma samples collected at weeks 24 and 48 showed tenofovir concentrations > 10 ng/mL (also protective). (Lalley-Chareczko et al. Antivir Ther 2017;22(7):639-641.) Case report of a 20 year-old male with acute-chronic inflammatory demyelinating polyneuropathy (IDP) who was successfully treated for HIV with **crushed ARVs (Truvada (tenofovir DF-emtricitabine + raltegravir) administered via gastrojejunostomy tube**. The viral load decreased from 100,123 copies/mL to < 20 after two weeks of ARVs. The patient was also undergoing plasmapheresis and ARVs were administered after the plasmapheresis sessions. (Lindholm et al. J AIDS Clin Res	

				2013;4(12):1-7.)	
INDIVIDUAL ANTIRETROVIRAL AGENTS:					
abacavir	yes	20 mg/mL oral solution; 240 mL bottle. Yellow, strawberry-banana flavoured liquid. Contains sorbitol 340 mg/mL (E-mail communication, ViiV, April 2017)	Store oral solution at room temperature.		Tablet is film-coated. Tablet can be crushed and added to a small amount of liquid or semi-solid food; consume immediately (Duggan et al. Am J Health-Syst Pharm. 2015; 72:1555-65.)
amprenavir	no-product discontinued	See fosamprenavir for liquid formulation.			
atazanavir	yes (US only)	50 mg/1.5 g dispersible oral powder packet	**Powder:** mix with food such as applesauce or yogurt (1 TBSP minimum). Mixing with a beverage (milk, formula, water-30 mL + additional 15 mL after to consume residual drug) can be used if infant is able to drink from a cup. For younger infants who cannot eat solid food, mix with infant formula (10 mL + additional 10 mL after to consume	**Capsules**: In an open label, multicentre study of atazanavir and atazanavir/ritonavir in children 91 days-21 years, the pharmacokinetics of atazanavir capsules and atazanavir orange-vanilla flavoured powder were studied. Day 7 atazanavir kinetics were compared in children of similar age receiving powder vs. capsules; the powder was found to be 40% less bioavailable at the same BSA-based dose. Therefore, suggest converting from powder to capsule by multiplying the powder dose by 0.6 and rounding up to the nearest 50 mg. (Kiser J et al. AIDS 2011;25:1489-96.)	**Capsules:** May be opened and the contents mixed with applesauce for immediate ingestion with a light meal. In-house study showed that the bioavailability of the contents of two 200-mg atazanavir capsules mixed with applesauce was 91.7% relative to atazanavir capsules taken intact. In addition, administration of the contents of two 200-mg capsules was well tolerated (Bristol Myers Squibb, Personal Communication, November 20, 2015).

			residual drug) and administer via oral syringe. Stable for 1 hour at room temperature once mixed in food or beverage. (Refer to Reyataz® US Product Monograph for additional information on mixing/administration).		
cabotegravir	no				For patients who cannot swallow, or have difficulty swallowing tablets whole, cabotegravir tablets may be split into halves immediately prior to administration. Additionally, cabotegravir tablets may be carefully crushed and added to a small amount of semi-solid food or liquid, all of which should be consumed immediately (ViiV, February 2023).
darunavir	yes- compassionate access through Janssen Canada (call Janssen Medical Information at 1-800-567-3331 or submit Compassionate Use form posted	100 mg/mL oral suspension	Store oral suspension at room temperature. Shake well before use.	In two patients, one with dysphagia and Candida esophagitis and one with a stomach tube, who received darunavir tablets **crushed and dissolved and administered with ritonavir oral solution**, adequate plasma darunavir levels were achieved along with good virologic response.(Scholten et al. J Int AIDS Soc 2010;13(Suppl	No pharmacokinetic data are available on chewing or crushing of Prezista® film-coated tablets. However, since the tablets are not formulated as an extended release formulation, no potential problem is anticipated if the tablets are chewed or crushed for administration through a nasogastric (NG) tube. It is unlikely that chewing or

	on website https://www.janssenmedicalinformation.ca/login?destination=compassionate-use; updated Feb 2020) Available in US	4):P114.) A case report describes an intubated 44 year-old man on tenofovir/emtricitabine, darunavir, and ritonavir in ICU who was given darunavir tablets via **orogastric tube crushed and dissolved in 15-20mls of water**. Viral load did not change significantly and adequate darunavir trough levels were achieved. (Kim et al. CJHP 2014;67(1):39-42.) An HIV-positive patient on continuous venovenous hemodiafiltration (CVVHDF) received raltegravir 400 mg BID, darunavir 600/100 mg BID, zidovudine 300 mg BID and 3TC 50 mg q24h in **suspension via gastric port** and simultaneous enteral feeding via the duodenal port of a double-lumen nasogastroduodenal tube. Pharmacokinetic sampling and analysis indicated that darunavir and raltegravir were removed by CVVHDF with approximately the same clearance as provided by a normally functioning kidney. **Absorption of both darunavir and raltegravir after suspension and application via the gastric port with continued administration of feed via the duodenal port of the double-lumen tube was good.** As such, dose adjustments are not required for patients receiving darunavir	crushing Prezista® tablets would have a significant impact on pharmacokinetics (Data on File, Tibotec, November 2006).

