

# Antiretroviral Formulations for Swallowing Difficulties

Revised April 2017

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## Nucleoside/tide Reverse Transcriptase Inhibitors

Antiretroviral	Formulation	Comments
<b>NRTIs</b>		
<b>Abacavir</b>	Oral Solution (Ziagen® and generic)	<ul style="list-style-type: none"> <li>Dosing is the same for oral solution and tablet.</li> <li>Store below 30°C. Discard 2 months after first opening.</li> <li>Contains 340 mg/ml sorbitol.</li> </ul>
	Tablet (Ziagen®)	<ul style="list-style-type: none"> <li>Bitter taste.</li> <li>Tablets can be crushed and added to a small amount of semi-solid food or liquid and taken immediately.</li> </ul>
<b>Didanosine</b>	Powder for Oral Solution (Videx® and generic)	<ul style="list-style-type: none"> <li>Prior to dispensing, the pharmacist must reconstitute the dry powder with water and immediately mix the resulting solution with antacid.</li> <li>Store at 2-8°C (in a fridge) after reconstitution. Discard 30 days after reconstitution.</li> </ul>
	Chewable/dispersible tablet (Videx®)	<ul style="list-style-type: none"> <li>Contains calcium and magnesium antacids. Patients &gt;1 year old must take at least 2 (but no more than 4) tablets in each dose to provide sufficient antacid against acid degradation of didanosine.</li> <li>Each tablet contains 342 mg sorbitol and 36.5 mg phenylalanine.</li> <li>Tablets must be thoroughly chewed and taken at least 30 minutes before or 2 h after food.</li> <li>To disperse tablets, stir into at least 30 ml water until a uniform dispersion forms, and drink the entire dispersion immediately. For additional flavouring, the dispersion may be diluted with 30 ml clear apple juice. Stir the further dispersion just prior to consumption.</li> </ul>
<b>Emtricitabine</b>	Oral Solution (Emtriva®)	<ul style="list-style-type: none"> <li>The oral solution and capsules are <b>NOT</b> bioequivalent: 240 mg (24 ml) oral solution = 200 mg capsule.</li> <li>Store at 2-8°C (in a fridge). After opening, must not be stored above 25°C. Discard 45 days after first opening.</li> <li>Contains Na<sup>+</sup> 460 µmol/ml.</li> </ul>
	Hard Capsule (Emtriva®)	<ul style="list-style-type: none"> <li>Capsules can be opened and contents dissolved in at least 30 ml water. [<i>EACS Guidelines, version 8.1, 2016</i>]</li> </ul>
<b>Lamivudine</b>	Oral Solution (EpiVir®)	<ul style="list-style-type: none"> <li>Dosing is the same for oral solution and tablets.</li> <li>The bioavailability of lamivudine solution has been shown to be significantly reduced in a dose dependent manner by sorbitol which is present in other liquid formulations (e.g., abacavir, nevirapine, cotrimoxazole) or in didanosine chewable/dispersible tablets. [<i>Adkison KK et al, CROI 2017, abstract 428</i>]</li> <li>Do not store above 25°C. Discard 1 month after first opening.</li> <li>Contains 1g/5ml sucrose.</li> </ul>
