NO. 91548

INTRAPERITONEAL CHEMOTHERAPY

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Instructions for use: This document is for informational purposes only. Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable. Eligibility and benefit coverage are determined in accordance with the terms of the member's plan in effect as of the date services are rendered. It is not an authorization, certification, explanation of benefits, or contract. Receipt of benefits is subject to satisfaction of all terms and conditions of coverage. Priority Health's medical policies are developed with the assistance of medical professionals and are based upon a review of published and unpublished information including, but not limited to, current medical literature, guidelines published by public health and health research agencies, and community medical practices in the treatment and diagnosis of disease. Because medical practice, information, and technology are constantly changing, Priority Health reserves the right to review and update its medical policies at its discretion. Priority Health's medical policies are intended to serve as a resource to the plan. They are not intended to limit the plan's ability to interpret plan language as deemed appropriate. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment they choose to provide.

Policy scope: This policy addresses advanced intraperitoneal chemotherapy techniques used in the treatment of peritoneal malignancies, including Hyperthermic Intraperitoneal Chemotherapy (HIPEC/IPHC) and Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC).

Related policies:

- CLINICAL TRIALS FOR SELF FUNDED GROUPS OPTING OUT OF PPACA # 91448
- CLINICAL TRIALS # 91606

I. MEDICAL NECESSITY CRITERIA

Inclusions:

A. Intraperitoneal Hyperthermic Chemotherapy (IPHC) / Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

1. Intraperitoneal Hyperthermic Chemotherapy (IPHC), also known as Hyperthermic Intraperitoneal Chemotherapy (HIPEC) may be considered medically necessary when recommended by applicable National Comprehensive Cancer Network (NCCN) Guidelines, including but not limited to the following indications:
   a. Colon Cancer
   b. Gastric Cancer

c. Mesothelioma: Peritoneal
d. Ovarian Cancer, including Epithelial Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Not Medically Necessary as Considered Experimental / Investigational:

A. Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC)

1. Pressurized intraperitoneal aerosol chemotherapy (PIPAC), including but not limited to PIPAC using oxaliplatin, cisplatin/doxorubicin, or other chemotherapeutic agents, is considered Experimental, Investigational, and Unproven (E/I/U) for **all** indications, as current evidence is insufficient to demonstrate a definitive clinical or survival benefit.

Note: Services provided in the context of a clinical trial are subject to the Plan's Clinical Trials policy and the member's benefit plan.

II. CENTERS FOR MEDICARE & MEDICAID SERVICES (CMS) COVERAGE DETERMINATION

Any applicable federal or state mandates will take precedence over this medical coverage policy.

Medicare: Refer to the CMS Online Manual System (IOMs) and Transmittals.
For the most current applicable CMS National Coverage Determination (NCD)/Local Coverage Determination (LCD)/Local Coverage Article (LCA) refer to CMS Medicare Coverage Database.

The information below is current as of the review date for this policy. However, the coverage issues and policies maintained by CMS are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. MAC jurisdiction for purposes of local coverage determinations is governed by the geographic service area where the Medicare Advantage plan is contracted to provide the service. Please refer to the Medicare Coverage Database website for the most current applicable NCD, LCD, LCA, and CMS Online Manual System/Transmittals.

National Coverage Determinations (NCDs)	
NCD - Hyperthermia for Treatment of Cancer (110.1)	
Local Coverage Determinations (LCDs)	
CGS Administrators, LLC	None identified
First Coast Service Options, Inc.	None identified
National Government Services, Inc.	None identified
Noridian Healthcare Solutions	None identified
Novitas Solutions, Inc.	None identified
Palmetto GBA	None identified
WPS Insurance Corporation	None identified

III. BACKGROUND

Intraperitoneal hyperthermic chemotherapy (IPHC) is used as an adjunct to surgery such as cytoreductive surgery (CRS) for the treatment of selected cancers that have

penetrated or metastasized within the peritoneal cavity. The goal of IPHC is to enhance the cytotoxic effect of chemotherapeutic agents through direct locoregional exposure and hyperthermia, thereby targeting residual disseminated tumor cells and reducing the risk of tumor recurrence.

IPHC involves using a heated sterile chemotherapy solution that is circulated throughout the abdominal cavity immediately following cytoreductive surgery (CRS). A heated chemotherapy solution (3 to 5 L) is circulated in the peritoneal cavity using a roller or peristaltic pump, a temperature-controlled container for the chemotherapy fluid, tubing to infuse chemotherapy to and from the patient, and temperature probes for the peritoneal cavity (Kok et al., 2020). Either an open or closed technique may be used. While there is no universally accepted standard for temperature and duration, the peritoneal infusate is typically maintained between 40 and 45°C (104–113°F), and exposure duration ranges from 30 to 120 minutes (Ji et al., 2021).

