

## MEDICAL POLICY – 2.03.07

# Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Select Intra-Abdominal and Pelvic Malignancies

BCBSA Ref. Policy: 2.03.07

Effective Date: Oct. 1, 2025

Last Revised: Mar. 18, 2026


Replaces: N/A

RELATED MEDICAL POLICIES:

None

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## Introduction

Chemotherapy can be delivered directly into the abdominal cavity to treat certain types of cancer. However, chemotherapy has trouble penetrating large tumors. That’s why surgery is done to remove as much cancer as possible before chemotherapy is directly given into the abdomen. Removing or reducing the size of the tumor—also called debulking—provides the chemotherapy drug the best chance to kill the remaining cancer cells. There are several different types of cancer in which this treatment has been tried. This policy describes when debulking surgery followed by direct application of chemotherapy may be considered medically necessary.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

## Policy Coverage Criteria

**Note:** This policy addresses “perioperative” intraperitoneal chemotherapy; that is intraperitoneal chemotherapy which occurs at the same operative session as the cytoreductive or interval cytoreductive surgery. This policy does not address intraperitoneal chemotherapy which is delivered directly into the abdominal cavity through an indwelling catheter with an access port given post-operatively either in an inpatient or outpatient setting.

Service	Medical Necessity
<p><b>Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (HIPEC)</b></p>	<p><b>Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (HIPEC) <u>at the time of surgery</u> may be considered medically necessary for the treatment of either of the following conditions:</b></p> <ul style="list-style-type: none"> <li>• Pseudomyxoma peritonei (malignant tumor of the appendix)</li> <li>• Diffuse malignant peritoneal mesothelioma</li> </ul> <p><b>The use of HIPEC may be considered medically necessary in newly diagnosed epithelial ovarian or fallopian tube cancer <u>at the time of interval cytoreductive surgery</u> when ALL of the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• The individual has newly diagnosed stage III disease (see <a href="#">Related Information</a>)</li> <li>• The individual is not eligible for primary cytoreductive surgery or surgery has been performed but was incomplete <b>and</b> the individual received 3 cycles of cis-platinum and paclitaxel systemic neoadjuvant chemotherapy immediately prior to interval-debulking surgery (see <a href="#">Related Information</a>);</li> <li>• Optimal cytoreduction (residual tumor nodules of less than 10 mm) is achievable at the time of the interval debulking surgery (see <a href="#">Related Information</a>)</li> </ul> <p><b>The use of HIPEC in all other settings to treat ovarian cancer, including, but not limited to stage IIIC or IV ovarian cancer is considered investigational.</b></p>



Service	Investigational
<b>Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (HIPEC)</b>	<b>Cytoreductive surgery plus HIPEC is considered investigational for:</b> <ul style="list-style-type: none"> <li>• Peritoneal carcinomatosis from colorectal cancer, gastric cancer, or endometrial cancer</li> </ul> <b>AND</b> <ul style="list-style-type: none"> <li>• All other indications, including goblet cell tumors of the appendix</li> </ul>

Documentation Requirements
<p><b>The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:</b></p> <ul style="list-style-type: none"> <li>• For Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (HIPEC) at the time of surgery: <ul style="list-style-type: none"> <li>○ Office visit notes that contain the relevant history and physical supporting any of the following diagnoses: <ul style="list-style-type: none"> <li>▪ Pseudomyxoma peritonei (malignant tumor of the appendix)</li> <li>▪ Diffuse malignant peritoneal mesothelioma</li> </ul> </li> </ul> </li> <li>• For HIPEC <ul style="list-style-type: none"> <li>○ Office visit notes that contain the relevant history and physical supporting: <ul style="list-style-type: none"> <li>▪ Recently diagnosed epithelial ovarian or fallopian tube cancer at the time of interval cytoreductive surgery and ALL of the following criteria: <ul style="list-style-type: none"> <li>▫ The individual has stage III disease</li> <li>▫ The individual is not eligible for primary cytoreductive surgery or surgery has been performed but was incomplete and the individual received 3 cycles of cis-platinum and paclitaxel systemic neoadjuvant chemotherapy immediately prior to interval-debulking surgery</li> <li>▫ Optimal cytoreduction (residual tumor nodules of &lt;10 mm) is achievable at the time of the interval debulking surgery</li> </ul> </li> </ul> </li> </ul> </li> </ul>

## Coding

The coding for this overall procedure would likely involve codes for the surgery and the intraperitoneal chemotherapy.