	Tablet (EpiVir® and generic)	<ul style="list-style-type: none"> <li>Tablets can be crushed and added to a small amount of semi-solid food or liquid and taken immediately.</li> </ul>
<b>Stavudine</b>	Powder for Oral Solution (Zerit® and generic)	<ul style="list-style-type: none"> <li>Dosing is the same for oral solution and capsules.</li> <li>Store at 2-8°C (in a fridge) after reconstitution. Discard 30 days after reconstitution.</li> <li>Contains 50 mg/ml sucrose.</li> </ul>
	Hard Capsule (Zerit® and generic)	<ul style="list-style-type: none"> <li>Capsules can be opened and mixed with food.</li> <li>Take on an empty stomach.</li> </ul>
<b>Tenofovir-DF</b>	Granules/Powder (Viread®)	<ul style="list-style-type: none"> <li>One level scoop delivers 1 g of granules/powder, containing 33 mg tenofovir-DF, and should be mixed with one tablespoon (15 ml) of soft food (e.g. apple sauce, yogurt) per scoop of granules/powder. The entire mixture should be ingested immediately to avoid bitter taste.</li> <li>The granules/powder should not be administered in a liquid as it may float on top of the liquid even after stirring.</li> </ul>
	Tablet (Viread® and generic)	<ul style="list-style-type: none"> <li>Bitter taste.</li> <li>Tablets may be disintegrated in at least 100 ml of water, orange juice, or grape juice.</li> <li>Manufacturer recommends dispersing tablets in exceptional circumstances only. Tenofovir granules/powder preferred.</li> </ul>
<b>Tenofovir-DF + Emtricitabine</b>	Tablet (Truvada®)	<ul style="list-style-type: none"> <li>Bitter taste.</li> <li>Tablets may be disintegrated in at least 100 ml of water, orange juice, or grape juice and taken immediately.</li> </ul>
<b>Zidovudine</b>	Oral Solution (Retrovir® and generic)	<ul style="list-style-type: none"> <li>Dosing is the same for oral solution and capsules.</li> <li>Do not store above 30°C. Discard 1 month after first opening bottle.</li> </ul>
	IV concentrate for solution for infusion (Retrovir® and generic)	<ul style="list-style-type: none"> <li>The required dose should be mixed with Glucose Intravenous Infusion 5% w/v to give a final zidovudine concentration of either 2 mg/ml or 4 mg/ml, which is stable for up to 48 hours at both 5°C and 25°C.</li> <li>Administer by slow intravenous infusion of the diluted product over 1 hour.</li> </ul>
<b>Zidovudine + Lamivudine</b>	Tablet (Combivir® and generic)	<ul style="list-style-type: none"> <li>Tablets may be crushed and mixed with a small amount of semi-solid food or liquid (at least 15 ml) which must be consumed immediately.</li> </ul>