With IPHC treatment, patients are connected to a series of tubes and a pumping device that bathe the abdominal cavity with a heated sterile solution containing anticancer (chemotherapeutic) drugs. The high temperature has been found to increase the drug's effect. The fluid goes through the abdomen to treat tumor cells that may remain after surgery. Both heat and direct contact with chemotherapy drugs kills the cancer cells.

Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a distinct intraperitoneal chemotherapy approach that differs fundamentally from HIPEC in both delivery method and clinical intent. PIPAC is administered laparoscopically without extensive cytoreduction and delivers chemotherapy as a pressurized aerosol within a closed abdominal cavity, aiming to improve drug distribution and tissue penetration through aerosolization and capnoperitoneum-associated pressure (Grass et al., 2017; Sgarbura et al., 2022). Unlike HIPEC, PIPAC is designed to be repeatable and is most often used in patients with unresectable, recurrent, or chemotherapy-refractory peritoneal metastases, frequently in combination with systemic therapy as part of a bidirectional approach (Jørgensen et al., 2025).

The largest real-world evaluation of PIPAC, derived from the ISSPP PIPAC database (1126 patients; 3224 procedures), demonstrates technical feasibility and an acceptable safety profile, with major surgical complications occurring in <1% of procedures and CTCAE grade ≥ 3 adverse events in approximately 5% of treatments. Histopathologic tumor response, measured by the Peritoneal Regression Grading Score (PRGS), was frequently observed and correlated with longer overall survival; however, due to the descriptive, non-comparative design and heterogeneous populations, an independent survival benefit attributable to PIPAC cannot be established (Jørgensen et al., 2025).

Across tumor types, evidence supporting PIPAC remains limited. In gastric cancer with peritoneal metastases, systematic reviews report modest survival outcomes with intraperitoneal chemotherapy strategies, with PIPAC demonstrating lower toxicity but generally shorter survival compared with catheter-based intraperitoneal paclitaxel; interpretation is limited by non-randomized designs and lack of standardized response measures (Guchelaar et al., 2024; Acs et al., 2024). In colorectal peritoneal metastases, a phase II trial of PIPAC oxaliplatin monotherapy demonstrated technical feasibility but limited clinical benefit, including no radiologic responses, modest survival, and non-trivial toxicity (Rovers et al., 2021). In pancreatic adenocarcinoma, intraperitoneal chemotherapy approaches—including PIPAC—have been evaluated primarily as

palliative interventions in heterogeneous, non-randomized studies, with uncertain clinical effectiveness (Frassini et al., 2022).

Early-phase and single-arm studies suggest that PIPAC, particularly when combined with systemic chemotherapy or immunotherapy, may demonstrate biological activity and histopathologic response; however, survival benefit remains unproven (Tonello et al., 2025; Sundar et al., 2024). An international expert consensus has emphasized the need for standardized protocols and explicitly states that PIPAC does not constitute standard of care, with dose escalation and novel indications restricted to clinical trials (Sgarbura et al., 2022). Ongoing randomized phase III trials, including PIPAC VEROne, are evaluating whether PIPAC improves resectability or survival when added to systemic therapy; until such data are available, PIPAC remains investigational (Casella et al., 2022).

IV. GUIDELINES / POSITION STATEMENTS

Medical/Professional Society	Guideline
NCCN	colon.pdf gastric.pdf meso_peritoneal.pdf ovarian.pdf
National Cancer Institute	Treatment of Ovarian Epithelial, Fallopian, & Peritoneal Cancers - NCI (2024)
ERAS Society	Guidelines for Perioperative Care in Cytoreductive Surgery (CRS) with or without hyperthermic IntraPEritoneal chemotherapy (HIPEC): Enhanced recovery after surgery (ERAS®) Society Recommendations - Part I: Preoperative and intraoperative management (2020)
Peritoneal Surface Oncology Gorup International (PSOGI)	The 2022 PSOGI International Consensus on HIPEC Regimens for Peritoneal Malignancies: Epithelial Ovarian Cancer | Annals of Surgical Oncology
American Cancer Society (The Chicago Consensus)	The Chicago Consensus on peritoneal surface malignancies: Management of peritoneal mesothelioma (2020)
American Society of Colon and Rectal Surgeons	The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Appendiceal Neoplasms (2025)

PSOGI/ EURACAN	Appendiceal tumours and pseudomyxoma peritonei: Literature review with PSOGI/EURACAN clinical practice guidelines for diagnosis and treatment - ClinicalKey (2021)
National Institute for Health and Care Excellence (NICE)	Cytoreduction surgery with hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis | Guidance | NICE (2021)

V. REGULATORY (US FOOD AND DRUG ADMINISTRATION)

See U.S. Food & Drug Administration (FDA) Medical Device Databases for the most current information.