				and/or raltegravir while undergoing CVVHDF and that absorption of darunavir and raltegravir is not significantly affected by postpyloric enteral feeding. (Taegtmeyer et al. AIDS 2011;25(10):1339-41.)	
delavirdine	no				Can dissolve 100 mg tablets in water to make slurry (20% ↑ bioavailability). Disperse tablets in at least 90 mL of water, allow to stand for a few minutes, stir and consume.
didanosine (ddI)	no Note: Canada-product was discontinued May 2019 by manufacturer and is no longer available via SAP; no longer available in US	Note: Product is discontinued. 4 g oral powder (pediatric solution); 10 mg/mL final concentration. Take on an empty stomach. Do not give with fruit juices or acidic drinks, feeds or milk. Chew Tablets discontinued (Canada and US)	30 days	Note: Product is discontinued. Reconstitute with commercially available antacid that contains as active ingredients aluminum hydroxide (400 mg per 5 mL), magnesium hydroxide (400 mg per 5 mL), and simethicone (40 mg per 5 mL)) If above strength not available, reconstitute with similar antacid of ½ strength using these alternative instructions: Add 400 mL of antacid in two, 200 mL portions, shaking the contents after each addition of 200 mL. The admixture may be dispensed in flint-glass or plastic bottles. Shake well before using. Stable for 30 days in fridge.	
dolutegravir	5 mg dispersible tablet for oral suspension (licensed in US).	Pediatric film-coated tablets (10, 25 mg)	After full dispersion, administer the oral suspension within 30 minutes of	In comparison to the commercially available tablet, dolutegravir exposures following administration of the granule formulation alone, with different types of water and with formula	10, 25 and 50 mg tablets should ideally be swallowed whole. All tablet strengths may also be split into halves followed by immediate ingestion of both halves or crushed and added to

	Two neonatal liquid formulations in development (5 mg/mL suspension in miglyol, and 2 mg/mL solution in glycerol). In an open label pharmacokinetic study in healthy adults, bioavailability for both formulations was comparable to the dolutegravir dispersible tablet formulation with marginally higher Cmax for the 2 mg/mL solution. Both formulations were well tolerated. (Singh et al. Int Workshop Clinical Pharmacol HIV Hep Antivirals 2020 Sep 28-30, abstract 8).	mixing.	exceeded that of the tablet, demonstrating the dolutegravir oral granule can be given without restriction on the type of liquid, or can be administered directly to mouth (e.g., when potable water is not available). (Patel et al. Antivir Ther 2014;19(3):229-33.) Case report of a critically ill patient with lymphoma requiring enteral administration of ARVs. Both abacavir and 3TC solutions were administered enterally. Crushed **dolutegravir 50 mg BID** (separated from enteral nutrition by 2 hours) and rilpivirine 25 mg daily (given with a 240-mL bolus of an enteral formula (2 kcal/mL)) were administered via orogastric tube. Crushed tablets were each mixed with 10 mL of water and flushed down the tube at separate administration times. Trough concentrations were: day 8, rilpivirine 30 ng/mL (reference range 40-120 ng/mL), and day 9, dolutegravir 820 ng/mL (reference range 830 ng/mL steady-state trough concentration for 50 mg once daily dose). Virologic suppression was maintained after ARV enteral administration (hospital day 29). Given somewhat decreased levels of these ARVs, the authors recommended consideration to increase dolutegravir to 150-200 mg total daily dose,	a small amount of semi-solid food or liquid, all of which should be consumed immediately. (ViiV Healthcare communication, February 2017) Tivicay PD (dispersible tablets for oral suspension): • Administer with or without food • Do not chew, cut or crush tablets • Swallow the tablets for oral suspension whole (if more than one tablet is required, swallow one tablet at a time to reduce the risk of choking), or • Fully disperse the tablets for oral suspension in 5 mL of drinking water (if using 1 or 3 tablets for oral suspension) or 10 mL (if using 4, 5, or 6 tablets for oral suspension) in the supplied cup; swirl the suspension so that no lumps remain. After full dispersion, administer the oral suspension within 30 minutes of mixing. See Triumeq® for additional information.

		particularly in integrase-experienced patients, and rilpivirine 50 mg daily (similar to dosing with an inducer such as rifabutin). (Turley et al. JIAPAC 2017;16(2):117-119.) Case report of complex HIV patient with MAC with intractable nausea/vomiting requiring ARVs (tenofovir DF 300 mg/emtricitabine 200 mg as Truvada® and **dolutegravir 50 mg daily)** via jejunostomy (J)-tube. ARVs were crushed, mixed with 3-5 mL or water, administered, and flushed with 10 mL of water. Concentrations of oral and J-tube administration of ARVs were assessed. DTG and TDF exposures were similar between J-tube and oral administration. FTC AUC was 38% lower for J-tube vs. oral. Compared to a reference population, overall AUC was lower for both routes- DTG 75-76% lower and TDF 55-61% lower. However, FTC via J-tube AUC was similar to the reference population and 71% higher when given orally. Reduced drug absorption was the primary cause for decreased drug exposure. TDM is recommended to assess drug concentrations in patients with the potential for impaired absorption (Brooks et al. Pharmacother 2017;37:e82-9.)	

		Case report of an HIV patient with difficulty swallowing pills who preferred ARV formulations that he could crush. Tenofovir DF-emtricitabine (Truvada®) 1 tab daily and **dolutegravir 50 mg daily** were crushed using a pill crusher, added to applesauce, and consumed immediately. The 4- week viral load decreased from 10,800 to < 20 copies/mL (Buscemi L. Am J Health-Syst Pharm 2016;73(15):1125-26.) Case report of a male with HIV and antiretroviral experienced with resistance mutations (K101E, M184V, M230L, A98G, L10I, E35D and M36I) with dysphagia due to eosinophilic esophagitis was successfully treated with crushed dolutegravir, crushed tenofovir AF (TAF), and liquid abacavir and emtricitabine. The viral load was suppressed after 10 months of follow-up. The patient was intolerant of crushed tenofovir DF (TDF) due to taste and nausea but tolerated crushed TAF. (Moore SE et al. Int J STD AIDS 2020;31(3):285-287.)	
doravirine	no	Case report describing administration of doravirine crushed and mixed with 60 mL warm water and administered via nasojejenunal tube, along with crushed dolutegravir and liquid lamivudine. Viral suppression was maintained.	Crushing or splitting Pifeltro® has not been studied and is not recommended. The product should be swallowed whole. The tablets are film coated (e-mail communication Merck Canada, Inc, September 2018).

