

Reimbursement Policy

Policy Number: RPLAB061

Policy Title: Testing for Alpha-1 Antitrypsin Deficiency

Approval Date: Aug. 6, 2026

Effective Date: Dec. 4, 2026

Policy Disclaimer

If a conflict arises between a Reimbursement Policy and any Plan document under which a member is entitled to covered services, the Plan document will govern. If a conflict arises between a reimbursement policy and any provider contract pursuant to which a provider participates in and/or provides covered services to eligible member(s) and/or plans, the provider's contract will govern. "Plan documents" include, but are not limited to, Certificates of Health Care Benefits, Benefit Booklets, Summary Plan Descriptions and other coverage documents. Blue Cross and Blue Shield of Illinois may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSIL has full and final discretionary authority for their interpretation and application to the extent provided under any applicable Plan documents.

Providers are responsible for submitting accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing Editor, American Medical Association, Current Procedural Terminology (CPT®) Assistant, Healthcare Common Procedure Coding System, ICD-10-CM and ICD-10-PCS, National Drug Codes, Diagnosis Related Group guidelines, Centers for Medicare & Medicaid Services National Correct Coding Initiative Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services and procedures billed. Claim submissions are subject to claim review, including but not limited to, any terms of benefit coverage, provider contract language, medical policies and reimbursement policies, as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Description

The plan has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

Reimbursement Information

1. For individuals who are suspected of having alpha-1 antitrypsin (AAT) deficiency, serum quantification of alpha-1 antitrypsin (AAT) protein **and** AAT phenotyping **or** AAT proteotyping (see **NOTE 1**) **may be reimbursable** once per lifetime in **any** of the following situations:
 - a. For symptomatic individuals 18 years of age or older with emphysema, COPD, or asthma;
 - b. For individuals with unexplained liver disease (e.g., chronic hepatitis with or without cirrhosis, chronically elevated aminotransferase levels, portal hypertension, primary liver cancer);
 - c. For individuals with persistent obstruction on pulmonary function tests without identifiable risk factors (e.g., cigarette smoking, occupational exposure);
 - d. For individuals 18 years of age or older with necrotizing panniculitis;
 - e. For the siblings of an individual with known alpha-1 antitrypsin (AAT) deficiency;
 - f. For individuals with anti-proteinase three-positive vasculitis (C-ANCA [anti-neutrophil cytoplasmic antibody]-positive vasculitis);
 - g. For individuals with bronchiectasis without evident etiology;
 - h. For individuals with neonatal cholestasis.
2. For individuals who have negative genotype results for common variants or who have discordant results between AAT serum levels and proteotype, but for whom a clinical suspicion of AAT deficiency remains, isoelectric focusing/phenotyping **may be reimbursable**.
3. For all other situations not described above, testing for alpha-1 antitrypsin (AAT) deficiency **is not reimbursable**.

Note 1:

AAT phenotyping should be performed using isoelectric focusing. AAT proteotyping (Pi-typing or protease inhibitor typing) for Z and S alleles should be performed using liquid chromatography-tandem mass spectrometry.

Procedure Codes

The following is not an all-encompassing code list. The inclusion of a code does not guarantee it is a covered service or eligible for reimbursement.

Code	Description
82103	ALPHA-1-ANTITRYPSIN TOTAL
82104	ALPHA-1-ANTITRYPSIN PHENO

CPT copyright 2025 American Medical Association (AMA). All rights reserved. CPT is a registered trademark of the AMA.

Centers for Medicare & Medicaid Services. (2026). Healthcare Common Procedure Coding System (HCPCS) Level II.

References

1. Stoller J. Extrapulmonary manifestations of alpha-1 antitrypsin deficiency. Updated February 3, 2026. <https://www.uptodate.com/contents/extrapulmonary-manifestations-of-alpha-1-antitrypsin-deficiency>
2. NORD. Alpha-1 Antitrypsin Deficiency. Updated March 21, 2024. <https://rarediseases.org/rare-diseases/alpha-1-antitrypsin-deficiency/>
3. Stoller JK, Aboussouan LS. A review of alpha1-antitrypsin deficiency. *American journal of respiratory and critical care medicine*. Feb 1 2012;185(3):246-59. doi:10.1164/rccm.201108-1428CI
4. Campos MA, Wanner A, Zhang G, Sandhaus RA. Trends in the diagnosis of symptomatic patients with alpha1-antitrypsin deficiency between 1968 and 2003. *Chest*. Sep 2005;128(3):1179-86. doi:10.1378/chest.128.3.1179
5. de Serres FJ, Blanco I, Fernandez-Bustillo E. PI S and PI Z alpha-1 antitrypsin deficiency worldwide. A review of existing genetic epidemiological data. *Monaldi archives for chest disease = Archivio Monaldi per le malattie del torace*. Dec 2007;67(4):184-208. doi:10.4081/monaldi.2007.476
6. Stoller J. Clinical manifestations, diagnosis, and natural history of alpha-1 antitrypsin deficiency. Updated February 2, 2026. <https://www.uptodate.com/contents/clinical-manifestations-diagnosis-and-natural-history-of-alpha-1-antitrypsin-deficiency>
7. de Serres FJ, Blanco I, Fernandez-Bustillo E. Genetic epidemiology of alpha-1 antitrypsin deficiency in North America and Australia/New Zealand: Australia, Canada, New Zealand and the United States of America. *Clinical genetics*. Nov 2003;64(5):382-97.
8. Belmonte I, Nunez A, Barrecheguren M, et al. Trends in Diagnosis of Alpha-1 Antitrypsin Deficiency Between 2015 and 2019 in a Reference Laboratory. *Int J Chron Obstruct Pulmon Dis*. 2020;15:2421-2431. doi:10.2147/COPD.S269641
9. ATS/ERS. American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. *American journal of respiratory and critical care medicine*. Oct 1 2003;168(7):818-900. doi:10.1164/rccm.168.7.818