Device	Premarket Approval, 513(f)(2)(De Novo), or 510(k) Number	Notice date
ThermaSolutions ThermoChem HT-1000 System ThermoChem HT-2000 System	 K993330 K131583	 12/30/1999 10/03/2013
Belmont Hyperthermia Treatment Pump	K152208	09/02/2015
BSD-2000 Hyperthermia System.	H090002	11/18/2011

VI. CODING

ICD-10 Codes that may support medical necessity

C45.1 Mesothelioma of peritoneum
C48.0 Malignant neoplasm of retroperitoneum
C48.1 Malignant neoplasm of specified parts of peritoneum
C48.2 Malignant neoplasm of peritoneum, unspecified
C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C78.6 Secondary malignant neoplasm of retroperitoneum and peritoneum

CPT/HCPCS Codes

49329 Unlisted laparoscopy procedure, abdomen, peritoneum and omentum

96547 Intraoperative hyperthermic intraperitoneal chemotherapy (HIPEC) procedure, including separate incision(s) and closure, when performed; first 60 minutes (List separately in addition to code for primary procedure)

96548 Intraoperative hyperthermic intraperitoneal chemotherapy (HIPEC) procedure, including separate incision(s) and closure, when performed; each additional 30 minutes (List separately in addition to code for primary procedure)

96446	Chemotherapy administration into peritoneal cavity
96549	Unlisted chemotherapy procedure

Coding Notes: CPT code 96446 identifies chemotherapy administration into the peritoneal cavity via implanted port or catheter. This procedure does not refer to external application of heat as described by CPT 77605. Heating of the chemotherapy agent for IPHC is not separately payable.

VII. MEDICAL NECESSITY REVIEW

Prior authorization for certain drugs, devices, services and procedures may or may not be required. In cases where prior authorization is required, providers will submit a request demonstrating that a drug, service or procedure is medically necessary. For more information, refer to the Priority Health Provider Manual.

Individual case review may allow coverage for care or treatment that is investigational yet promising for the conditions described. Requests for individual consideration require prior plan approval. All determinations of coverage for experimental, investigational, or unproven treatment will be made by a Priority Health medical director or clinical pharmacist. The exclusion of coverage for experimental, investigational, or unproven treatment may be reviewed for exception if the condition is either a terminal illness, or a chronic, life threatening, severely disabling disease that is causing serious clinical deterioration.

VIII. APPLICATION TO PRODUCTS

Coverage is subject to the member's specific benefits. Group-specific policy will supersede this policy when applicable.

- **HMO/EPO**: This policy applies to insured HMO/EPO plans.
- **POS**: This policy applies to insured POS plans.
- **PPO**: This policy applies to insured PPO plans. Consult individual plan documents as state mandated benefits may apply. If there is a conflict between this policy and a plan document, the provisions of the plan document will govern.
- **ASO**: For self-funded plans, consult individual plan documents. If there is a conflict between this policy and a self-funded plan document, the provisions of the plan document will govern.
- **INDIVIDUAL**: For individual policies, consult the individual insurance policy. If there is a conflict between this medical policy and the individual insurance policy document, the provisions of the individual insurance policy will govern.
- **MEDICARE**: Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, this policy applies.
- **MEDICAID/HEALTHY MICHIGAN PLAN**: For Medicaid/Healthy Michigan Plan members, this policy will apply. Coverage is based on medical necessity criteria being met and the appropriate code(s) from the coding section of this policy being included on the Michigan Medicaid Fee Schedule. If there is a discrepancy between this policy and the Michigan Medicaid Provider Manual, the Michigan Medicaid Provider Manual will govern. If there is a discrepancy or lack of guidance in the Michigan Medicaid Provider Manual, the Priority Health contract with Michigan Medicaid will govern. For Medical Supplies/DME/Prosthetics and

Orthotics, please refer to the Michigan Medicaid Fee Schedule to verify coverage.

IX. REFERENCES

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SUMMARY OF CHANGES

Additions:

- Added Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) as an experimental/investigational/unproven (E/I/U) technology for all indications.
- Updated coding to include codes relevant to PIPAC.

Changes:

- Updated background and references.
- Policy scope and name revised to reflect inclusion of PIPAC.
- Removed section “B” regarding clinical trial coverage for HIPEC not recommended by NCCN; and added a note clarifying that services in clinical trials are subject to the Plan’s Clinical Trials policy and member benefits.

Past committee review dates:02/2008, 2/2009, 02/2010, 02/2011, 02/2012, 02/2013, 02/2014, 02/2015, 02/2016, 02/2017, 02/2018, 02/2019, 02/2020,02/2021, 02/2022, 02/2023, 02/2024, 02/2025, 02/2026, 05/2026

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