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## Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

Antiretroviral	Formulation	Comments
<b>NNRTIs</b>		
<b>Efavirenz</b>	Tablet and Hard Capsule (Sustiva® and generic)	<ul style="list-style-type: none"> <li>• Capsules can be opened and the contents administered with a small amount of food using the capsule sprinkle method of administration.</li> <li>• Tablets may be divided for ease of swallowing.</li> <li>• No additional food should be consumed for up to 2 hours after efavirenz administration.</li> </ul>
<b>Etravirine</b>	Tablet (Intelence®)	<ul style="list-style-type: none"> <li>• Patients who are unable to swallow whole tablets may disperse the tablets in water. Place the tablet(s) in 5 ml of water, or at least enough liquid to cover, and stir well. If desired, add more water or alternatively orange juice or milk (do not place the tablets in orange juice or milk without first adding water). Drink immediately and rinse the glass several times to ensure the entire dose is taken.</li> <li>• The use of grapefruit juice or warm (&gt;40°C) or carbonated beverages should be avoided.</li> </ul>
<b>Nevirapine</b>	Oral Suspension (Viramune® and generic)	<ul style="list-style-type: none"> <li>• Viramune tablets and oral suspension are comparably bioavailable and interchangeable at doses up to 200 mg.</li> <li>• Use within 6 months of opening.</li> <li>• Contains 150 mg/ml sucrose and 162 mg/ml sorbitol.</li> </ul>
	Film Coated Tablet (Viramune® and generic)	<ul style="list-style-type: none"> <li>• Tablets can be crushed and dissolved in water but any extended release effect will be lost. If the extended release effect is lost, twice daily administration is recommended in patients with higher body weight (≥90 kg) as sub-therapeutic trough levels may occur following administration of nevirapine 400 mg once daily immediate release. [<i>EACS Guidelines, version 8.1, 2016</i>]</li> </ul>
<b>Protease Inhibitors</b>		
<b>Atazanavir</b>	Oral Powder (Reyataz®)	<ul style="list-style-type: none"> <li>• It is preferable to mix atazanavir oral powder with food such as apple sauce or yogurt. However, atazanavir oral powder can be mixed with milk, infant formula, or water for infants who can drink from a cup, or mixed with infant formula and given using an oral dosing syringe to young infants (&lt;6 months) who cannot eat solid food or drink from a cup. Using an infant bottle is not recommended as the full dose may not be delivered.</li> <li>• The dose should be administered within one hour of preparation and may be left at room temperature during this one hour period.</li> </ul>
<b>Darunavir</b>	Oral Suspension (Prezista®)	<ul style="list-style-type: none"> <li>• Dosing is the same for oral suspension and tablets.</li> <li>• Do not store above 30°C.</li> </ul>
	Tablet (Prezista®)	<ul style="list-style-type: none"> <li>• Tablets can be crushed and added to a small amount of semi-solid food or liquid and taken immediately. [<i>EACS Guidelines, version 8.1, 2016</i>]</li> <li>• Take with food.</li> </ul>
<b>Fosamprenavir</b>	Oral Suspension (Telzir®)	<ul style="list-style-type: none"> <li>• Bioequivalence was <b>not</b> demonstrated when oral suspension was given with food.</li> <li>• Adults should take the oral suspension on an empty stomach; patients under 18 years should take the oral suspension with food.</li> </ul>
<b>Lopinavir/ritonavir</b>	Oral Solution (Kaletra® and generic)	<ul style="list-style-type: none"> <li>• Dosing is the same for oral solution and tablets.</li> <li>• Store in a refrigerator (2-8°C). In use storage: if kept outside of the refrigerator, do not store above 25°C. Discard any unused contents after 42 days (6 weeks).</li> <li>• Contains 153 mg/ml propylene glycol and alcohol (42%).</li> </ul>
<b>Ritonavir</b>	Oral Solution (Norvir®)	<ul style="list-style-type: none"> <li>• Dosing is the same for oral solution and capsules/tablets.</li> <li>• Bitter taste can be masked by mixing with chocolate milk; must NOT be mixed with water, measuring cup must be dry.</li> <li>• Store below 25°C. Do not refrigerate or freeze.</li> <li>• Contains alcohol (43%).</li> </ul>
	Powder for Oral Suspension (Norvir®)	<ul style="list-style-type: none"> <li>• Each sachet contains 100 mg ritonavir.</li> <li>• The entire contents of a sachet can be poured over a small amount of soft food or suspended in 9.4 ml of liquid (water, chocolate milk, or infant formula).</li> <li>• Once the powder is mixed, the prepared food/suspension should be used within 2 hours.</li> <li>• The bitter aftertaste may be lessened if peanut butter, hazelnut chocolate spread, or black currant syrup are taken immediately after dose administration.</li> <li>• The prescribed dose can be administered via a feeding tube after being mixed with water.</li> </ul>
<b>Saquinavir</b>	Capsule (Invirase®)	<ul style="list-style-type: none"> <li>• Capsules can be opened and mixed with 15 ml sugar/sorbitol syrup, or 3 teaspoons of jam.</li> </ul>
<b>Tipranavir</b>	Oral solution (Aptivus®)	<ul style="list-style-type: none"> <li>• Bioavailability of the oral solution is higher than that of the capsules and is <b>NOT</b> interchangeable.</li> <li>• Patients should check the solution for crystallisation and the bottle replaced if more than a thin layer of crystals forms.</li> <li>• Take with/after food, and separate from indigestion remedies.</li> <li>• Do not store below 15°C. Do not refrigerate or freeze.</li> <li>• Contains 78 mg/ml Vitamin E.</li> </ul>

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## Entry Inhibitors, Integrase Inhibitors and Co-formulations