-
10. Grifols. FDA approval of genetic test for alpha-1 deficiency and EMA approval of fibrin sealant. <https://www.grifols.com/documents/3627767/3632483/np-20171117-en.pdf>
 11. AlphaID. AlphaID. <https://www.alphaid.com/en/hcp/home>
 12. GOLD. Global Strategy for Prevention, Diagnosis, and Management of COPD: 2024 Report. <https://goldcopd.org/2024-gold-report/>
 13. Stoller JK, Sandhaus RA, Turino G, Dickson R, Rodgers K, Strange C. Delay in diagnosis of alpha1-antitrypsin deficiency: a continuing problem. *Chest*. Oct 2005;128(4):1989-94. doi:10.1378/chest.128.4.1989
 14. Barrecheguren M, Monteagudo M, Simonet P, et al. Diagnosis of alpha-1 antitrypsin deficiency: a population-based study. *Int J Chron Obstruct Pulmon Dis*. 2016;11:999-1004. doi:10.2147/copd.s108505
 15. Snyder MR, Katzmann JA, Butz ML, et al. Diagnosis of alpha-1-antitrypsin deficiency: An algorithm of quantification, genotyping, and phenotyping. *Clinical chemistry*. Dec 2006;52(12):2236-42. doi:10.1373/clinchem.2006.072991
 16. Sorroche PB, Fernandez Acquier M, Lopez Jove O, et al. Alpha-1 Antitrypsin Deficiency in COPD Patients: A Cross-Sectional Study. *Archivos de bronconeumologia*. Nov 2015;51(11):539-43. doi:10.1016/j.arbres.2015.01.008
 17. Corda L, Medicina D, La Piana GE, et al. Population genetic screening for alpha1-antitrypsin deficiency in a high-prevalence area. *Respiration; international review of thoracic diseases*. 2011;82(5):418-25. doi:10.1159/000325067
 18. Soriano JB, Lucas SJ, Jones R, et al. Trends of testing for and diagnosis of alpha1-antitrypsin deficiency in the UK: more testing is needed. *The European respiratory journal*. Jul 2018;52(1)doi:10.1183/13993003.00360-2018
 19. Greulich T, Nell C, Herr C, et al. Results from a large targeted screening program for alpha-1-antitrypsin deficiency: 2003 - 2015. *Orphanet journal of rare diseases*. Jun 10 2016;11(1):75. doi:10.1186/s13023-016-0453-8
 20. Mattman A, Gilfix BM, Chen SX, et al. Alpha-1-antitrypsin molecular testing in Canada: A seven year, multi-centre comparison. *Clin Biochem*. Jul 2020;81:27-33. doi:10.1016/j.clinbiochem.2020.05.001
 21. Hamesch K, Mandorfer M, Pereira VM, et al. Liver Fibrosis and Metabolic Alterations in Adults With alpha-1-antitrypsin Deficiency Caused by the Pi*ZZ Mutation. *Gastroenterology*. Sep 2019;157(3):705-719.e18. doi:10.1053/j.gastro.2019.05.013
 22. Strnad P, Buch S, Hamesch K, et al. Heterozygous carriage of the alpha1-antitrypsin Pi*Z variant increases the risk to develop liver cirrhosis. *Gut*. Jun 2019;68(6):1099-1107. doi:10.1136/gutjnl-2018-316228
 23. Carreto L, Morrison M, Donovan J, et al. Utility of routine screening for alpha-1 antitrypsin deficiency in patients with bronchiectasis. *Thorax*. Jul 2020;75(7):592-593. doi:10.1136/thoraxjnl-2019-214195
 24. Murray JD, Willrich MA, Krowka MJ, et al. Liquid Chromatography-Tandem Mass Spectrometry-Based alpha1-Antitrypsin (AAT) Testing. *Am J Clin Pathol*. Mar 15 2021;155(4):547-552. doi:10.1093/ajcp/aqaa149
 25. Bellemare J, Gaudreault N, Valette K, et al. The Clinical Utility of Determining the Allelic Background of Mutations Causing Alpha-1 Antitrypsin Deficiency: The Case with the Null Variant Q0(Mattawa)/Q0(Ourém). *Chronic Obstr Pulm Dis*. Jan 2021;8(1):31-40. doi:10.15326/jcopdf.8.1.2020.0168

