

If a conflict arises between a Clinical Payment and Coding Policy (“CPCP”) 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. BCBSIL 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 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 (“HIPAA”) approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing (“UB”) Editor, American Medical Association (“AMA”), Current Procedural Terminology (“CPT®”), CPT® Assistant, Healthcare Common Procedure Coding System (“HCPCS”), ICD-10 CM and PCS, National Drug Codes (“NDC”), Diagnosis Related Group (“DRG”) guidelines, Centers for Medicare and Medicaid Services (“CMS”) National Correct Coding Initiative (“NCCI”) 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

Policy Number: CPCPLAB056

Version 1.0

Enterprise Medical Policy Committee Approval Date: January 25, 2022

Plan Effective Date: May 1, 2022

Description

BCBSIL 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:

The testing described below is applicable only for adult individuals aged 18 years and older.

1. Serum GGT testing* (See Note 1) **may be reimbursable** in individuals with elevated alkaline phosphatase activity.
2. Serum GGT testing* (See Note 1) to assess liver injury, function, and/or disease **may be reimbursable** in individuals who meet at least one of the following:

- a. Chronic alcohol or drug ingestion
- 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. Serum GGT testing **is not reimbursable** as part of a wellness check or for general encounters without abnormal findings.

***Note 1:** A maximum of one unit of GGT per week will be reimbursed for adult individuals. In accordance with NCD 190.32, “When used to assess liver dysfunction secondary to existing non-hepatobiliary disease with no change in signs, symptoms, or treatment, it is generally not necessary to repeat a GGT determination after a normal result has been obtained unless new indications are present (CMS, 2019).”

Procedure Codes

Codes
82977

References:

AACC. (2020). Gamma-Glutamyl Transferase (GGT). Retrieved from <https://labtestsonline.org/tests/gamma-glutamyl-transferase-ggt>

Agin, M., Tumgor, G., Alkan, M., Ozden, O., Satar, M., & Tuncer, R. (2016). Clues to the diagnosis of biliary atresia in neonatal cholestasis. *Turk J Gastroenterol*, 27(1), 37-41. doi:10.5152/tjg.2015.150379

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. doi: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. doi:10.1016/j.jalz.2019.09.086

Arasteh, S., Moohebaty, M., Avan, A., Esmaili, H., Ghazizadeh, H., Mahdizadeh, A., . . . 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. doi: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. doi:10.1097/adm.0000000000000668

BSPGHAN. (2020). UK Fatty Liver Guideline. Retrieved from https://bspghan.org.uk/wp-content/uploads/2020/08/LSG_UK-Fatty-Liver-Guideline-August-2020.pdf

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. doi:10.1016/j.jhep.2015.04.006

Celik, O., Cakmak, H. A., Satilmis, S., Gungor, B., Akin, F., Ozturk, D., . . . 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. doi:10.1002/clc.22307

Chen, X., Dong, R., Shen, Z., Yan, W., & Zheng, S. (2016). Value of Gamma-Glutamyl Transpeptidase for Diagnosis of Biliary Atresia by Correlation With Age. *J Pediatr Gastroenterol Nutr*, 63(3), 370-373. doi:10.1097/mpg.0000000000001168

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. doi:10.2147/ndt.S203855

Chung, H. S., Lee, J. S., Kim, J. A., Roh, E., Lee, Y. B., Hong, S. 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). doi:10.3390/jcm8060832

CMS. (2019, 10/2019). National Coverage Determination (NCD) for Gamma Glutamyl Transferase (190.32). Retrieved from <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?ncdid=153>

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. Retrieved from <https://onlinelibrary.wiley.com/doi/abs/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., . . . Lawlor, D. A. (2019). Liver Function and Risk of Type 2 Diabetes: Bidirectional Mendelian Randomization Study. *Diabetes*, 68(8), 1681-1691. doi: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. doi:10.1177/0004563216659887

Dong, R., Jiang, J., Zhang, S., Shen, Z., Chen, G., Huang, Y., . . . Zheng, S. (2018). Development and Validation of Novel Diagnostic Models for Biliary Atresia in a Large Cohort of Chinese Patients. *EBioMedicine*, 34, 223-230. doi:10.1016/j.ebiom.2018.07.025

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. doi:10.1053/ejso.2002.1405

Fawaz, R., Baumann, U., Ekong, U., Fischler, B., Hadzic, N., Mack, C. L., . . . Karpen, S. J. (2017). Guideline for the Evaluation of Cholestatic Jaundice in Infants: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr*, 64(1), 154-168. doi:10.1097/mpg.0000000000001334

Friedman, L. (2020). Approach to the patient with abnormal liver biochemical and function tests - UptoDate. Retrieved from https://www.uptodate.com/contents/approach-to-the-patient-with-abnormal-liver-biochemical-and-function-tests?search=Gamma-glutamyl%20Transferase&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2

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). doi: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. Retrieved from <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. doi:10.1161/01.ATV.0000253905.13219.4b