			(Porter et al. J Pharm Pract 2022 May 24;8971900221104258. doi: 10.1177/08971900221104258)	
efavirenz	no Note: pediatric suspension is no longer available internationally (2014)	30 mg/mL; 180 mL bottle- not available Consider use of capsule formulation as described in Clinical Compounding	**Tablets**: A pediatric pharmacokinetic intensive study that utilized weight band dosing and a combination of capsules or half of a 600 mg tablet reported low overall plasma efavirenz concentrations in both groups (higher doses need to be investigated). They found no significant differences across weight bands, suggesting no discernible effect of using half tablets. (Fillekes et al. JAIDS 2011;58(4):392-8.) **Capsules:** may be opened and added to 1-2 tsp of liquids or foods (e.g. applesauce, grape jelly, yogurt, reconstituted infant formula at room temperature) but may result in peppery taste. Grape jelly may mask taste. Specific instructions: (Kaul et al. AJHP 2010;67(3):217-22.) 1. Hold the capsule horizontally over a small container and twist open to avoid spillage. 2. Pull the capsule away from the body of the capsule carefully, sprinkle and mix the contents with 1-2 tsp of food or formula. 3. Administer the mixture with a spoon as soon as possible but no more than 30 minutes after mixing. 4. After administration of the efavirenz–food mixture, an	Splitting efavirenz tablets has not been well studied. With the exception of the study by (Fillekes et al. JAIDS 2011;58(4):392-8.), there are no well controlled pharmacokinetic studies evaluating a split tablet vs. a whole tablet. Efavirenz is not water soluble. The use of the capsule formulation is preferred when possible. (see Case Reports/Clinical Compounding)

				additional 2 tsp of food or infant formula must be added to the container, stirred, and given to the patient. For nasogastric administration, may open **capsules** and mix with either 5 mL MCT oil or 15 mL Ora-Sweet/any aqueous vehicle (grind powder first to enhance dissolution). Do NOT mix with polyethylene glycol (will ↓ bioavailability). Splitting **tablets** is not recommended (Email communication, Bristol-Myers Squibb, June 1, 2011).	
elvitegravir	no			Case report describing successful virological suppression with crushed Stribild® in juice (Fulco et al. AJHP 2014 71(10);784-6.)	Crushing or splitting Genvoya® tablets has not been studied and is not recommended. While emtricitabine and TAF are soluble in water, cobicistat and elvitegravir are practically insoluble in water. See Genvoya® for more information. (Communication from Gilead Canada, March 2016). See Stribild® for more information.
emtricitabine (FTC)	no (US only)	10 mg/mL oral solution	Store oral solution refrigerated; stable for 3 mos at room temperature.		200 mg capsules may be opened and mixed with water.
etravirine	no	See Crushing and Splitting section for dispersion information.	Consume immediately.	The absorption of raltegravir, etravirine, emtricitabine, and tenofovir was not compromised when the drugs were crushed, dissolved in 60 mL warm water, and administered by gastrostomy tube to a 52 year old HIV-positive male with	Patients who are unable to swallow etravirine tablets whole may disperse the tablets in a glass of water. A bioavailability study has shown that the PK of etravirine tablets when swallowed whole and when taken after dispersion in a glass

				ulcerative esophagitis. (Sandkovsky et al. Pharmacother 2012;32(2):142-7.)	of water are comparable. Both the 100 mg and 200 mg tablet formulations of etravirine may be dispersed in water (Kakuda et al. Int J Clin Pharmacol Ther 2013;51(9):725-37.) Place the tablet in 5 mL of cold water or at least enough liquid to cover the medication. Stir until a homogenous, white, cloudy, suspension is obtained. If desired, add more water or alternatively orange juice or milk. Once dispersed, patients should stir the dispersion well and drink it immediately. The glass should be rinsed with water, orange juice or milk several times and each rinse completely swallowed to ensure the entire dose is consumed. Avoid the use of grapefruit juice, warm liquids (> 40°C) or carbonated beverages. (Intelence® Product Monograph, 2014).
fosamprenavir	yes	50 mg/mL oral suspension, 225 mL bottle. 0.6% propylene glycol Grape bubblegum and peppermint flavour. In adults, oral suspension should be taken on an empty stomach (1 hr before or 2 hours after food). In	Store oral suspension between 2-30°C. Do not freeze. Discard the suspension 28 days after first opening.		No information on crushing or dissolution of 700 mg tablets. Fosamprenavir calcium tablets and suspension are equivalent on a mg per mg basis.