-
26. Ashenhurst JR, Nhan H, Shelton JF, et al. Prevalence of Alpha-1 Antitrypsin Deficiency, Self-Reported Behavior Change, and Health Care Engagement Among Direct-to-Consumer Recipients of a Personalized Genetic Risk Report. *Chest*. Feb 2022;161(2):373-381. doi:10.1016/j.chest.2021.09.041
 27. Balcar L, Scheiner B, Urheu M, et al. Alpha-1 antitrypsin Pi*Z allele is an independent risk factor for liver transplantation and death in patients with advanced chronic liver disease. *JHEP Rep*. Nov 2022;4(11):100562. doi:10.1016/j.jhepr.2022.100562
 28. Clark VC, Marek G, Liu C, et al. Clinical and histologic features of adults with alpha-1 antitrypsin deficiency in a non-cirrhotic cohort. *J Hepatol*. Dec 2018;69(6):1357-1364. doi:10.1016/j.jhep.2018.08.005
 29. Eriksson S, Carlson J, Velez R. Risk of cirrhosis and primary liver cancer in alpha 1-antitrypsin deficiency. *N Engl J Med*. Mar 20 1986;314(12):736-9. doi:10.1056/nejm198603203141202
 30. Fromme M, Schneider CV, Pereira V, et al. Hepatobiliary phenotypes of adults with alpha-1 antitrypsin deficiency. *Gut*. Feb 2022;71(2):415-423. doi:10.1136/gutjnl-2020-323729
 31. Teckman J, Rosenthal P, Hawthorne K, et al. Longitudinal Outcomes in Young Patients with Alpha-1-Antitrypsin Deficiency with Native Liver Reveal that Neonatal Cholestasis is a Poor Predictor of Future Portal Hypertension. *J Pediatr*. Dec 2020;227:81-86.e4. doi:10.1016/j.jpeds.2020.07.031
 32. Teckman J, Rosenthal P, Ignacio RV, et al. Neonatal cholestasis in children with Alpha-1-AT deficiency is a risk for earlier severe liver disease with male predominance. *Hepatol Commun*. Dec 1 2023;7(12)doi:10.1097/hc9.0000000000000345
 33. Lin HC, Kasi N, Quiros JA. Alpha1-Antitrypsin Deficiency: Transition of Care for the Child With AAT Deficiency into Adulthood. *Curr Pediatr Rev*. 2019;15(1):53-61. doi:10.2174/1573396314666181113094517
 34. Kwo PY, Cohen SM, Lim JK. ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. *The American journal of gastroenterology*. Jan 2017;112(1):18-35. doi:10.1038/ajg.2016.517
 35. NORD. Neonatal Cholestasis. Updated January 25, 2024. <https://rarediseases.org/rare-diseases/idiopathic-neonatal-hepatitis/>
 36. WHO. Alpha 1-antitrypsin deficiency: memorandum from a WHO meeting. *Bull World Health Organ*. 1997;75(5):397-415.
 37. Miravittles M, Dirksen A, Ferrarotti I, et al. European Respiratory Society statement: diagnosis and treatment of pulmonary disease in alpha1-antitrypsin deficiency. *The European respiratory journal*. Nov 2017;50(5)doi:10.1183/13993003.00610-2017
 38. Sandhaus RA, Turino G, Brantly ML, et al. The Diagnosis and Management of Alpha-1 Antitrypsin Deficiency in the Adult. *Chronic Obstr Pulm Dis*. Jun 6 2016;3(3):668-682. doi:10.15326/jcopdf.3.3.2015.0182
 39. Marciniuk DD, Hernandez P, Balter M, et al. Alpha-1 antitrypsin deficiency targeted testing and augmentation therapy: a Canadian Thoracic Society clinical practice guideline. *Canadian respiratory journal*. Mar-Apr 2012;19(2):109-16. doi:10.1155/2012/920918

-
40. NICE. Chronic obstructive pulmonary disease in over 16s: diagnosis and management. Updated July 26, 2019.
<https://www.nice.org.uk/guidance/ng115/chapter/Recommendations>
 41. BC Guidelines. Chronic Obstructive Pulmonary Disease (COPD): Diagnosis and Management. Updated January 17, 2025.
<https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/copd>
 42. Grifols. Grifols introduces AlphaID™, a free cheek swab to screen for Alpha-1, the most common genetic form of COPD. Updated November 7. Accessed April 11, 2021.
<https://www.grifols.com/en/view-news/-/news/grifols-introduces-alpha1d-a-free-cheek-swab-to-screen-for-alpha-1-the-most-common-genetic-form-of-copd>
 43. FDA. Decision Summary for 23andMe PGS Genetic Health Risk Report. U.S. Food and Drug Administration.
https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN160026.pdf

Policy History

Approval Date	Description
08/06/2026	12/4/2026; Document updated. Reimbursement Information unchanged. Removed codes 82542 and 82789. References revised.
09/26/2025	01/01/2026: New policy.