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<b>Entry Inhibitors</b>		
<b>Maraviroc</b>	Oral Solution (Selzentry®)	<ul style="list-style-type: none"> <li>Dosing is the same for oral solution and tablets.</li> <li>Store at 20-25°C.</li> </ul>
	Tablet (Celsentri/Selzentry®)	<ul style="list-style-type: none"> <li>No specific pharmacokinetic data on file. Crushing the tablet is not expected to have a negative effect on bioavailability. [EACS Guidelines, version 8.1, 2016]</li> </ul>
<b>Integrase Inhibitors</b>		
<b>Dolutegravir</b>	Tablet (Tivicay®)	<ul style="list-style-type: none"> <li>Tablets can be split or crushed and added to a small amount of semi-solid food or liquid and taken immediately. [EACS Guidelines, version 8.1, 2016]</li> </ul>
<b>Raltegravir</b>	Granules/Powder for Oral Suspension (Isentress®)	<ul style="list-style-type: none"> <li>Isentress for oral suspension is <b>NOT</b> bioequivalent with Isentress film coated tablets.</li> <li>Each sachet contains approximately 0.5 mg fructose, 1.5 mg sorbitol and 4.7 mg sucrose.</li> <li>Each sachet contains 100 mg of raltegravir which is to be suspended in 5 ml of water giving a final concentration of 20 mg/ml. The volume (dose) of suspension should be administered orally within 30 minutes of mixing and any remaining suspension discarded.</li> <li>Maximum dose of oral suspension is 100 mg twice daily. Patients can remain on the oral suspension as long as their weight is below 20 kg.</li> </ul>
	Chewable Tablet (Isentress®)	<ul style="list-style-type: none"> <li>Isentress chewable tablets are <b>NOT</b> bioequivalent with Isentress film coated tablets; 300 mg chewable tablet = 400 mg film-coated tablet.</li> <li>Contains fructose, phenylalanine and sorbitol (see label for quantities per 25/100 mg tablet).</li> <li>Maximum dose of chewable tablets is 300 mg twice daily.</li> <li>Chewable tablets may be chewed or swallowed whole. The 100 mg tablet can be divided into equal 50 mg doses.</li> <li>Store in original package with the bottle tightly closed. Keep the desiccant in the bottle to protect from moisture.</li> </ul>
	Film coated Tablet (Isentress®)	<ul style="list-style-type: none"> <li>Crushing tablets is not recommended in the product label, however, absorption of raltegravir was not compromised when tablets were crushed and dissolved in 60 ml warm water and administered by gastrostomy tube. [Sandkovsky U, et al, 2012]</li> </ul>
<b>Co-formulations</b>		
<b>Tenofovir-DF + Emtricitabine + Elvitegravir + Cobicistat</b>	Tablet (Stribild®)	<ul style="list-style-type: none"> <li>Crushing tablets is not recommended in the product label, however, there was no significant effect on the pharmacokinetics of the components of the tablet following oral administration of a crushed and suspended tablet. [Colbers A et al, CROI 2016, abstract 431]</li> </ul>
<b>Abacavir + Lamivudine + Dolutegravir</b>	Tablet (Triumeq®)	<ul style="list-style-type: none"> <li>Tablets can be split or crushed and added to a small amount of semi-solid food or liquid and taken immediately. The pharmacokinetic profiles of the components of the tablet were not modified to a clinically significant extent when Triumeq was crush and administered suspended in water or enteral nutrition. [Roskam-Kwint M, et al, CROI 2017, abstract 429]</li> </ul>

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## Formulations which the product label advises to be swallowed intact