		pediatric patients, oral suspension should be given with food.			
indinavir	no			10 mg/mL indinavir syrup complex compounding formulation. Stable for 14 days in refrigerator, store in glass bottle. (Hugen et al. AJHP 2000; 57(14):1332-9.)	Do NOT open capsules (bitter taste; stability uncertain).
lamivudine (3TC)	yes	10 mg/mL oral solution; 240 mL bottle. Pale yellow, strawberry-banana flavoured solution); (NB: contains 6% v/v ETOH & 3g sugar). Does not contain sorbitol.	Store at room temperature.		Can also crush or split tablets. Pharmacokinetic study in adults on co-administration of 3TC 300 mg and sorbitol solution (low (3.2 g), medium (10.2 g) and high (13.4 g) sorbitol doses) given with 240 mL water in the fasting state. A dose-dependent decrease in 3TC exposure was seen and is likely due to decreased absorption and bioavailability of 3TC (accelerated small intestinal transit time mediated by sorbitol). Higher doses of sorbitol resulted in lower 3TC concentrations (decreased $AUC_{0-\infty}$ by 14%, 32%, and 36%, respectively). Caution is warranted with chronic administration of 3TC solution and other liquid drugs containing sorbitol (e.g. abacavir, nevirapine, cotrimoxazole). (Adkison et al. Clin Pharmacol Ther 2018;103:402-8.) In addition, in pediatric patients, ensure lamivudine dose is optimized based on weight.(Choi et al. Clin Pharmacol Ther

			2018;104:785-7.)
lenacapavir	no	Administration via nasogastric (NG) tube: There are currently no known published clinical data or patient outcomes regarding the administration of LEN tablets via NG tube: the safety and efficacy of administering LEN via NG tube have not been established. An in vitro feasibility study of LEN tablet administration via NG tube conducted at Gilead Sciences demonstrated that the physical passage of a LEN tablet suspension through NG tubes of various sizes is possible under laboratory conditions. One 300 mg LEN tablet was dispersed in 120 mL deionized water and stirred for up to 18 minutes. The resulting suspension was passed through nasogastric tubes of sizes 5 Fr, 8 Fr, and 12 Fr (1 Fr = 0.33 mm diameter) using a syringe. The suspension passed through all tube sizes, with no pressure build-up or obstruction. Additional rinsing and passage of remaining material passed through the tube without incident. [Gilead Sciences Inc. Data on file]. This in vitro feasibility study found that LEN tablets can be suspended in water and physically administered through NG tubes of 5 Fr, 8 Fr, and 12 Fr sizes without incident. The information provided is not	Lenacapavir is practically insoluble in water. Crushing lenacapavir tablets and adding into a liquid medium has not been studied and is not recommended. Currently, there are no studies evaluating the oral bioavailability of a crushed lenacapavir tablet dispersed into a liquid medium (eg, milk, water, juice) compared to a whole tablet. Similarly, splitting lenacapavir tablets has not been studied and it is not recommended. Gilead US Medical Information, October 2024.

				intended to serve as a clinical recommendation or guidance for patient care. https://www.askgileadmedical.com/docs/yeztugo/yeztugo-crushing-or-splitting-tablets	
lopinavir/ ritonavir	yes	80 mg/20 mg per mL; 160 mL bottle. Cotton-candy flavoured yellow-orange oral solution. Oral solution contains the excipients alcohol (42.4% v/v) and propylene glycol (15.3% w/v). Increased risk of toxicity in preterm infants. 40mg/10 mg oral pellets packaged in capsules approved by FDA for use in PEPFAR Program (not available in US or Canada).	Stable in refrigerator until expiry date; stable at room temperature for 42 days.	Adults with COVID-19: Adequate exposures of lopinavir and ritonavir were observed with crushed lopinavir/ritonavir administered via NG tube in 11 adults hospitalized with COVID-19 disease.(Naghani et al. Eur J Hosp Pharm 2021 May 14) Children: Administration of crushed 200/50 mg lopinavir/ritonavir tablets to children significantly reduced lopinavir and ritonavir exposure with a decrease in AUC by 45% and 47%, respectively.(Best et al. JAIDS 2011;58:385-91.)	Adult and pediatric Kaletra® tablets should be swallowed whole and not chewed, broken, or crushed. Risk of tablets shattering if broken/crushed. Tablets are film-coated and formulated using Meltrex (Melt Extrusion Technology) which improves the poor solubility of lopinavir/ritonavir by dissolving drug in a polymer and allowing drug to remain in dispersion as the polymer hardens. The extruded material can then be processed into tablets. (Klein et al. JAIDS 2007;44:401-410.) Lopinavir/ritonavir pellets are contained in capsules and should NOT be swallowed whole; should be administered with food. The dose is weight-based and ranges from 2 capsules (80 mg LPV) to 10 capsules (400 mg LPV). The entire content of the capsule should be sprinkled on food and the entire amount consumed, followed by drinking water. Do not crush or chew oral pellets. (Lopinavir and Ritonavir Oral Pellets 40 mg/10 mg, CIPLA LTD, India, 2015). In the CHAPAS 2 study (infants

					3-6 mos) oral lopinavir-ritonavir pellets were added to a small volume of expressed breast milk in a spoon and given to the infant or put directly on the infant's tongue prior to breastfeeding. (Fact Sheet on LPV/R Oral Pellets, WHO, Sept 28, 2015).
maraviroc	yes (US only); not available via SAP in Canada	20 mg/ml clear, colourless, strawberry flavoured oral solution		Successful administration of abacavir, lamivudine, raltegravir and maraviroc given via a percutaneous endoscopic gastrostomy (PEG) tube in a 40 year old male with HIV and PML. Abacavir and lamivudine oral liquid formulations were used. Maraviroc and raltegravir tablets were each crushed and separately mixed with 60 mL sterile water. Maraviroc trough concentrations were therapeutic. (Fulco PP et al. AJHP 2019;76:265-7.)	Film coated immediate release tablet. No pharmacokinetic data available for crushing/chewing tablet. (Data on File, Pfizer). While the company does not have any specific kinetic information, crushing or cutting the tablets is not expected to negatively affect bioavailability.
nelfinavir	no; discontinued in Canada & US	Discontinued in Canada & US; 50 mg/g oral powder; 144 g bottle. (1g = 1 level scoop)	**Oral Powder:** mix with small amount of water, milk, formula, or dietary supplements (acidic food or juice such as apple juice, orange juice, apple sauce not recommended-bitter taste); consume immediately;		For infants, can also dissolve tablets (i.e. 250 mg tablet) in 5 mL sterile water to yield a 50 mg/mL liquid. Use syringe with 1 mL increments to measure. Round dose to nearest 50 mg and consume immediately. Tablets also readily dissolve in water and produce a dispersion that can be mixed with milk/chocolate milk. Tablets can be crushed and given with pudding. Tablet may be mixed with food or liquid and taken immediately. Do not mix with

