02-40000-22

Original Effective Date: 08/15/01

Reviewed: 08/22/24

Revised: 09/15/24

Subject: Cryoablation of Liver Tumors

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Hepatic tumors can be due to primary liver cancer or metastases to the liver from nonhepatic primary tumors. Primary liver cancer can arise from hepatocellular tissue (hepatocellular carcinoma) or intrahepatic biliary ducts (cholangiocarcinoma).

Various locoregional therapies for unresectable liver tumors have been evaluated, including cryosurgical ablation (cryosurgery). Cryosurgical ablation occurs in tissue that has been frozen by at least 3 mechanisms: (1) formation of ice crystals within cells, thereby disrupting membranes and interrupting cellular metabolism among other processes; (2) coagulation of blood, thereby interrupting blood flow to the tissue, in turn causing ischemia and apoptosis; and (3) induction of apoptosis.

Summary and Analysis of Evidence: The NCCN Clinical Practice Guideline for Hepatocellular Carcinoma (HCC) (V2.2024) states, "(l)ocoregional therapy should be considered in patients who are not candidates for surgical curative treatments, or as a part of a strategy to bridge patients for other curative therapies. These are broadly categorized into ablation, arterially directed therapies, and radiotherapy. Multidisciplinary review is recommended." The CPG also includes, "(a)blation alone may be curative in treating tumors less than or equal to 3 cm. In well-selected patients with small properly located tumors, ablation should be considered as definitive treatment in the context of a multidisciplinary review. Lesions 3 to 5 cm may be treated to prolong survival using arterially directed therapies, or with combination of an arterially directed therapy and ablation as long as tumor location is accessible for ablation."

The American Association for the Study of Liver Diseases (AASLD) practice guideline (Heimbach et al, 2018) for HCC states, "(b)ecause cirrhosis is one of the primary risk factors for HCC, the selection of treatment modality depends as much on the underlying liver function and the degree of portal

hypertension as on the oncologic stage of the tumor. Therefore, whereas therapeutic options are limited for patients who present with advanced liver disease and/or advanced tumor stages, multiple options exist for those presenting with well-compensated cirrhosis and smaller, potentially resectable tumors. These include ablative strategies such as radiofrequency, microwave, chemical, and cryoablation, as well as surgical resection." The guideline further notes that ablation is the most effective treatment option for early stage HCC in candidates who are not suitable for resection or liver transplant, and that the most effective treatment is generally dependent on size and location of lesions.

Gosalia et al (2017) stated, "Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related deaths worldwide. Liver transplant is considered the gold standard for curative therapy for HCC when patients are not candidates for surgical resection or ablation. Because a subset of patients with HCC have a survival rate with liver transplantation that is comparable to that of cirrhotic patients without tumors, the organ allocation system allows for increased priority for transplant in potential recipients within the Milan criteria. Treatment of HCC has rapidly evolved with interventional radiology. Percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation, and TACE are the major modalities utilized to control growth of HCC lesions. Cryoablation has been less utilized as more advanced ablative techniques have emerged, but still plays a role in select patients. The technique requires laparoscopy with direct application of a cryoprobe, with either liquid nitrogen or argon gas placed on the HCC lesion. Freezing induces irreversible damage to the tissue. Typically, 2 to 3 cycles are performed in a single session, and intraoperative ultrasound is used to monitor tumor destruction in real time. Cryoablation can be used as monotherapy or as part of a multimodal treatment approach. There are no RCTs evaluating the efficacy of cryoablation compared to other ablative modalities, although retrospective trials and case series have evaluated the efficacy of cryoablation. One large series of patients receiving cryotherapy demonstrated a 39.8% 5-year survival rate, and among the subset of patients with lesions less than 5 cm, survival was 55.4%.47 The main disadvantage of cryoablation is that it is most often performed laparoscopically and may cause morbidity in patients with advanced cirrhosis. Complication rates have been reported to be upwards of 50% and include coagulopathy, cardiac arrhythmia, and liver fracture. However, percutaneous application of cryoablation may mitigate these risks. Cryoablation may have a role in special situations, such as treatment of residual disease at resection margins, but is rarely considered as a first-line therapy in the treatment of HCC."

POSITION STATEMENT:

Cryoablation of tumors in the liver **meets the definition of medical necessity** for the treatment of primary hepatic tumors or metastatic tumors, when the following criteria are met:

- The disease is non-resectable, **OR**
- The individual is a poor candidate for surgery due to comorbid disease

BILLING/CODING INFORMATION:

CPT Coding

47371	Laparoscopy, surgical, ablation or one or more liver tumor(s); cryosurgical
47381	Ablation, open, or one or more liver tumor(s); cryosurgical

47383	Ablation, 1 or more liver tumor(s), percutaneous, cryoablation

LOINC Codes

The following information may be required documentation to support medical necessity: physician history and physical, physician progress notes, treatment plan, radiology and/or other diagnostic studies, documentation of co-morbid disease.

