If a conflict arises between a Clinical Payment and Coding 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 CPCP 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 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 Texas may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSTX has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of 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 PCS, National Drug Codes, Diagnosis Related Group guidelines, Centers for Medicare and 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/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Gamma-glutamyl Transferase in Adults

Policy Number: CPCPLAB056

Version 1.0

Approval Date: February 5, 2025

Plan Effective Date: May 15, 2025

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:

NOTE: This policy is specific to individuals 18 years of age or older. Criteria below do not apply to individuals less than 18 years of age.

1. For individuals with elevated alkaline phosphatase activity, serum GGT testing no more than once every two weeks **may be reimbursable**.

2. To assess for liver injury, function, and/or disease, serum GGT testing no more than once every two weeks **may be reimbursable** for individuals with at least **one** of the following:
    a. Chronic alcohol use;
    b. Long-term drug therapy known to have a potential for causing liver toxicity;
    c. Exposure to hepatotoxins;
    d. Viral hepatitis, amoebiasis, tuberculosis, psittacosis, or similar infections that may cause hepatic injury;
    e. Primary or secondary malignant neoplasms;
    f. Diabetes mellitus;
    g. Malnutrition;
    h. Disorders of iron and mineral metabolism;
    i. Sarcoidosis;
    j. Amyloidosis;
    k. Lupus;
    l. Hypertension;
    m. Gastrointestinal disease;
    n. Pancreatic disease;
    o. As part of liver function assessment subsequent to liver transplantation.

3. For asymptomatic individuals, serum GGT testing during a wellness visit or a general exam without abnormal findings **is not reimbursable**.

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.

Codes
82977

References:

AACC. (2024). *Gamma-Glutamyl Transferase (GGT)*. https://www.labtestsonline.org/tests/gamma-glutamyl-transferase-ggt

Andrade, R., Aithal, G., Björnsson, E., Kaplowitz, N., Kullak-Ublick, G., Larrey, D., & Karlsen, T. (2019). EASL Clinical Practice Guidelines: Drug-induced liver injury. *J Hepatol*, *70*(6), 1222-1261. https://doi.org/10.1016/j.jhep.2019.02.014

Andrews, S. J., Goate, A., & Anstey, K. J. (2020). Association between alcohol consumption and Alzheimer's disease: A Mendelian randomization study. *Alzheimers Dement*, *16*(2), 345-353. https://doi.org/10.1016/j.jalz.2019.09.086

Arasteh, S., Moohebati, M., Avan, A., Esmaeili, H., Ghazizadeh, H., Mahdizadeh, A., Rahmani, F., Mohamamdazade, E., Ferns, G. A., Parizadeh, M. R., & Ghayour-Mobarhan, M. (2018). Serum level of gamma-glutamyl transferase as a biomarker for predicting stenosis severity in patients with coronary artery disease. *Indian Heart J*, *70*(6), 788-792. https://doi.org/10.1016/j.ihj.2017.11.017

ASAM. (2020). The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management. *J Addict Med*, *14*(3S Suppl 1), 1-72. https://doi.org/10.1097/adm.0000000000000668

Berzigotti, A., Tsochatzis, E., Boursier, J., Castera, L., Cazzagon, N., Friedrich-Rust, M., Petta, S., & Thiele, M. (2021). EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. *J Hepatol*, *75*(3), 659-689. https://doi.org/10.1016/j.jhep.2021.05.025

Castera, L., Chan, H., Arrese, M., Afdhal, N., Bedossa, P., Friedrich-Rust, M., & Han KH, P., M. (2015). EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis. *J Hepatol*, *63*(1), 237-264. https://doi.org/10.1016/j.jhep.2015.04.006

Celik, O., Cakmak, H. A., Satilmis, S., Gungor, B., Akin, F., Ozturk, D., Yalcin, A. A., Ayca, B., Erturk, M., Atasoy, M. M., & Uslu, N. (2014). The relationship between gamma-glutamyl transferase levels and coronary plaque burdens and plaque structures in young adults with coronary atherosclerosis. *Clin Cardiol*, *37*(9), 552-557. https://doi.org/10.1002/clc.22307