			may be stored in fridge for up to 6 hours.		acidic food/juice (orange or apple juice) due to bitter taste.
nevirapine	Yes (SAP)	10 mg/mL;240 mL bottle suspension Contains sorbitol 162 mg/mL (Personal communication, Boehringer Ingelheim Canada, April 2017).	Stable at room temperature. Shake well before use.	Recipe for nevirapine 5 mg/mL oral suspension: 1) Crush nevirapine 200 mg tablet; 2) Measure out 40 mL of simple syrup in a bottle; 3) Triturate crushed tablet with 10 mL of simple syrup; 4) Add nevirapine mixture back into the bottle of remaining syrup and shake well. Refrigerate. Stable for 24 hours. (Data on file, Foothills Hospital Pharmacy Department, Alberta Health Services, Calgary, Alberta, Canada)	Can crush immediate release (200 mg) nevirapine tablets in water. NB: Extended-release (400 mg XR) tablets must be swallowed whole; they must not be chewed, crushed or divided. (Viramune Product Monograph, Burlington, ON, Nov 18, 2013).
raltegravir	Yes-SAP in Canada; available in US	20 mg/mL oral banana flavoured granular powder (single-use packet of 100 mg raltegravir) 25 mg & 100 mg pediatric chewable tablets (Canada & US)	The oral suspension should be administered orally within 30 minutes of mixing	An HIV-positive patient on continuous venovenous hemodiafiltration (CVVHDF) received raltegravir 400 mg BID, darunavir 600/100 mg BID, zidovudine 300 mg BID and 3TC 50 mg q24h in suspension via gastric port and simultaneous enteral feeding via the duodenal port of a double-lumen nasogastroduodenal tube. Pharmacokinetic sampling and analysis indicated that darunavir and raltegravir were removed by CVVHDF with approximately the same clearance as provided by a normally functioning kidney. **Absorption of both darunavir and raltegravir after suspension and application via the gastric port with**	Crushing 400 mg and 600 mg HD film coated tablets is not recommended. (Data on file, Merck US, November 29, 2017). Granules (sub-units of the tablet) dissolve faster than intact tablets and may result in faster release of drug which could affect in-vivo performance. (Data on file, Merck Frosst, May 2008). Drug has a bitter taste which is masked by the film coating. Chewable tablets may be chewed or swallowed whole. Oral suspension, chewable tablets and film-coated tablets are NOT interchangeable. The maximum dose of the chewable

		continued administration of feed via the duodenal port of the double-lumen tube was good. As such, dose adjustments are not required for patients receiving darunavir and/or raltegravir while undergoing CVVHDF and that absorption of darunavir and raltegravir is not significantly affected by postpyloric enteral feeding. (Taegtmeyer et al. AIDS 2011;25(10):1339-41.)	tablets is 300 mg BID and the maximum dose of the oral suspension is 100 mg BID. Pharmacokinetic study in HIV patients administered raltegravir 400 mg HD tablet BID either whole (n=67) or chewed (n=13). In the chewed raltegravir group the Cmax, AUC_{0-12}, and trough increased by 73%, 27% and 55%, respectively. There was less interpatient variability in the pharmacokinetics of this group. Most patients who chewed raltegravir found the palatability to be fair. There were no reported adverse events. Crushed tablets tested in water or in a pH 6.8 buffer exhibited prompt and complete dissolution of raltegravir. (Cattaneo et al, Antimicrob Agents Chemother 2012;56(12):132-6.) In healthy volunteers, raltegravir 800 mg daily (chewed) vs. 400 mg BID (swallowed intact) resulted in a 2-fold increase AUC, 4-fold increase in Cmax, similar Cmin concentrations, and less pharmacokinetic variability in the 800 mg daily group. (Cattaneo et al. Ther Drug Monit 2015;37(1):119-25.)
rilpivirine	Dispersible tablet (2.5 mg) and granule (2.5 mg/g)	Case report of a 60 year old woman with squamous cell carcinoma requiring administration of ARVs via	Film coated tablet. No data available on stability of splitting or crushing rilpivirine tablets. Rilpivirine is insoluble in water

	formulations under investigation- Janssen Ireland (https://clinicaltrials.gov/ct2/show/NCT02561936) (not available in Canada)	gastrotomy tube. Initially the patient received rilpivirine, dolutegravir and emtricitabine, with darunavir/ritonavir later being added. Rilpivirine and dolutegravir were crushed and dissolved prior to administration. Rilpivirine concentrations were within the expected range and the patient achieved viral suppression. (Ragonnet et al. Br J Clin Pharmacol 2024;90:895-9.) Case report of a critically ill patient with lymphoma requiring enteral administration of ARVs. Both abacavir and 3TC solutions were administered enterally. Crushed dolutegravir 50 mg BID (separated from enteral nutrition by 2 hours) and rilpivirine 25 mg daily (given with a 240-mL bolus of an enteral formula (2 kcal/mL)) were administered via orogastric tube. Crushed tablets were each mixed with 10 mL of water and flushed down the tube at separate administration times. Trough concentrations were: day 8, rilpivirine 30 ng/mL (reference range 40-120 ng/mL), and day 9, dolutegravir 820 ng/mL (reference range 830 ng/mL steady-state trough concentration for 50 mg once daily dose). Virologic suppression was maintained after ARV enteral administration (hospital day 29). Given somewhat decreased levels of	over wide pH range. (Email communication, Janssen, July 2012). Crushed tablets added to a small amount of semisolid food or liquid is not expected to have an adverse effect if consumed immediately. Since tablets are small, ensure the whole dose is consumed. (Huesgen et al. Pharmacother 2016;36(11):1145-65.)