Code	Description
<b>CPT</b>	
96446	Chemotherapy administration into the peritoneal cavity via indwelling port or catheter
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)

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

## Cytoreduction

There is no specific CPT code for the surgical component of this complex procedure. It is likely that a series of CPT codes would be used to describe exploratory laparotomies of various components of the abdominal cavity, in addition to specific codes for resection of visceral organs, depending on the extent of the carcinomatosis.

## Intraperitoneal Chemotherapy

CPT code 96446 identifies "chemotherapy administration into the peritoneal cavity via indwelling port or catheter." When performed using a temporary catheter or performed intraoperatively, the unlisted code 96549 (unlisted chemotherapy procedure) would be reported.

## Hyperthermia

This procedure does not refer to external application of heat as described by CPT code 77605. There are no codes for the heating of the chemotherapy.

## Related Information



### **Ovarian cancer staging is as follows:**

**Stage I:** The cancer is confined to the ovary or fallopian tube.

**Stage II:** The cancer involves one or both ovaries with pelvic extension.

**Stage III:** The cancer has spread within the abdomen.

**Stage IV:** The cancer is widely spread throughout the body.

Eligibility for neoadjuvant chemotherapy and interval debulking surgery is based on a high perioperative risk profile (i.e., the individual is a poor candidate to withstand an aggressive initial cytoreductive procedure) or a low likelihood of achieving cytoreduction to less than 1 cm (i.e., the individual has extensive disease that precludes upfront optimal cytoreduction) or surgery has been performed but was incomplete (i.e., after surgery, one or more residual tumors measuring >1 cm in diameter were present).

Complete cytoreduction is defined as no visible disease and optimal cytoreduction as one or more residual tumors measuring 10 mm or less in diameter remaining.

## Evidence Review

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### **Description**

Cytoreductive surgery (CRS) includes peritonectomy (i.e., peritoneal stripping) procedures and multivisceral resections, depending on the extent of intra-abdominal tumor dissemination. CRS may be followed by infusion of intraperitoneal chemotherapy with or without heating, which is intended to improve the tissue penetration of the chemotherapy. When heated, this is referred to as hyperthermic intraperitoneal chemotherapy (HIPEC). CRS and HIPEC have been proposed for a number of intra-abdominal and pelvic malignancies such as pseudomyxoma peritonei and peritoneal carcinomatosis from colorectal, gastric, or endometrial cancer.



## Background

### Pseudomyxoma Peritonei

Pseudomyxoma peritonei is a clinicopathologic disease characterized by the production of mucinous ascites and mostly originates from epithelial neoplasms of the appendix. Appendix cancer is diagnosed in fewer than 1000 Americans each year; less than half are epithelial neoplasms.<sup>1</sup> The incidence of pseudomyxoma peritonei is estimated at two cases per 1 million individuals.<sup>2</sup> As mucin-producing cells of the tumor proliferate, the narrow lumen of the appendix becomes obstructed and subsequently leads to appendiceal perforation. Neoplastic cells progressively colonize the peritoneal cavity and produce copious mucin, which collects in the peritoneal cavity. Pseudomyxoma peritonei ranges from benign (disseminated peritoneal adenomucinosis) to malignant (peritoneal mucinous carcinomatosis), with some intermediate pathologic grades. Clinically, this syndrome ranges from early pseudomyxoma peritonei, usually discovered during imaging or laparotomy performed for another reason, to advanced cases with a distended abdomen, bowel obstruction, and starvation.

### Treatment

The conventional treatment of pseudomyxoma peritonei is surgical debulking, repeated as necessary to alleviate pressure effects. However, repeated debulking surgeries become more difficult due to progressively thickened intra-abdominal adhesions, and this treatment is palliative, leaving visible or occult disease in the peritoneal cavity.<sup>3</sup>

### Peritoneal Carcinomatosis of Colorectal Origin

Peritoneal dissemination develops in 10% to 15% of individuals with colon cancer.

### Treatment

Despite the use of increasingly effective regimens of chemotherapy and biologic agents to treat advanced disease, peritoneal metastases are associated with a median survival of six to seven months.