Antiretroviral	Formulation	Comments
<b>NRTIs</b>		
<b>Didanosine</b>	Gastro-resistant Capsule (Videx® and generic) Delayed-release Capsule (Videx EC® and generic)	<ul style="list-style-type: none"> <li>The gastro-resistant capsule should be taken intact with at least 100 ml of water. Capsules should not be opened to facilitate administration, since this could reduce absorption.</li> <li>Delayed-release capsules should be swallowed intact.</li> </ul>
<b>NNRTIs</b>		
<b>Nevirapine</b>	Extended/Prolonged Release Tablet (Viramune XR® and generic)	<ul style="list-style-type: none"> <li>The prolonged-release tablets must be swallowed whole and should not be chewed, crushed, or divided if an extended release effect is required. If the extended release effect is lost, dose modification may be required.</li> <li>If the extended release effect is lost, twice daily administration is recommended in patients with higher body weight (≥90 kg) as sub-therapeutic trough levels may occur following administration of nevirapine 400 mg once daily immediate release. [EACS Guidelines, version 8.1, 2016]</li> </ul>
<b>Protease Inhibitors</b>		
<b>Atazanavir</b>	Capsule (Reyataz® and generic)	<ul style="list-style-type: none"> <li>Swallow the capsules whole. Do not open the capsules.</li> </ul>
<b>Indinavir</b>	Hard Capsule (Crixivan®)	<ul style="list-style-type: none"> <li>The hard capsules should be swallowed whole.</li> </ul>
<b>Lopinavir</b>	Tablet (Kaletra®)	<ul style="list-style-type: none"> <li>Kaletra tablets must be swallowed whole and not chewed, broken or crushed.</li> </ul>
<b>Ritonavir</b>	Tablet (Norvir® and generic)	<ul style="list-style-type: none"> <li>Tablets should be swallowed whole and not chewed, broken or crushed.</li> </ul>
<b>Saquinavir</b>	Tablet (Invirase®)	<ul style="list-style-type: none"> <li>Invirase film-coated tablets should be swallowed whole</li> </ul>
<b>Integrase Inhibitors</b>		
<b>Elvitegravir</b>	Tablet (Vitekta®)	<ul style="list-style-type: none"> <li>The film-coated tablet should not be chewed or crushed.</li> </ul>
<b>Others</b>		
<b>Cobicistat</b>	Tablet (Tybost®)	<ul style="list-style-type: none"> <li>The film-coated tablet should not be chewed or crushed.</li> </ul>
<b>Co-formulations</b>		
<b>Atazanavir + Cobicistat</b>	Tablet (Evotaz®)	<ul style="list-style-type: none"> <li>The film-coated tablet should be swallowed whole and must not be chewed, broken, cut or crushed.</li> </ul>
<b>Darunavir + Cobicistat</b>	Tablet (Rezolsta®, Prezcoibix®)	<ul style="list-style-type: none"> <li>To ensure administration of the entire dose of both darunavir and cobicistat, the tablet should be swallowed whole.</li> </ul>
<b>Efavirenz + Emtricitabine + Tenofovir-DF</b>	Tablet (Atripla®)	<ul style="list-style-type: none"> <li>Atripla tablets should be swallowed whole with water.</li> </ul>
<b>Rilpivirine + Emtricitabine + Tenofovir-DF</b>	Tablet (Eviplera®, Complera®)	<ul style="list-style-type: none"> <li>The film-coated tablet should not be chewed, crushed or split as it may impact the absorption of Eviplera.</li> </ul>
<b>Emtricitabine + Tenofovir alafenamide</b>	Tablet (Descovy®)	<ul style="list-style-type: none"> <li>The film-coated tablet should not be chewed, crushed, or split.</li> </ul>
<b>Emtricitabine + Tenofovir alafenamide + Elvitegravir + Cobicistat</b>	Tablet (Genvoya®)	<ul style="list-style-type: none"> <li>The film-coated tablet should not be chewed, crushed, or split.</li> </ul>
<b>Emtricitabine + Tenofovir alafenamide + Rilpivirine</b>	Tablet (Odefsey®)	<ul style="list-style-type: none"> <li>The film-coated tablet should not be chewed, crushed or split.</li> </ul>

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