Choe, Y. M., Lee, B. C., Choi, I. G., Suh, G. H., Lee, D. Y., & Kim, J. W. (2019). Combination of the CAGE and serum gamma-glutamyl transferase: an effective screening tool for alcohol use disorder and alcohol dependence. *Neuropsychiatr Dis Treat*, *15*, 1507-1515. https://doi.org/10.2147/ndt.s203855

Chung, H. S., Lee, J. S., Kim, J. A., Roh, E., Lee, Y. B., Hong, S. H., Yoo, H. J., Baik, S. H., Kim, N. H., Seo, J. A., Kim, S. G., Kim, N. H., & Choi, K. M. (2019). gamma-Glutamyltransferase Variability and the Risk of Mortality, Myocardial Infarction, and Stroke: A Nationwide Population-Based Cohort Study. *J Clin Med*, *8*(6). https://doi.org/10.3390/jcm8060832

CMS. (2023, 1/2023). *National Coverage Determination (NCD) for Gamma Glutamyl Transferase (190.32)*. Centers for Medicare & Medicaid Services. Retrieved 03/03/2020 from https://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/Downloads/R17NCD.pdf

Conigrave, K. M., Degenhardt, L. J., Whitfield, J. B., Saunders, J. B., Helander, A., & Tabakoff, B. (2002). CDT, GGT, and AST as markers of alcohol use: the WHO/ISBRA collaborative project. *Alcohol Clin Exp Res*, *26*(3), 332-339. https://doi.org/10.1111/j.1530-0277.2002.tb02542.x

De Silva, N. M. G., Borges, M. C., Hingorani, A. D., Engmann, J., Shah, T., Zhang, X., Luan, J., Langenberg, C., Wong, A., Kuh, D., Chambers, J. C., Zhang, W., Jarvelin, M. R., Sebert, S., Auvinen, J., Gaunt, T. R., & Lawlor, D. A. (2019). Liver Function and Risk of Type 2 Diabetes: Bidirectional Mendelian Randomization Study. *Diabetes*, *68*(8), 1681-1691. https://doi.org/10.2337/db18-1048

Dillon, J. F., & Miller, M. H. (2016). Gamma glutamyl transferase 'To be or not to be' a liver function test? *Ann Clin Biochem*, *53*(6), 629-631. https://doi.org/10.1177/0004563216659887

Dixit, S., & Singh, P. (2015). Usefulness of Gamma Glutamyl Transferase as Reliable Biological Marker in Objective Corroboration of Relapse in Alcohol Dependent Patients. *J Clin Diagn Res*, *9*(12), Vc01-vc04. https://doi.org/10.7860/jcdr/2015/14752.6895

Engelken, F. J., Bettschart, V., Rahman, M. Q., Parks, R. W., & Garden, O. J. (2003). Prognostic factors in the palliation of pancreatic cancer. *Eur J Surg Oncol*, *29*(4), 368-373. https://doi.org/10.1053/ejso.2002.1405

Friedman, L. (2024, April 8). *Approach to the patient with abnormal liver biochemical and function tests*. https://www.uptodate.com/contents/approach-to-the-patient-with-abnormal-liver-biochemical-and-function-tests

Gori, E., Pierini, A., Lippi, I., Boffa, N., Perondi, F., & Marchetti, V. (2019). Urinalysis and Urinary GGT-to-Urinary Creatinine Ratio in Dogs with Acute Pancreatitis. *Vet Sci*, *6*(1). https://doi.org/10.3390/vetsci6010027

Gowda, S., Desai, P. B., Hull, V. V., Math, A. A., Vernekar, S. N., & Kulkarni, S. S. (2009). A review on laboratory liver function tests. *Pan Afr Med J*, *3*, 17. https://www.ncbi.nlm.nih.gov/pubmed/21532726