## Peritoneal Carcinomatosis of Gastric Origin

Peritoneal carcinomatosis is detected in more than 30% of individuals with advanced gastric cancer and is a poor prognostic indicator. The median survival is three months, and five-year survival is less than 1%.<sup>4</sup> Sixty percent of deaths from gastric cancer are attributed to peritoneal carcinomatosis.<sup>5</sup>

### Treatment

Current chemotherapy regimens are nonstandard, and peritoneal seeding is considered unresectable for cure.<sup>6</sup>

## Peritoneal Mesothelioma

Malignant mesothelioma is a relatively uncommon malignancy that may arise from the mesothelial cells lining the pleura, peritoneum, pericardium, and tunica vaginalis testis. In the US, 200 to 400 new cases of diffuse malignant peritoneal mesothelioma (DMPM) are registered every year, accounting for 10% to 30% of all-type mesothelioma.<sup>7</sup> DMPM has traditionally been considered a rapidly lethal malignancy with limited and ineffective therapeutic options. The disease is usually diagnosed at an advanced stage and is characterized by multiple variably sized nodules throughout the abdominal cavity. As the disease progresses, the nodules become confluent to form plaques, masses, or uniformly cover peritoneal surfaces. In most individuals, death eventually results from locoregional progression within the abdominal cavity. In historical case series, treatment by palliative surgery, systemic or intraperitoneal chemotherapy, and abdominal irradiation has resulted in a median survival of 12 months.

### Treatment

Surgical cytoreduction (resection of visible disease) in conjunction with HIPEC is designed to remove visible tumor deposits and residual microscopic disease. By delivering chemotherapy intraperitoneally, drug exposure to the peritoneal surface is increased some 20-fold compared with systemic exposure. In addition, previous animal and in vitro studies have suggested that the cytotoxicity of mitomycin C is enhanced at temperatures greater than 39°C (102.2°F).



## Ovarian Cancer

Several different types of malignancies can arise in the ovaries; epithelial carcinoma is the most common, accounting for 90% of malignant ovarian tumors. Epithelial ovarian cancer is the fifth most common cause of cancer death in women in the US. Most ovarian cancer patients (>70%) present with widespread disease, and annual mortality is 65% of the incidence rate. In addition, African American women reportedly have a higher prevalence of presenting with more advanced tumors, being undertreated or untreated, and having shorter disease-free survival compared to other racial groups.<sup>8</sup>

### Treatment

Current management of advanced epithelial ovarian cancer is CRS followed by combination chemotherapy. Tumor recurrences are common, and the prognosis for recurrent disease is poor.

CRS plus HIPEC in combination with systemic chemotherapy is being studied for primary and recurrent disease. Because HIPEC is administered at the time of surgery, treatment-related morbidity may be reduced compared with intraperitoneal chemotherapy administered postoperatively.

### Summary of Evidence

For individuals who have pseudomyxoma peritonei who receive CRS plus HIPEC, the evidence includes cohort studies and a systematic review. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity.

Retrospective cohort studies and systematic reviews have reported median survival ranging from 47 to 156 months and 5-year overall survival ranging from 41% to 96% for individuals with primary treatment for pseudomyxoma peritonei treated with CRS plus HIPEC. Two retrospective studies reported results of CRS plus HIPEC for recurrence with five-year overall survival rates of 34% to 79%. Although no direct comparisons between CRS plus HIPEC and other interventions have been published, traditional surgical debulking is not curative, and complete CRS alone (without HIPEC) has been associated with a five-year OS of approximately 50%, along with high recurrence rates (91%, with a median disease-free survival of 24 months). Median progression-free survival with CRS plus HIPEC as primary treatment has been reported as 40 to 78 months, with five-year progression-free survival rates of 38% to 80%. Procedure-related morbidity and mortality have generally decreased over time. Because the prevalence of pseudomyxoma