			these ARVs, the authors recommended consideration to increase dolutegravir to 150-200 mg total daily dose, particularly in integrase-experienced patients, and rilpivirine 50 mg daily (similar to dosing with an inducer such as rifabutin). (Turley et al. JIAPAC 2017;16(2):117-119.)	
ritonavir	No- solution discontinued in Canada and the US.	100 mg Oral Powder (100 mg/packet)- Available in the US only. Ritonavir oral powder not available via SAP in Canada. (AbbVie Canada, Data on file, May 2019).		**Tablet dissolved in water**: A manufacturer study demonstrated that a ritonavir 100 mg tablet produced an aqueous suspension when placed whole in 10, 20, 40 or 60 mL of water at room temperature for 4 hours without stirring. The tablet fully eroded after 4 hours. Hourly stirring or placing the tablet in warm water did not impact the dissolution time. This dosing strategy is only recommended for full doses in 100 mg increments. In vivo, the performance and bioavailability of the suspension is expected to be the same as ritonavir powder for oral suspension. Of note, ritonavir powder for oral suspension demonstrated bioequivalence to the discontinued oral solution when administered after a moderate-fat meal (Data on file, AbbVie Canada, ATR-17-00389). **Oral powder (100 mg/packet):** The entire packet should be mixed with soft food such as

saquinavir	no	Liquid not being formulated due to unpalatability	In an open-label, randomized, 4 period study in adults, the bioavailability of 1000 mg opened saquinavir capsules suspended in simple syrup, baby formula and jelly jam (plus ritonavir 100 mg oral solution) was approximately 10%, 60% and 40% higher, respectively, than 1000 mg unopened saquinavir capsules plus ritonavir. In terms of palatability, saquinavir suspended in simple syrup or jelly jam ranked higher than saquinavir suspended in baby food.(McKay et al. 8th Int Workshop Clin Pharm HIV Ther 2007, abstract 6.) An extemporaneously prepared saquinavir suspension (60 mg/mL) from saquinavir (Fortovase®) soft gelatin capsules was stable at both 5 and 25 degrees C for at least 30 days.(Tan et al. J Clin Pharm Ther 2000;28:457-63.)	apple sauce or vanilla pudding, or mixed with liquid such as water, chocolate milk, or infant formula. All soft food or liquid should be consumed within 2 hours of preparation. The bitter taste may be decreased if taken with food. The powder should be used in 100 mg increments only. The oral powder can also be administered via feeding tube after being mixed with water. **Note: Only Invirase® 500 mg tablets are marketed in Canada & US.** Invirase® and Fortovase® capsules are discontinued (verified April 2019). Hard gel caps (Invirase®) may be opened and powder sprinkled on food, simple syrup or water (unpleasant taste). Take with food. 6 x 200 mg Fortovase® (soft-gel caps) whole caps mixed with 50 mL of whole milk or Advera nutritional supplement took 5-15 minutes to dissolve when heated to 40, 60 or 80°C. The mixture remained in solution for up to 1 hour at room temperature. If refrigerated for 24 hours, it turned into a gel, but reliquified after reheating to 30 degrees C. The drug was still stable at 24 hours. (data on file, Hoffmann-LaRoche)

stavudine (d4T)	No longer available in Canada via SAP; product discontinued in Canada (Sept 30, 2018) & US	1 mg/mL oral suspension; 200 ml bottle. Fruit-flavoured. Shake well (no longer available in Canada & US)	Stable 30 days in fridge.		Can open up stavudine capsules and give in small portion of food or 5-10 mL cool tap water.
tenofovir AF	no			Case report of a male with HIV, antiretroviral experienced with resistance mutations (K101E, M184V, M230L, A98G, L10I, E35D and M36I), and dysphagia due to eosinophilic esophagitis who was successfully treated with crushed dolutegravir, crushed tenofovir AF (TAF), and liquid abacavir and emtricitabine. The viral load was suppressed after 10 months of follow-up. The patient was intolerant of crushed tenofovir DF (TDF) due to taste and nausea but tolerated crushed TAF. (Moore SE et al. Int J STD AIDS 2020;31(3):285-287.)	Available as Vemlidy® tablets containing tenofovir alafenamide 25 mg for hepatitis B treatment indication.
tenofovir DF	yes (US only)	40 mg per 1 gram of oral powder formulation. Oral powder should be mixed in a container with 2 to 4 ounces (60 to 120 mL) of soft food not requiring chewing (e.g., applesauce, baby food, yogurt). Do	Administer immediately to avoid a bitter taste.		Crushed tablet dissolves in 100 mL water in 20 minutes; grape juice may also be used. Consume immediately. NB: crushed tablets have very disagreeable taste. May also try splitting tablets and inserting into empty gelatin capsules to mask taste.