Grundy, S. M. (2007). Gamma-glutamyl transferase: another biomarker for metabolic syndrome and cardiovascular risk. *Arterioscler Thromb Vasc Biol*, *27*(1), 4-7. https://doi.org/10.1161/01.atv.0000253905.13219.4b

Hong, S. H., Han, K., Park, S., Kim, S. M., Kim, N. H., Choi, K. M., Baik, S. H., Park, Y. G., & Yoo, H. J. (2020). Gamma-Glutamyl Transferase Variability and Risk of Dementia in Diabetes Mellitus: A Nationwide Population-Based Study. *J Clin Endocrinol Metab*, *105*(3). https://doi.org/10.1210/clinem/dgaa019

Huang, C. F., Yeh, M. L., Tsai, P. C., Hsieh, M. H., Yang, H. L., Hsieh, M. Y., Yang, J. F., Lin, Z. Y., Chen, S. C., Wang, L. Y., Dai, C. Y., Huang, J. F., Chuang, W. L., & Yu, M. L. (2014). Baseline gamma-glutamyl transferase levels strongly correlate with hepatocellular carcinoma development in non-cirrhotic patients with successful

hepatitis C virus eradication. *J Hepatol*, *61*(1), 67-74. https://doi.org/10.1016/j.jhep.2014.02.022
Jousilahti, P., Rastenyte, D., & Tuomilehto, J. (2000). Serum gamma-glutamyl transferase, self-reported alcohol drinking, and the risk of stroke. *Stroke*, *31*(8), 1851-1855. https://doi.org/10.1161/01.str.31.8.1851
Kaneko, K., Yatsuya, H., Li, Y., Uemura, M., Chiang, C., Hirakawa, Y., Ota, A., Tamakoshi, K., & Aoyama, A. (2019). Association of gamma-glutamyl transferase and alanine aminotransferase with type 2 diabetes mellitus incidence in middle-aged Japanese men: 12-year follow up. *J Diabetes Investig*, *10*(3), 837-845. https://doi.org/10.1111/jdi.12930
Koenig, G., & Seneff, S. (2015). Gamma-Glutamyltransferase: A Predictive Biomarker of Cellular Antioxidant Inadequacy and Disease Risk. *Dis Markers*, *2015*, 818570. https://doi.org/10.1155/2015/818570
Korantzopoulos, P., Tzimas, P., Kalantzi, K., Kostapanos, M., Vemmos, K., Goudevenos, J., Elisaf, M., & Milionis, H. (2009). Association between serum gamma-glutamyltransferase and acute ischemic nonembolic stroke in elderly subjects. *Arch Med Res*, *40*(7), 582-589. https://doi.org/10.1016/j.arcmed.2009.07.012
Kunutsor, S. K., Abbasi, A., & Adler, A. I. (2014). Gamma-glutamyl transferase and risk of type II diabetes: an updated systematic review and dose-response meta-analysis. *Ann Epidemiol*, *24*(11), 809-816. https://doi.org/10.1016/j.annepidem.2014.09.001
Kwo, P. Y., Cohen, S. M., & Lim, J. K. (2017). ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. *Am J Gastroenterol*, *112*(1), 18-35. https://doi.org/10.1038/ajg.2016.517
LabCorp. (2021). *γ-Glutamyl Transferase (GGT)*. https://www.labcorp.com/tests/001958/glutamyl-transferase-ggt
Lee, D. Y., Han, K., Yu, J. H., Park, S., Seo, J. A., Kim, N. H., Yoo, H. J., Kim, S. G., Kim, S. M., Choi, K. M., Baik, S. H., Park, Y. G., & Kim, N. H. (2020). Prognostic value of long-term gamma-glutamyl transferase variability in individuals with diabetes: a nationwide population-based study. *Scientific Reports*, *10*(1), 15375. https://doi.org/10.1038/s41598-020-72318-7
Lee, J., Kim, M. Y., Kang, S. H., Kim, J., Uh, Y., Yoon, K. J., & Kim, H. S. (2018). The gamma-glutamyl transferase to platelet ratio and the FIB-4 score are noninvasive markers to determine the severity of liver fibrosis in chronic hepatitis B infection. *Br J Biomed Sci*, *75*(3), 128-132. https://doi.org/10.1080/09674845.2018.1459147
Lee, M. Y., Hyon, D. S., Huh, J. H., Kim, H. K., Han, S. K., Kim, J. Y., & Koh, S. B. (2019). Association between Serum Gamma-Glutamyltransferase and Prevalence of Metabolic Syndrome Using Data from the Korean Genome and Epidemiology Study. *Endocrinol Metab (Seoul)*, *34*(4), 390-397. https://doi.org/10.3803/enm.2019.34.4.390
Li, S., Liao, X., Pan, Y., Xiang, X., & Zhang, Y. (2022). Gamma-glutamyl transferase levels are associated with the occurrence of post-stroke cognitive impairment: a