Hong, S. H., Han, K., Park, S., Kim, S. M., Kim, N. H., Choi, K. M., . . . 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). doi:10.1210/clinem/dgaa019

Huang, C. F., Yeh, M. L., Tsai, P. C., Hsieh, M. H., Yang, H. L., Hsieh, M. Y., . . . 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. doi: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. doi:10.1161/01.str.31.8.1851

Kaneko, K., Yatsuya, H., Li, Y., Uemura, M., Chiang, C., Hirakawa, Y., . . . 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. doi: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. doi:10.1155/2015/818570

Korantzopoulos, P., Tzimas, P., Kalantzi, K., Kostapanos, M., Vemmos, K., Goudevenos, J., . . . Millionis, H. (2009). Association between serum gamma-glutamyltransferase and acute ischemic nonembolic stroke in elderly subjects. *Arch Med Res*, 40(7), 582-589. doi: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. doi: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. doi:10.1038/ajg.2016.517

LabCorp. (2019). γ -Glutamyl Transferase (GGT). Retrieved from <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., . . . 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. doi: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. doi: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. doi:10.3803/EnM.2019.34.4.390

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. doi: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. doi:10.1016/j.exger.2018.02.026

Minuk, G. Y. (1998). Canadian Association of Gastroenterology Practice Guidelines: evaluation of abnormal liver enzyme tests. *Can J Gastroenterol*, 12(6), 417-421. doi:10.1155/1998/943498

Moyer, V., Freese, D. K., Whittington, P. F., Olson, A. D., Brewer, F., Colletti, R. B., & Heyman, M. B. (2004). Guideline for the evaluation of cholestatic jaundice in infants: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr*, 39(2), 115-128. doi:10.1097/00005176-200408000-00001

Nano, J., Muka, T., Ligthart, S., Hofman, A., Darwish Murad, S., Janssen, H. L. A., . . . Dehghan, A. (2017). Gamma-glutamyltransferase levels, prediabetes and type 2 diabetes: a Mendelian randomization study. *Int J Epidemiol*, 46(5), 1400-1409. doi: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. doi:10.1016/j.cca.2017.11.026

Ndrepepa, G., Holdenrieder, S., Cassese, S., Fusaro, M., Xhepa, E., Laugwitz, K. L., . . . 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. doi:10.1016/j.numecd.2017.09.005

Ndrepepa, G., & Kastrati, A. (2016). Gamma-glutamyl transferase and cardiovascular disease. *Ann Transl Med*, 4(24), 481. doi:10.21037/atm.2016.12.27

Newsome, P. N., Cramb, R., Davison, S. M., Dillon, J. F., Foulerton, M., Godfrey, E. M., . . . Yeoman, A. (2018). Guidelines on the management of abnormal liver blood tests. *Gut*, 67(1), 6-19. doi: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. doi: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. doi:10.5812/numonthly.13652
- Rosoff, D. B., Charlet, K., Jung, J., Lee, J., Muench, C., Luo, A., . . . Lohoff, F. W. (2019). Association of High-Intensity Binge Drinking With Lipid and Liver Function Enzyme Levels. *JAMA Netw Open*, 2(6), e195844. doi: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. doi: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. doi: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. Retrieved from <http://ispub.com/IJS/9/2/7169>
- Thursz, M., Gual, A., Lackner, C., Mathurin, P., Moreno, C., Spahr, L., . . . Cortez -Pinto, H. (2018). EASL Clinical Practice Guidelines: Management of alcohol-related liver disease. *J Hepatol*, 69(1), 154-181. doi:10.1016/j.jhep.2018.03.018
- Vos, M. B., Abrams, S. H., Barlow, S. E., Caprio, S., Daniels, S. R., Kohli, R., . . . 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. doi:10.1097/mpg.0000000000001482
- Vroon, D., & Israili, Z. (1990). *Clinical Methods: The History, Physical, and Laboratory Examinations*. 3rd edition.
- 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. doi:10.1177/0300060516664638
- Wang, S., Zhang, J., Zhu, L., Song, L., Meng, Z., Jia, Q., . . . Jia, Q. (2017). Association between liver function and metabolic syndrome in Chinese men and women. *Sci Rep*, 7, 44844. doi: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. doi:10.5582/ddt.2014.01025
- Xu, T., Wang, W., Zhai, L., Zhang, Y. F., Zhou, H. Z., Wu, X. M., . . . Ke, K. F. (2017). Serum Gamma-glutamyl Transferase Levels Predict Functional Outcomes after Aneurysmal Subarachnoid Hemorrhage. *Biomed Environ Sci*, 30(3), 170-176. doi:10.3967/bes2017.024

Yamada, J., Tomiyama, H., Yambe, M., Koji, Y., Motobe, K., Shiina, K., . . . 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. doi: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. doi: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. doi:10.1038/s41598-019-56569-7

Yavuz, B. B., Yavuz, B., Halil, M., Cankurtaran, M., Ulger, Z., Cankurtaran, E. S., . . . 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. doi: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. doi:10.1038/s41598-020-58306-x

Policy Update History:

5/1/2022	New policy
----------	------------