MEDICAL POLICY

POLICY TITLE	CRYOSURGICAL ABLATION OF PRIMARY OR METASTATIC LIVER TUMORS
POLICY NUMBER	MP 1.121

CLINICAL BENEFIT	☒ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☐ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	5/1/2025

I. POLICY

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Cryosurgical ablation of either primary or metastatic tumors in the liver is considered **investigational**. There is insufficient evidence to support a general conclusion concerning the health outcomes of benefits associated with these procedures.

Cross-References:

MP 1.088 Cryosurgical Ablation of Miscellaneous Solid Tumors other than Liver, Prostate or Dermatologic Tumors
MP 1.055 Radiofrequency Ablation of Primary or Metastatic Liver Tumors
MP 1.084 Radiofrequency Ablation of Miscellaneous Solid Tumors, Excluding Liver Tumors

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:
https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

III. DESCRIPTION/BACKGROUND

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Hepatic tumors can be primary or metastatic. Primary liver cancer can arise from hepatocellular tissue (hepatocellular carcinoma [HCC]) or intrahepatic biliary ducts (cholangiocarcinoma).

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Multiple tumors metastasize to the liver, but there is particular interest in the treatment of hepatic metastases from colorectal carcinoma (CRC) given the propensity of CRC to metastasize to the liver and the high prevalence. Liver metastases from neuroendocrine tumors present a unique clinical situation. Neuroendocrine cells produce and secrete a variety of regulatory hormones (or neuropeptides), which include neurotransmitters and growth factors. Overproduction of the specific neuropeptides by cancerous cells causes various symptoms, depending on the hormone produced.

Treatment

Treatment of liver tumors is done to reduce endocrine-related symptoms, as well as prolong survival and reduce symptoms related to the hepatic mass.

Surgical resection with tumor-free margins or liver transplantation are the primary treatments available that have curative potential. Many hepatic tumors are unresectable at diagnosis, due either to their anatomic location, size, number of lesions, or underlying liver reserve. Local therapy for hepatic metastasis is indicated only when there is no extrahepatic disease, which rarely occurs for patients with primary cancers other than CRC or certain neuroendocrine malignancies. For liver metastases from CRC, postsurgical adjuvant chemotherapy has been reported to decrease recurrence rates and prolong time to recurrence. Combined systemic and hepatic arterial chemotherapy may increase disease-free intervals for patients with hepatic metastases from CRC but apparently is not beneficial for those with unresectable HCC.

Various ablative therapies for unresectable liver tumors have been evaluated: cryosurgical, radiofrequency (RFA), microwave ablation (MWA), laser. Other therapies include transhepatic arterial embolization, chemoembolization, or radioembolization with yttrium-90 microspheres; microwave coagulation; and percutaneous ethanol injection.

Guided cryoablation via many imaging methods induces ice-ball formation and tumor necrosis and is an attractive option for treating unresectable liver tumors. There are several advantages to using cryoablation for the treatment of liver cancer: it can be performed percutaneously, intraoperatively, and laparoscopically; ice-ball formation can be monitored; it has little impact on nearby large blood vessels; and it induces a cryo-immunological response in situ.

Clinically, primary research has shown that percutaneous cryoablation of liver cancer is relatively safe and efficient, and it can be combined with other methods, such as radiation therapy, chemotherapy, and immunology, to control disease.

Procedure-Related Complications

Cryosurgery is not a benign procedure. Treatment-related deaths occur in approximately 2% of study populations and are most often caused by cryoshock, liver failure, hemorrhage, pneumonia/sepsis, and acute myocardial infarction. Clinically significant nonfatal complication rates in the reviewed studies ranged from 0% to 83% and were generally due to the same causes as treatment-related deaths. The likelihood of complications arising from cryosurgery might be predicted, in part, by the extent of the procedure, but much of the treatment-related morbidity and mortality reflect the generally poor health status of patients with advanced hepatic disease.

Regulatory Status

Several cryosurgical devices have been cleared by the U.S. Food and Drug Administration (FDA). For example, in 1996, the Endocare™ Cryocare System (Endocare) was cleared for marketing through the 510(k) process. I Use includes general surgery, urology, gynecology, oncology, neurology, dermatology, ENT [ears, nose, throat], proctology, pulmonary surgery, and thoracic surgery. The system is designed to freeze/ablate tissue by the application of extreme cold temperatures.

IV. RATIONALE

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SUMMARY OF EVIDENCE

For individuals who have unresectable primary HCC amenable to locoregional therapy who receive cryosurgical ablation, the evidence includes a randomized controlled trial (RCT), several nonrandomized comparative studies, and multiple noncomparative studies. Relevant outcomes are overall survival, disease-specific survival, and treatment-related mortality and morbidity. The available RCT comparing cryoablation with radiofrequency ablation demonstrated lower rates of local tumor progression with cryoablation, but no differences in survival outcomes between groups. Although this trial provided suggestive evidence that cryoablation is comparable with radiofrequency ablation, trial limitations would suggest findings need to be replicated. Nonrandomized comparative studies have failed to find consistent benefit with cryoablation in outcomes related to tumor recurrence and survival. Additional randomized comparative evidence is needed to permit conclusions about the effectiveness of cryoablation compared with other locoregional therapies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable liver metastases from neuroendocrine tumors amenable to locoregional therapy who receive cryosurgical ablation, the evidence includes a Cochrane review and case series. Relevant outcomes are overall survival, disease-specific survival, symptoms, and treatment-related mortality and morbidity. The available evidence base is very limited. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable liver metastases from colorectal cancer amenable to locoregional therapy who have cryosurgical ablation, the evidence includes an RCT, several nonrandomized comparative and noncomparative studies, and systematic reviews of these studies. Relevant outcomes are overall survival, disease-specific survival, and treatment-related mortality and morbidity. The available RCT comparing surgical resection with cryoablation was judged at high risk of bias. Some nonrandomized comparative studies have reported improved survival outcomes for patients managed with cryotherapy compared with those managed with resection alone; however, these studies were subject to bias in the selection of patients for treatments. Additional controlled studies are needed to permit conclusions about the effectiveness of cryoablation compared with other locoregional therapies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

V. DEFINITIONS

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DENATURATION refers to a change in conditions (temperature, addition of a substance) that causes irreversible change in a protein's structure, usually resulting in precipitation of the protein.

EXTRAHEPATIC refers to outside or unrelated to the liver.

HEPATIC pertains to the liver.

HYPERTHERMIA refers to the use of microwave or radiofrequency energy to increase body temperature.

METASTASIS is the movement of body cells (esp. cancer cells) from one part of the body to another.

NEUROENDOCRINE MALIGNANCIES refer to a diverse group of tumors, such as carcinoid, islet cell tumors, neuroblastoma, and small-cell carcinomas of the lung.

PERCUTANEOUS refers to that which is passed or affected through the skin.

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations are based on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross' medical policies are developed to assist in administering a member's benefits. These medical policies do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined

by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational, and therefore not covered:

Procedure Codes								
47371	47381	47383	47399					

IX. REFERENCES

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X. POLICY HISTORY

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MP 1.121	**06/26/2020 Minor Review.** Changed Cryosurgical ablation from investigational to medically necessary with criteria added. Description, Rationale and References updated.
	10/20/2021 Consensus Review. No changes to policy statement. NCCN statement and denial statement added. References updated. FEP language updated.
	11/14/2022 Consensus Review. No change to policy stance. Updated background. Updated references. Code 47399 added.
	11/06/2023 Consensus Review. No change to statement, updated background, and references.
	11/06/2024 Minor Review. Cryosurgical ablation is now investigational. Updated references.

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