multicenter cohort study. *BMC Neurology*, *22*(1), 65. https://doi.org/10.1186/s12883-022-02587-4
Lippi, I., Perondi, F., Meucci, V., Bruno, B., Gazzano, V., & Guidi, G. (2018). Clinical utility of urine kidney injury molecule-1 (KIM-1) and gamma-glutamyl transferase (GGT) in the diagnosis of canine acute kidney injury. *Vet Res Commun*, *42*(2), 95-100. https://doi.org/10.1007/s11259-018-9711-7
Liu, C. F., Zhou, W. N., Lu, Z., Wang, X. T., & Qiu, Z. H. (2018). The associations between liver enzymes and the risk of metabolic syndrome in the elderly. *Exp Gerontol*, *106*, 132-136. https://doi.org/10.1016/j.exger.2018.02.026
Lothar, T. (2022). Enzymes In *Clinical Laboratory Diagnostics* https://www.clinical-laboratory-diagnostics.com/k01.html
Minuk, G. Y. (1998). Canadian Association of Gastroenterology Practice Guidelines: evaluation of abnormal liver enzyme tests. *Can J Gastroenterol*, *12*(6), 417-421. https://doi.org/10.1155/1998/943498
Mujawar, S. J., Suchitra, G., Kosandal, K. A., Choudhari, S., Inamdar, N. A., & Ahmed, K. B. (2020). Evaluation of salivary gamma-glutamyl transpeptidase as a biomarker in oral squamous cell carcinoma and precancerous lesions. *Journal of oral and maxillofacial pathology : JOMFP*, *24*(3), 584-584. https://doi.org/10.4103/jomfp.JOMFP_73_20
Nano, J., Muka, T., Ligthart, S., Hofman, A., Darwish Murad, S., Janssen, H. L. A., Franco, O. H., & Dehghan, A. (2017). Gamma-glutamyltransferase levels, prediabetes and type 2 diabetes: a Mendelian randomization study. *Int J Epidemiol*, *46*(5), 1400-1409. https://doi.org/10.1093/ije/dyx006
Ndrepepa, G., Colleran, R., & Kastrati, A. (2018). Gamma-glutamyl transferase and the risk of atherosclerosis and coronary heart disease. *Clin Chim Acta*, *476*, 130-138. https://doi.org/10.1016/j.cca.2017.11.026
Ndrepepa, G., Holdenrieder, S., Cassese, S., Fusaro, M., Xhepa, E., Laugwitz, K. L., Schunkert, H., & Kastrati, A. (2018). A comparison of gamma-glutamyl transferase and alkaline phosphatase as prognostic markers in patients with coronary heart disease. *Nutr Metab Cardiovasc Dis*, *28*(1), 64-70. https://doi.org/10.1016/j.numecd.2017.09.005
Ndrepepa, G., & Kastrati, A. (2016). Gamma-glutamyl transferase and cardiovascular disease. *Ann Transl Med*, *4*(24), 481. https://doi.org/10.21037/atm.2016.12.27
Newsome, P. N., Cramb, R., Davison, S. M., Dillon, J. F., Foulerton, M., Godfrey, E. M., Hall, R., Harrower, U., Hudson, M., Langford, A., Mackie, A., Mitchell-Thain, R., Sennett, K., Sheron, N. C., Verne, J., Walmsley, M., & Yeoman, A. (2018). Guidelines on the management of abnormal liver blood tests. *Gut*, *67*(1), 6-19. https://doi.org/10.1136/gutjnl-2017-314924
Nivukoski, U., Bloigu, A., Bloigu, R., Aalto, M., Laatikainen, T., & Niemela, O. (2019). Liver enzymes in alcohol consumers with or without binge drinking. *Alcohol*, *78*, 13-19. https://doi.org/10.1016/j.alcohol.2019.03.001
Noborisaka, Y., Ishizaki, M., Yamazaki, M., Honda, R., & Yamada, Y. (2013). Elevated Serum Gamma-Glutamyltransferase (GGT) Activity and the Development of