peritonei is very low, conducting comparative trials is difficult. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peritoneal carcinomatosis of colorectal origin who receive CRS plus HIPEC, the evidence includes randomized controlled trials (RCTs), systematic reviews, and a large number of observational studies. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. A meta-analysis of controlled studies found that CRS plus HIPEC, compared with traditional therapy without HIPEC, was associated with significantly higher survival rates, and was not associated with significantly higher treatment-related morbidity rates. One RCT, in which individuals with peritoneal carcinomatosis due to colorectal cancer were followed for at least six years, demonstrated improved survival in individuals who received CRS plus HIPEC, and systemic chemotherapy compared with individuals who received systemic chemotherapy alone. However, procedure-related morbidity and mortality were relatively high, and systemic chemotherapy regimens did not use currently available biologic agents. A more recent RCT found no survival benefit with CRS plus HIPEC over CRS alone, and a higher rate of adverse events 31 to 60 days post-procedure in the CRS plus HIPEC group. The lack of benefit seen with HIPEC in this trial may have been due to several factors, including the short duration of HIPEC treatment, the extensive use of preprocedural systemic chemotherapy, and the high rates of complete cytoreduction achieved in both groups. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peritoneal carcinomatosis of gastric origin who receive CRS plus HIPEC, the evidence includes two small RCTs, observational studies, and two systematic reviews. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. A 2017 meta-analysis identified two RCTs and 12 controlled nonrandomized studies comparing surgery plus HIPEC with standard surgical management in individuals who had peritoneal carcinomatosis due to gastric cancer. One meta-analysis found significantly better survival in the surgery plus HIPEC group at one year but not at two or three years. Another meta-analysis found survival benefit was reported in the CRS plus HIPEC groups at one, two and three years. A 2024 meta-analysis identified 16 RCTs evaluating CRS plus HIPEC and found it to be a promising prophylactic and treatment therapy option, however the scarcity of large cohort studies and the heterogeneity of the included studies prevented authors from making a definitive recommendation for use. A phase 3 RCT (N=105) found no difference in OS between CRS plus HIPEC or CRS alone. One small (N=17) preliminary RCT showed improved survival in individuals with peritoneal carcinomatosis due to gastric cancer who received CRS plus HIPEC compared with individuals who received chemotherapy alone. Another (N=68) RCT showed improved survival in individuals who received CRS plus HIPEC compared with CRS alone.



The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peritoneal carcinomatosis of endometrial origin who receive CRS plus HIPEC, the evidence includes cohort studies and a systematic review of these studies. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Only uncontrolled retrospective cohort studies were available, with the largest including only 43 individuals. Randomized trials that compare CRS plus HIPEC with standard treatment (e.g., CRS alone or systemic chemotherapy alone) are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peritoneal mesothelioma who receive CRS plus HIPEC, the evidence includes retrospective cohort studies and systematic reviews. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Retrospective cohort studies have shown median and 5-year overall survival ranging from 30 to 92 months and from 33% to 68%, respectively, for individuals with peritoneal mesothelioma treated with CRS plus HIPEC. Although no RCTs or comparative studies have been published, historical case series have reported a median survival of 12 months with treatment by palliative surgery, systemic or intraperitoneal chemotherapy, and abdominal irradiation. Procedure-related morbidity and mortality rates with CRS plus HIPEC have remained relatively steady over time, at approximately 35% and 5%, respectively. Because the prevalence of peritoneal mesothelioma is very low, conducting comparative trials is difficult. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have newly diagnosed stage III ovarian cancer who receive CRS plus HIPEC, the evidence includes systematic reviews and RCTs. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. For individuals with newly diagnosed stage III ovarian cancer who received neoadjuvant chemotherapy, HIPEC increased the time to disease recurrence and reduced mortality. HIPEC did not increase serious adverse events compared with surgery alone. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have recurrent stage IIIC or IV ovarian cancer who receive CRS plus HIPEC, the evidence includes RCTs and systematic reviews. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. For recurrent stage IIIC or IV disease (second-line setting), evidence from an RCT indicated that CRS plus HIPEC improved survival compared with CRS without HIPEC. However, interpretation of this study is limited because treatment groups in this RCT were unbalanced at baseline (variation in the completeness of cytoreduction), which has been shown to be associated with survival.



Another RCT reported that CRS plus HIPEC did not result in superior outcomes compared to CRS without HIPEC for individuals with platinum-sensitive recurrent disease. The most recent RCTs combining HIPEC with CRS in patients with recurrent disease are conflicting, and the survival benefit of HIPEC with CRS compared with CRS alone remains unclear. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have appendiceal goblet cell tumors who receive CRS plus HIPEC, the evidence includes retrospective cohort studies. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. A propensity score-matched analysis found that CRS plus HIPEC was associated with improved median survival compared to surgery alone. However, this analysis was limited by the retrospective nature of the data and small sample size (N=44). Rates of complete cytoreduction were not reported or accounted for in this study, so between-group differences in this or other variables may have influenced the observed outcomes. Additional studies are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

## Ongoing and Unpublished Clinical Trials

Some currently ongoing or unpublished trials that might influence this review are listed in [Table 1](#).