		not attempt to mix in a liquid as the powder may float on top even after stirring.			
tipranavir	yes (US only; not in Canada)	100 mg/mL oral solution; contains 116 IU/mL vitamin E.	Store oral solution and room temperature (25ºC). Use solution within 60 days of opening the bottle.		250 mg capsule. Avoid splitting or crushing capsule.
zalcitabine (ddC)	no	Investigational oral solution is no longer available.			
zidovudine (AZT)	yes	10 mg/mL oral syrup; 240 mL bottle. Strawberry-flavoured.	Store at room temperature.		May open capsules & give in small portion of food or 5-10 mL cool tap water.
DIRECT ACTING ANTIVIRALS (DAAs)					
daclatasvir	no				Manufacturer recommends not chewing or crushing the tablet as it has a very unpleasant taste. (Daklinza Summary of Product Characteristics, EU, Feb 19, 2019).
elbasvir/ grazoprevir (Zepatier®)	no			Sustained virologic response was achieved in a 63 year old non-cirrhotic, treatment-naive man who received 16 weeks of crushed elbasvir/grazoprevir administered through a percutaneous endoscopic gastrostomy (PEG) tube. (Yap et al. J Clin Pharm Ther	The Zepatier® tablet uses an enabled formulation (i.e. not a simple enteric coated formulation) and breakage of the tablet integrity should not affect its bioavailability in presence of increased pH. (Reau et al. Hepatol Commun 2017;1(8):757-764.) However,

		2018;43:730-2.)	no pharmacokinetic studies have been performed, and caution is advised.
glecaprevir/ pibrentasvir (Maviret®, Mavyret®)	no	Case report of a 41 year-old female (36 kg) with treatment naive chronic HCV, spina bifida and hydrocephalus who received crushed glecaprevir/pibrentasvir (GLE/PIB) x 8 weeks via PEG tube feeds and achieved a 12-week sustained virologic response post-treatment. Prior to PEG tube administration, GLE/PIB was crushed into powder and suspended with water. The regimen was well-tolerated (constipation reported). (Tanaka et al. Clin J Gastroenterol 2019;12:588-91.) 25 patients who received a heart transplant from HCV donors were given GLE/PIB on call to the OR and continued for 8 weeks. Of these, eight (32%) received GLE/PIB crushed via enteral tube (median 6 days). No difference was found in SVR or rapidity of HCV clearance in patients who received crushed GLE/PIB. (Waldman et al. J Heart Lung Transplant 2020;39:S95-96.) In a retrospective case series of 10 patients (60% HCV GT1a) on **SOF/VEL (50%), LED/SOF (30%) and GLE/PIB (20%),**	In healthy adults, cutting the tablet in half had minimal impact on glecaprevir and pibrentasvir exposures (≤15% difference) compared to swallowing the whole tablets. In contrast, grinding or crushing the tablets resulted in 27-61% lower exposures for glecaprevir and 21-83% higher exposures for pibrentasvir. (Oberoi et al. J Pharm Sci 2018;107:1724-30.) These data suggest that Maviret® tablets may be cut in half for people who have difficulty swallowing whole tablets. Solubility: Glecaprevir has a solubility of less than 0.1 to 0.3 mg/mL across a pH range of 2–7 at 37ºC and is practically insoluble in water, but is sparingly soluble in ethanol. (Maviret Product Monograph; St-Laurent, QC. Aug 16, 2017).

		patients either crushed (70%) or split (30%) their DAA tablets. All patients were prescribed 12 weeks of DAA therapy and had undetectable HCV viral loads by day 56. All patients with available data (7/7) had SVR12; 3 patients had undetectable viral loads at end of treatment but no follow-up data were available. No patients experienced severe adverse events. (Whelchel K et al. Open Forum Infect Dis 2021;8:ofab525).	
ledipasvir/ sofosbuvir (Harvoni®)	no	In a retrospective case series of 10 patients (60% HCV GT1a) on **SOF/VEL (50%), LED/SOF (30%) and GLE/PIB (20%),** patients either crushed (70%) or split (30%) their DAA tablets. All patients were prescribed 12 weeks of DAA therapy and had undetectable HCV viral loads by day 56. All patients with available data (7/7) had SVR12; 3 patients had undetectable viral loads at end of treatment but no follow-up data were available. No patients experienced severe adverse events. (Whelchel K et al. Open Forum Infect Dis 2021;8:ofab525). A patient with HIV, hepatitis C and high-grade postresection sarcoma of the throat received crushed ledipasvir/sofosbuvir daily for 12 weeks and achieved	

		SVR. The ledipasvir/sofosbuvir was crushed and dissolved in water and administered via PEG tube.(Huffman V et al. Am J Health-Syst Pharm 2020;78:36-40.) In a treatment-experienced patient with compensated cirrhosis, SVR12 was achieved after 24 weeks of treatment with crushed ledipasvir/sofosbuvir administered via a percutaneous endoscopic gastrostomy (PEG) tube. (Jindracek et al. J Pharm Pract 2018;31:522-4.) A 19-year old woman with HCV genotype 1 and HIV coinfection achieved SVR12 after 12 weeks of crushed ledipasvir/sofosbuvir administered via gastrosomy button. Each ledipasvir/sofosbuvir tablet was crushed, mixed with 10 mL warm water, and administered via syringe. Additional warm water was used to obtain all the powder. (Fulco et al. AJHP 2017;74:1761-2.)	
sofosbuvir	no		Sofosbuvir tablets can be disintegrated in water, juice, or milk with minor stirring and pressure with a spoon. However, the stability of sofosbuvir in these liquids is unknown at this time. Furthermore, there are no studies evaluating the