Chronic Kidney Disease (CKD) in Cigarette Smokers. *Nephrourol Mon*, *5*(5), 967-973. https://doi.org/10.5812/numonthly.13652

Rosoff, D. B., Charlet, K., Jung, J., Lee, J., Muench, C., Luo, A., Longley, M., Mauro, K. L., & Lohoff, F. W. (2019). Association of High-Intensity Binge Drinking With Lipid and Liver Function Enzyme Levels. *JAMA Netw Open*, *2*(6), e195844. https://doi.org/10.1001/jamanetworkopen.2019.5844

Sette, L. H., & Almeida Lopes, E. P. (2014). Liver enzymes serum levels in patients with chronic kidney disease on hemodialysis: a comprehensive review. *Clinics (Sao Paulo)*, *69*(4), 271-278. https://doi.org/10.6061/clinics/2014(04)09

Shibabaw, T., Dessie, G., Molla, M. D., Zerihun, M. F., & Ayelign, B. (2019). Assessment of liver marker enzymes and its association with type 2 diabetes mellitus in Northwest Ethiopia. *BMC Res Notes*, *12*(1), 707. https://doi.org/10.1186/s13104-019-4742-x

Singh, M., Tiwary, S., Patil, D., Sharma, D., & Shukla, V. (2006). Gamma-Glutamyl Transpeptidase (GGT) As A Marker In Obstructive Jaundice. *The Internet Journal of Surgery*, *9*. http://ispub.com/IJS/9/2/7169

Thursz, M., Gual, A., Lackner, C., Mathurin, P., Moreno, C., Spahr, L., Sterneck, M., & Cortez-Pinto, H. (2018). EASL Clinical Practice Guidelines: Management of alcohol-related liver disease. *J Hepatol*, *69*(1), 154-181. https://doi.org/10.1016/j.jhep.2018.03.018

Vos, M. B., Abrams, S. H., Barlow, S. E., Caprio, S., Daniels, S. R., Kohli, R., Mouzaki, M., Sathya, P., Schwimmer, J. B., Sundaram, S. S., & Xanthakos, S. A. (2017). NASPGHAN Clinical Practice Guideline for the Diagnosis and Treatment of Nonalcoholic Fatty Liver Disease in Children: Recommendations from the Expert Committee on NAFLD (ECON) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). *J Pediatr Gastroenterol Nutr*, *64*(2), 319-334. https://doi.org/10.1097/mpg.0000000000001482

Vroon, D., & Israili, Z. (1990). *Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition.* https://www.ncbi.nlm.nih.gov/books/NBK203/