Documentation Table	LOINC Codes	LOINC Time Frame Modifier Code	LOINC Time Frame Modifier Codes Narrative
Physician history and physical	28626-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Attending physician visit note	18733-6	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Treatment plan	18776-5	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Radiology report	18726-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Diagnostic studies (non-lab)	27899-4	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.
Co-morbidities and complications	42126-3	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim.

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline reviewed date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Cryosurgical ablation: a surgical procedure where cancerous or diseased cells are destroyed using extreme cold; also called cryoablation, cryosurgery, cryotherapy.

Extra-hepatic metastases: cancer that has spread from its original location to other sites within the body, other than the liver.

Hepatic metastases: cancer that has spread from its original location in the body to the liver.

Primary hepatocellular cancer: a cancer that originates within liver cells, as opposed to having spread from other organs; malignant hepatoma.

Unresectable: a property of a tumor where it is unable to be removed surgically.

RELATED GUIDELINES:

Radiofrequency Ablation of Liver Tumors, 02-40000-23
Cryosurgical Ablation of the Prostate (CSAP), 02-54000-14
Cryosurgical Ablation of Solid Tumors Other Than Liver or Prostate Tumors, 02-99221-12

OTHER:

None applicable.

REFERENCES:

1. AHRQ National Guideline Clearinghouse. ACR Appropriateness Criteria® hepatic malignancy. Guideline Summary NGC-5989. January 2007.
2. AHRQ National Guideline Clearinghouse. Management of hepatocellular carcinoma: an update. Guideline Summary NGC-8006. November 2005 (revised July 2010).
3. AHRQ National Guideline Clearinghouse. Society of Interventional Radiology position statement on chemoembolization of hepatic malignancies. Guideline Summary NGC-8342. July 2009.
4. Benson AB, Abrams TA et al. NCCN Practice Guidelines in Oncology. Hepatobiliary Cancers. V2.2010. ©2010 National Comprehensive Cancer Network, Inc.
5. Benson AB, Abrams TA et al. NCCN Practice Guidelines in Oncology. Hepatobiliary Cancers. V2.2012. 10/28/11. ©2011 National Comprehensive Cancer Network, Inc.
6. Blue Cross Blue Shield Association Evidence Positioning System®. 7.01.75 – Cryosurgical ablation of Primary or Metastatic Liver Tumors, 10/23.

7. Blue Cross Blue Shield Association TEC Assessments. Cryosurgical Ablation of Unresectable Hepatic Tumors & Radiofrequency Ablation Unresectable Hepatic Tumors, (11/00).
8. “Cryotherapy for hepatic colorectal carcinoma metastases”, Ellis Fischel Cancer Center University of Missouri Health Care", (03/01).
9. Di Martino M, Rompianesi G, Mora-Guzmán I, Martín-Pérez E, Montalti R, Troisi RI. Systematic review and meta-analysis of local ablative therapies for resectable colorectal liver metastases. Eur J Surg Oncol. 2020 May;46(5):772-781. doi: 10.1016/j.ejso.2019.12.003. Epub 2019 Dec 4. PMID: 31862133.
10. ECRI Health Technology Forecast. “Expanding indications for cryosurgery for malignant tumors” (06/25/07).
11. Glazer DI, et al. Percutaneous Image-Guided Cryoablation of Hepatic Tumors: Single-Center Experience With Intermediate to Long-Term Outcomes. AJR Am J Roentgenol. 2017 Dec;209(6):1381-1389. doi: 10.2214/AJR.16.17582. Epub 2017 Sep 27.
12. Gosalia AJ, Martin P, Jones PD. Advances and Future Directions in the Treatment of Hepatocellular Carcinoma. Gastroenterol Hepatol (N Y). 2017 Jul;13(7):398-410.
13. Hayes Medical Technology Directory, Cryosurgery for Primary And Metastatic Cancers Of The Liver (10/04; update 11/19/06).
14. Heimbach JK, Kulik LM, Finn RS, Sirlin CB, Abecassis MM, Roberts LR, Zhu AX, Murad MH, Marrero JA. AASLD guidelines for the treatment of hepatocellular carcinoma. Hepatology. 2018 Jan;67(1):358-380. doi: 10.1002/hep.29086.
15. Irvin M. Modlin, Igor Latich, Mark Kidd, Michelle Zikusoka, Geeta Eick et al. Therapeutic Options for Gastrointestinal Carcinoids. Clinical Gastroenterology and Hepatology Vol. 4, Issue 5, Pages 526-547. May 2006.
16. Kim DK, Han K, Won JY, Kim GM, Kwon JH, Kim MD. Percutaneous cryoablation in early stage hepatocellular carcinoma: analysis of local tumor progression factors. Diagn Interv Radiol. 2020 Mar;26(2):111-117. doi: 10.5152/dir.2019.19246.
17. Kim R, Kang TW, et al. Percutaneous cryoablation for perivascular hepatocellular carcinoma: Therapeutic efficacy and vascular complications. Eur Radiol. 2019 Feb;29(2):654-662. doi: 10.1007/s00330-018-5617-6. Epub 2018 Jul 24. PMID: 30043160.
18. Luo J, Dong Z, Xie H, et al. Efficacy and safety of percutaneous cryoablation for elderly patients with small hepatocellular carcinoma: A prospective multicenter study. Liver Int. 2022 Apr;42(4):918-929. doi: 10.1111/liv.15169. Epub 2022 Feb 6. PMID: 35065003.
19. Mahnken AH, König AM, Figiel JH. Current Technique and Application of Percutaneous Cryotherapy. Fortschr Röntgenstr 2018; 190: 836-846.
20. Marrero JA, Kulik LM, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology, VOL. 68, NO. 2, 2018.
21. National Cancer Institute (NCI) Adult Primary Liver Cancer PDQ: Treatment (Physician’s Data Query).
22. National Cancer Institute (NCI). Adult primary liver cancer treatment (PDQ) – health professional version (updated March 24, 2019). Accessed at. http://www.cancer.gov.
23. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Hepatobiliary Cancers, Version 2.2019; Version 2.2022; Version 2.2024.
24. National Institute for Health and Clinical Excellence. Cryotherapy for the treatment of liver metastases: Guidance document IPG369. Last updated December 15, 2010. Copyright© 2010 National Institute for Health and Clinical Excellence.