**Table 1. Summary of Key Trials**

NCT No.	Title	Enrollment	Completion Date
<b>Ongoing</b>			
<b>Colorectal and appendiceal cancer</b>			
<a href="#">NCT01815359</a>	ICARuS Post-operative Intraperitoneal Chemotherapy (EPIC) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) After Optimal Cytoreductive Surgery (CRS) for Neoplasms of the Appendix, Colon or Rectum With Isolated Peritoneal Metastasis	292	Sep 2026
<b>Gastric cancer</b>			
<a href="#">NCT05300945</a>	HIPEC Combined Gastrectomy in Patients With Advanced Gastric Cancer Received Neoadjuvant Chemotherapy	200	Dec 2028



NCT No.	Title	Enrollment	Completion Date
<a href="#">NCT01882933</a>	GASTRICHIP : D2 Resection and HIPEC (Hyperthermic Intraperitoneal Chemoperfusion) in Locally Advanced Gastric Carcinoma. A Randomized and Multicentric Phase III Study	367	May 2026
<b>Ovarian cancer</b>			
<a href="#">NCT06544460</a>	Secondary Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy for Recurrent Ovarian Cancer Patients With PARP Inhibitors Resistance: a Phase II Clinical Study	94	Dec 2026
<a href="#">NCT05827523</a>	Phase III Randomized Trial of HIPEC in Primary Stage Three & Four Ovarian Cancer After Interval Cytoreductive Surgery (FOCUS)	520	Dec 2030
<a href="#">NCT05316181</a>	Randomized Phase III Trial of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Platinum-Resistant Recurrent Ovarian Cancer	140	Dec 2029
<a href="#">NCT01767675</a>	A Phase II Randomized Study: Outcomes After Secondary Cytoreductive Surgery With or Without Carboplatin Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Followed by Systemic Combination Chemotherapy for Recurrent Platinum-Sensitive Ovarian, Fallopian Tube, or Primary Peritoneal Cancer	99	Jan 2026
<a href="#">NCT02124421</a>	Phase II Randomized Study: Cytoreductive Surgery (CRS) With/Without Carboplatin Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Followed by Adjuvant Chemotherapy as Initial Treatment of Ovarian, Fallopian Tube, & Primary Peritoneal Cancer	32	Apr 2028
<a href="#">NCT01376752</a>	A Phase III Randomized Study Evaluating Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC) in the Treatment of Relapse Ovarian Cancer	415	May 2027
<a href="#">NCT03772028</a>	Phase III Randomized Clinical Trial for Stage III Epithelial Ovarian Cancer Randomizing Between Primary Cytoreductive Surgery With or Without Hyperthermic Intraperitoneal Chemotherapy	538	Apr 2026
<b>Unpublished</b>			
<b>Gastric cancer</b>			
<a href="#">NCT02240524</a>	A Phase III Study of Hyperthermic Intraperitoneal Chemotherapy in the Treatment of Locally Advanced Gastric Cancer After radical Gastrectomy With D2 Lymphadenectomy	582	July 2019 (unknown)
<b>Ovarian cancer</b>			



NCT No.	Title	Enrollment	Completion Date
NCT01628380	Stage IIIC Unresectable Epithelial Ovarian/Tubal Cancer With Partial or Complete Response After 1st Line Neoadjuvant Chemotherapy (3 Cycles CBDCA+Paclitaxel): a Phase 3 Prospective Randomized Study Comparing Cytoreductive Surgery + Hyperthermic Intraperitoneal Chemotherapy (CDDP+Paclitaxel) + 3 Cycles CBDCA+Paclitaxel vs Cytoreductive Surgery Alone + 3 Cycles CBDCA+Paclitaxel	94	Jul 2018 (unknown)

NCT: National Clinical Trial

### Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

### American Society of Clinical Oncology

In 2022, the American Society of Clinical Oncology (ASCO) published recommendations for the treatment of metastatic colorectal cancer.<sup>53</sup> The guidelines recommend cytoreductive surgery (CRS) plus systemic chemotherapy for select patients. However, they recommend against CRS with oxaliplatin-based hyperthermic peritoneal chemotherapy based on evidence that this combination results in worse adverse events than CRS plus chemotherapy and little or no survival benefit.

ASCO published a guideline update for neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer in 2025.<sup>54</sup> The update states, "For patients diagnosed with FIGO [International Federation of Gynecology and Obstetrics] stage III disease who have good PS [performance status], adequate renal function, and treated with NACT [neoadjuvant chemotherapy], HIPEC [hyperthermic intraperitoneal chemotherapy] may be offered during ICS [interval cytoreductive surgery] through a shared decision-making process that considers patient



preferences, quality of life, and availability. Participation in HIPEC clinical trials is encouraged. (Evidence quality: Moderate; Strength of recommendation: Conditional)".