			pharmacokinetic parameters of the disintegrated or crushed sofosbuvir tablet versus the whole tablet. In addition, a disintegrated or crushed sofosbuvir tablet may have an unpleasant taste. (Personal communication, Gilead Sciences Canada, December 2013).
sofosbuvir/ velpatasvir (Epclusa®)	no	In a retrospective case series of 10 patients (60% HCV GT1a) on **SOF/VEL (50%), LED/SOF (30%) and GLE/PIB (20%),** patients either crushed (70%) or split (30%) their DAA tablets. All patients were prescribed 12 weeks of DAA therapy and had undetectable HCV viral loads by day 56. All patients with available data (7/7) had SVR12; 3 patients had undetectable viral loads at end of treatment but no follow-up data were available. No patients experienced severe adverse events. (Whelchel K et al. Open Forum Infect Dis 2021;8:ofab525). A case report of a 70 year-old female with an oropharyngectomy and infected with HCV genotype 1b studied drug absorption and exposure of crushed sofosbuvir/velpatasvir 400/100 mg tablet daily taken with an acidic beverage and meal (to enhance absorption). TDM showed that the absorption of both was increased compared	Manufacturer states that Epclusa® tablets are not enteric-coated and are not sustained-release. Tablets can be disintegrated in water, juice, or milk with minor stirring and pressure with a spoon. A disintegrated, crushed or split tablet may have an unpleasant taste and there are no studies evaluating the pharmacokinetics of these methods of administration. (Gilead Sciences Canada, Data on File, Nov 11, 2018).

		to historical controls and the steady-state trough concentration (Css) of velpatasvir at weeks 1 and 10 showed concentrations above historical reference with no accumulation. Although the trough Css of sofosbuvir was below the limit of quantification, this was anticipated/expected given the short half-life of the drug (30 minutes). The drugs were well tolerated with improved liver parameters. The HCV viral load became undetectable after 4 weeks and remained undetectable 12 weeks post-treatment. (Lalanne et al. Ther Drug Monit 2020;42:163-4.) A case report of a 62 year-old female with dysphagia and hepatitis C genotype 4 infection (non-cirrhotic, treatment naïve) was treated with sofosbuvir/velpatasvir given mixed with soft foods (e.g. apple sauce). The patient was adherent to therapy and it was well tolerated. The viral load was undetectable at weeks 4 and 12 of therapy and a 12 week sustained virologic response was achieved. Liver transaminases normalized during treatment. (Mogul et al. Am J Health Syst Pharm 2020;77:417-8.) A case report of a 54 year-old	

		male with hepatitis genotype 2b infection requiring PEG tube administration of medications due to left-sided hemiparesis post-stroke. Sofosbuvir/velpatasvir was crushed, dissolved in water and administered via PEG tube. Rinsing of tablet crusher and syringe to get residual drug was recommended. Steady-state pharmacokinetics (24 hour curve) of SOF-VEL via PEG tube was done on day 15 and on day 16 a second shorter 4-hour curve was done after the patient took the tablet whole under medical observation. SOF exposure was similar for crushed vs whole tablet. Crushed VEL Cmax was decreased by 35% and AUC decreased by 25% compared to whole tablet. However, the crushed concentrations were comparable or higher than whole tablet values in population-based references. The HCV viral load decreased to 49.6 IU/mL after 2 weeks, therefore treatment was continued for the full 12 weeks and a 12-week sustained virological response was achieved. (van Seyen et al. Int J Antimicrob Agents 2020;55:105934) A case series of 19 patients who received crushed SOF/VEL administered via oral = 8, NG tube = 3, PEG tube = 7, J-tube	

				=1) demonstrated high HCV cure rates and safety.(Joshi et al. AASLD 2021, poster 950).	
sofosbuvir/ velpatasvir/ voxilaprevir (Vosevi®)	no				Manufacturer states that Vosevi® tablets are not enteric-coated and are not sustained-release. Tablets can be disintegrated in water, juice, or milk with minor stirring and pressure with a spoon. A disintegrated, crushed or split tablet may have an unpleasant taste and there are no studies evaluating the pharmacokinetics of these methods of administration. (Gilead Sciences Canada, Data on File, Nov 19, 2018).
OTHER:					
acyclovir	yes	200 mg/5 mL;125 mL bottle. Banana-flavoured suspension.	Store between 15-25 ºC		
azithromycin	yes	pediatric oral powder/suspension 100 mg/5 mL (300 mg bottle) OR 200 mg/5 mL (600 & 900 mg bottles). Cherry-flavoured suspension.	Store reconstituted suspension between 5-30ºC. Dispose unused suspension after 10 days.		May also open capsules and mix with water (ingest immediately on empty stomach, follow with full glass of water).
clarithromycin	yes	125 mg/5 mL (55, 105, 150 mL bottles) OR 250 mg/5mL (105 mL bottles). Fruit-flavoured suspension. Shake well before	Store reconstituted liquid at room temperature.		

		use.			
hydroxyurea	no				Can open up capsules and mix with water; take immediately. Some inert material (used as a vehicle in capsule) may not dissolve and may float on top. Do not allow powder to come in contact with skin and mucous membranes. Avoid inhalation of powder when opening capsules.
rifabutin	no				Can open capsules (experience in pediatrics: OK to mix with applesauce, syrup, cherry syrup); drug not soluble in water
Trimethoprim/ sulfamethox-azole (TMP/SMX)	yes	pediatric suspension TMP/SMX 40 mg/200 mg per 5 mL (= ½ SS tablet); 100 & 400 mL bottles Contains sorbitol. Example : Teva-Trimel suspension contains sorbitol 4 g/5 mL- (Personal communication, Teva Canada, April 2017)	Store at room temperature. Shake well before use.		

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