25. Pusceddu C, Mascia L, Ninniri C, et al. The Increasing Role of CT-Guided Cryoablation for the Treatment of Liver Cancer: A Single-Center Report. Cancers (Basel). 2022 Jun 19;14(12):3018. doi: 10.3390/cancers14123018.
26. Sandra L. Wong, Pamela B. Mangu, Michael A. Choti, Todd S. Crocenzi, Gerald D. Dodd III, Gary S. Dorfman, Cathy Eng, Yuman Fong, Andrew F. Giusti, David Lu, Thomas A. Marsland, Rob Michelson, Graeme J. Poston, Deborah Schrag, Jerome Seidenfeld and Al B. Benson III. American Society of Clinical Oncology 2009 Clinical Evidence Review on Radiofrequency Ablation of Hepatic Metastases from Colorectal Cancer. Journal of Clinical Oncology. Volume 28. Number 3. January 20, 2010.
27. Thomas, Melanie B. Hepatocellular Carcinoma: The Need for Progress. Journal of Clinical Oncology, 23:2892-2899. 05/01/05.
28. UpToDate. Localized hepatocellular carcinoma: Liver-directed therapies for nonsurgical candidates who are eligible for local ablation. 2024. Accessed at uptodate.com.
29. UpToDate. Overview of treatment approaches for hepatocellular carcinoma. 2024. Accessed at uptodate.com.
30. Wu B, Xiao Y-Y, Zhang X, Zhang A-L, Li H-J, Gao D-F. Magnetic resonance imaging-guided percutaneous cryoablation of hepatocellular carcinoma in special regions. Hepatobiliary Pancreat Dis Int. 2010 Aug;9(4):384-92.
31. Zhou L, Yang Y-P, Feng Y-Y, Lu Y-Y, Wang C-P, Wang X-Z, An L-J, Zhang X, Wang F-S. Clinical Research Paper: Efficacy of argon-helium cryosurgical ablation on primary hepatocellular carcinoma. A pilot clinical study. Chinese Journal of Cancer 28:1, 45-48; January 2009]; ©2009 Sun Yat-Sen University Cancer Center.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 08/22/24.

GUIDELINE UPDATE INFORMATION:

08/15/01	Medical Coverage Guideline reformatted.
01/01/02	HCPCS changes.
12/15/02	Annual review for investigational; no change.
11/15/03	Changed policy number from 04-77260-15 to 02-40000-22.
02/15/04	Reviewed Radiofrequency/Cryoablation of Liver Tumors MCG #02-40000-22 and separated into two different policies Radiofrequency Ablation of Liver Tumors and Cryosurgical Ablation of Liver Tumors.
03/15/05	Scheduled review; no change in coverage statement; Program Exception added for Medicare Advantage products.
02/15/06	Scheduled review; investigational status removed; coverage criteria and ICD-9 diagnosis codes added.
08/15/07	Scheduled review; reformatted guideline; updated references.
02/15/09	Scheduled review; no change in position statement.
10/15/10	Revision; related ICD-10 codes added.
02/15/11	Annual review; no change in position statement. Revised description section; added CPT code 76940; updated references; reformatted guideline.
09/15/11	Revision; formatting changes.

02/15/12	Scheduled review; no change in position statement. Revised description section and updated references.
05/11/14	Revision: Program Exceptions section updated.
01/01/15	Annual CPT/HCPCS update. Added 47383.
11/01/15	Revision: ICD-9 Codes deleted.
10/01/16	Revision: Billing/Coding Information section updated.
04/20/17	Revision: deleted code 76490 and reformatted guideline.
09/15/19	Scheduled review. Revised description and CPT coding. Maintained position statement. Updated references.
02/15/21	Scheduled review. Revised description, maintained position statement, and updated references.
10/15/22	Scheduled review. Maintained position statement and updated references.
05/25/23	Update to Program Exceptions section.
01/01/24	Position statements maintained.
09/15/24	Scheduled review. Revised description, maintained position statement, and updated references.