

Table 15c. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Gastrointestinal Effects (Last updated April 16, 2019; last reviewed April 14, 2020) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Nausea/Vomiting	All ARV drugs, but most notably RTV-boosted PIs	<p>Onset:</p> <ul style="list-style-type: none"> • Early <p>Presentation:</p> <ul style="list-style-type: none"> • Nausea and emesis, both of which may be associated with anorexia and/or abdominal pain 	Varies by ARV agent; generally <15%	Unknown	<p>Instruct patient to take PIs with food.</p> <p>Monitor for weight loss and ARV adherence.</p>	<p>Reassure patient that these adverse effects generally improve over time (usually in 6–8 weeks).</p> <p>Consider switching to ARV drugs with smaller tablet sizes (see Appendix A, Table 2).</p> <p>Provide supportive care.</p> <p>In extreme or persistent cases, use antiemetics or switch to another ARV regimen.</p>
Diarrhea	All ARV drugs, but most notably RTV-boosted PIs	<p>Onset:</p> <ul style="list-style-type: none"> • Early <p>Presentation:</p> <ul style="list-style-type: none"> • More frequent bowel movements and stools that are generally soft 	Varies by ARV agent; generally <15%	Unknown	Monitor for weight loss and dehydration.	<p>In prolonged or severe cases, exclude infectious or noninfectious (e.g., lactose intolerance) causes of diarrhea.</p> <p>Reassure patient that this adverse effect generally improves over time (usually in 6–8 weeks). Consider switching to another ARV regimen in persistent and severe cases.</p> <p>Treatment data in children are lacking; however, the following strategies may be useful when the ARV regimen cannot be changed:</p> <ul style="list-style-type: none"> • Dietary modification • Using bulk-forming agents (e.g., psyllium) • Using antimotility agents (e.g., loperamide) • Using crofelemer, which is approved by the FDA to treat ART-associated diarrhea in adults aged ≥18 years; no pediatric data are available.

Table 15c. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Gastrointestinal Effects (Last updated April 16, 2019; last reviewed April 14, 2020) (page 2 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Pancreatitis	Rare, but may occur with NRTIs or RTV-boosted PIs	<p>Onset:</p> <ul style="list-style-type: none"> Any time, usually after months of therapy <p>Presentation:</p> <ul style="list-style-type: none"> Emesis, abdominal pain, elevated amylase and lipase levels (asymptomatic hyperamylasemia or elevated lipase do not in and of themselves indicate pancreatitis) 	<2% in a recent case series	<p>Use of concomitant medications that are associated with pancreatitis (e.g., TMP-SMX, pentamidine, ribavirin)</p> <p>Hypertriglyceridemia</p> <p>Advanced HIV infection</p> <p>Previous episode of pancreatitis</p> <p>Alcohol use</p>	Measure serum amylase and lipase concentrations if persistent abdominal pain develops.	<p>Discontinue offending agent and avoid reintroduction.</p> <p>Manage symptoms of acute episodes.</p> <p>If pancreatitis is associated with hypertriglyceridemia, consider using interventions to lower TG levels.</p>

Key: ART = antiretroviral therapy; ARV = antiretroviral; FDA = Food and Drug Administration; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RTV = ritonavir; TG = triglyceride; TMP-SMX = trimethoprim sulfamethoxazole

References

- Buck WC, Kabue MM, Kazembe PN, Kline MW. Discontinuation of standard first-line antiretroviral therapy in a cohort of 1434 Malawian children. *J Int AIDS Soc.* 2010;13:31. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20691049>.
- Nachman SA, Chernoff M, Gona P, et al. Incidence of noninfectious conditions in perinatally HIV-infected children and adolescents in the HAART era. *Arch Pediatr Adolesc Med.* 2009;163(2):164-171. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19188649>.
- Hoffmann CJ, Fielding KL, Charalambous S, et al. Antiretroviral therapy using zidovudine, lamivudine, and efavirenz in South Africa: tolerability and clinical events. *AIDS.* 2008;22(1):67-74. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18090393>.
- Malan N, Su J, Mancini M, et al. Gastrointestinal tolerability and quality of life in antiretroviral-naive HIV-1-infected patients: data from the CASTLE study. *AIDS Care.* 2010;22(6):677-686. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20467943>.
- Manfredi R, Calza L. HIV infection and the pancreas: risk factors and potential management guidelines. *Int J STD AIDS.* 2008;19(2):99-105. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18334062>.
- Tukei VJ, Asiimwe A, Maganda A, et al. Safety and tolerability of antiretroviral therapy among HIV-infected children and adolescents in Uganda. *J Acquir Immune Defic Syndr.* 2012;59(3):274-280. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22126740>.
- Wegzyn CM, Fredrick LM, Stubbs RO, Woodward WC, Norton M. Diarrhea associated with lopinavir/ritonavir-based therapy: results of a meta-analysis of 1469

- HIV-1-infected participants. *J Int Assoc Physicians AIDS Care (Chic)*. 2012;11(4):252-259. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22544446>.
8. Oumar AA, Diallo K, Dembele JP, et al. Adverse drug reactions to antiretroviral therapy: prospective study in children in sikasso (mali). *J Pediatr Pharmacol Ther*. 2012;17(4):382-388. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23411444>.
 9. Wattanuchariya N, Sirisanthana V, Oberdorfer P. Effectiveness and safety of protease inhibitor-based regimens in HIV-infected Thai children failing first-line treatment. *HIV Med*. 2013;14(4):226-232. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23094820>.
 10. Van Dyke RB, Wang L, Williams PL, Pediatric AIDS Clinical Trials Group C Team. Toxicities associated with dual nucleoside reverse-transcriptase inhibitor regimens in HIV-infected children. *J Infect Dis*. 2008;198(11):1599-1608. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19000014>.
 11. Clay PG, Crutchley RD. Noninfectious diarrhea in HIV seropositive individuals: a review of prevalence rates, etiology, and management in the era of combination antiretroviral therapy. *Infect Dis Ther*. 2014. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25388760>.
 12. Szoke D, Ridolfo A, Valente C, Galli M, Panteghini M. Frequency of pancreatic hyperamylasemia in human immunodeficiency virus-positive patients in the highly active antiretroviral therapy era. *Am J Clin Pathol*. 2016;145(1):128-133. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26712880>.
 13. Castro JG, Chin-Beckford N. Crofelemer for the symptomatic relief of non-infectious diarrhea in adult patients with HIV/AIDS on anti-retroviral therapy. *Expert Rev Clin Pharmacol*. 2015;8(6):683-690. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26517110>.
 14. Dikman AE, Schonfeld E, Srisarajivakul NC, Poles MA. Human Immunodeficiency virus-associated diarrhea: still an issue in the era of antiretroviral therapy. *Dig Dis Sci*. 2015;60(8):2236-2245. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25772777>.
 15. Logan C, Beadsworth MB, Beeching NJ. HIV and diarrhoea: what is new? *Curr Opin Infect Dis*. 2016;29(5):486-494. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27472290>.