Wang, R. Q., Zhang, Q. S., Zhao, S. X., Niu, X. M., Du, J. H., Du, H. J., & Nan, Y. M. (2016). Gamma-glutamyl transpeptidase to platelet ratio index is a good noninvasive biomarker for predicting liver fibrosis in Chinese chronic hepatitis B patients. *J Int Med Res*, *44*(6), 1302-1313. https://doi.org/10.1177/0300060516664638

Wang, S., Zhang, J., Zhu, L., Song, L., Meng, Z., Jia, Q., Li, X., Liu, N., Hu, T., Zhou, P., Zhang, Q., Liu, L., Song, K., & Jia, Q. (2017). Association between liver function and metabolic syndrome in Chinese men and women. *Sci Rep*, *7*, 44844. https://doi.org/10.1038/srep44844

Wang, Z., Song, P., Xia, J., Inagaki, Y., Tang, W., & Kokudo, N. (2014). Can gamma-glutamyl transferase levels contribute to a better prognosis for patients with hepatocellular carcinoma? *Drug Discov Ther*, *8*(3), 134-138. https://doi.org/10.5582/ddt.2014.01025

Xing, M., Gao, M., Li, J., Han, P., Mei, L., & Zhao, L. (2022). Characteristics of peripheral blood Gamma-glutamyl transferase in different liver diseases. *Medicine*, *101*(1), e28443-e28443. https://doi.org/10.1097/md.0000000000028443

Xu, T., Wang, W., Zhai, L., Zhang, Y. F., Zhou, H. Z., Wu, X. M., Li, A. H., Xie, L. L., Ning, X. J., Ji, Y. T., Wang, H. M., & Ke, K. F. (2017). Serum Gamma-glutamyl Transferase Levels Predict Functional Outcomes after Aneurysmal Subarachnoid Hemorrhage. *Biomed Environ Sci*, *30*(3), 170-176. https://doi.org/10.3967/bes2017.024

Yamada, J., Tomiyama, H., Yambe, M., Koji, Y., Motobe, K., Shiina, K., Yamamoto, Y., & Yamashina, A. (2006). Elevated serum levels of alanine aminotransferase and gamma glutamyltransferase are markers of inflammation and oxidative stress independent of the metabolic syndrome. *Atherosclerosis*, *189*(1), 198-205. https://doi.org/10.1016/j.atherosclerosis.2005.11.036

Yang, W., Kang, D. W., & Lee, S. H. (2020). Effects of Gamma-Glutamyl Transferase on Stroke Occurrence Mediated by Atrial Fibrillation. *J Clin Neurol*, *16*(1), 60-65. https://doi.org/10.3988/jcn.2020.16.1.60

Yao, T., Li, J., Long, Q., Li, G., Ding, Y., Cui, Q., & Liu, Z. (2019). Association between Serum Gamma-glutamyl transferase and Intracranial Arterial Calcification in Acute Ischemic Stroke Subjects. *Sci Rep*, *9*(1), 19998. https://doi.org/10.1038/s41598-019-56569-7

Yavuz, B. B., Yavuz, B., Halil, M., Cankurtaran, M., Ulger, Z., Cankurtaran, E. S., Aytemir, K., & Ariogul, S. (2008). Serum elevated gamma glutamyltransferase levels may be a marker for oxidative stress in Alzheimer's disease. *Int Psychogeriatr*, *20*(4), 815-823. https://doi.org/10.1017/s1041610208006790

Yoo, D., Kim, R., Jung, Y. J., Han, K., Shin, C. M., & Lee, J. Y. (2020). Serum gamma-glutamyltransferase activity and Parkinson's disease risk in men and women. *Sci Rep*, *10*(1), 1258. https://doi.org/10.1038/s41598-020-58306-x

Policy Update History:

Approval Date	Effective Date; Summary of Changes
02/05/2025	05/15/2025; Document updated with literature review. The following changes were made to Reimbursement Information: Note added clarifying the criteria in the policy applies only to individuals ages 18 years or older. References revised. Title changed from Gamma-glutamyl Transferase.
09/13/2024	01/01/2025: New policy.