## American Society of Colon and Rectal Surgeons

In 2022, the practice guidelines on the treatment of colon cancer by the American Society of Colon and Rectal Surgeons stated that "in patients with resectable colorectal cancer peritoneal metastases, cytoreductive surgery with or without intraperitoneal chemotherapy should be considered as part of a multimodality treatment plan (strong recommendation based on moderate quality evidence, 1B)".<sup>55</sup>

In 2019, the American Society of Colon and Rectal Surgeons guidelines on the management of appendiceal neoplasms stated that "in selected patients with appendiceal epithelial neoplasms, intraperitoneal chemotherapy may offer additional benefit for reducing peritoneal disease recurrence compared with CRS alone." The guidelines mention that HIPEC performed concurrently with CRS is the most common method of delivering this intraperitoneal chemotherapy.<sup>56</sup>

## Chicago Consensus Working Group

In 2020, the Chicago Consensus Working Group for the Management of Peritoneal Surface Malignancies published a consensus statement on the management of ovarian neoplasms.<sup>57</sup> The consensus statement mentions HIPEC and includes it in its management pathway for individuals with peritoneal metastasis from epithelial ovarian cancer. However, the authors also state that "level I evidence is lacking for HIPEC at the time of primary CRS or for stage IV disease" and "similarly, no level I evidence exists for HIPEC use in patients with rare ovarian histologies." Other consensus statements from this group on appendiceal neoplasms, peritoneal mesothelioma, gastric metastases, and colorectal metastases include CRS plus intraperitoneal chemotherapy or CRS +/- intraperitoneal chemotherapy in their management pathways; however, they do not specify whether this intraperitoneal chemotherapy should be HIPEC or another form of intraperitoneal chemotherapy.<sup>58-61</sup>



## National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN) guidelines include the following relevant recommendations for colon cancer (v.3.2025): "The panel currently believes that complete cytoreductive surgery and/or intraperitoneal chemotherapy can be considered in experienced centers for selected individuals with limited peritoneal metastases for whom R0 resection can be achieved. However, the significant morbidity and mortality associated with HIPEC, as well as the conflicting data on clinical efficacy, make this approach very controversial."<sup>62</sup> They additionally state that for patients with appendiceal adenocarcinoma with metastatic disease limited to the peritoneum, "Patients deemed possible surgical candidates should be evaluated at a high-volume center for candidacy for hyperthermic intraperitoneal chemotherapy (HIPEC). These candidates are suggested to receive chemotherapy for up to 6 months, preferably in the neoadjuvant setting. Additional chemotherapy may be considered for patients who are not resectable at initial diagnosis with the possibility of converting to resectable disease."

The NCCN guidelines on gastric cancer (v.2.2025) state that HIPEC "may be a therapeutic alternative for carefully selected patients with peritoneal carcinoma as only disease".<sup>6</sup> In addition they recommend "IC [intraperitoneal chemotherapy]/HIPEC can be used in conjunction with cytoreductive surgery for patients with low PCI [peritoneal cancer index] ( $\leq 10$ ) who are candidates to undergo complete cytoreduction. In patients with a higher burden of peritoneal disease (PCI >10), IC/HIPEC may be considered in the setting of a clinical trial. The role of prophylactic IC/HIPEC/PIPAC [pressurized intraperitoneal aerosolized chemotherapy] is currently investigational for patients with non-metastatic cancers and should only be performed in the setting of a clinical trial."

The NCCN guidelines on uterine neoplasms (v.3.2025) and rectal cancer (v.2.2025) do not discuss cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC).<sup>63,64</sup>

The NCCN guidelines on ovarian cancer (v.2.2025) state that "patients with low volume residual disease after surgical cytoreduction for invasive epithelial ovarian or peritoneal cancer are potential candidates for intraperitoneal chemotherapy" and " HIPEC with cisplatin (100 mg/m<sup>2</sup>) can be considered at the time of interval debulking surgery for stage III disease."

HIPEC can also be considered for suitable stage IV patients (category 2B) who have had a favorable response to neoadjuvant therapy both intraperitoneally and extraperitoneally, or in whom stage IV disease sites have completely resolved (e.g., resolution of malignant pleural effusion) or are now deemed resectable."<sup>65</sup> The guidelines also suggest consideration of HIPEC in poor surgical candidates or those with low likelihood of optimal cytoreduction who have had a response or have stable disease after neoadjuvant therapy.



## Medicare National Coverage

There is no national coverage determination.

## Regulatory Status

Mitomycin, oxaliplatin, carboplatin, and other drugs used for HIPEC have not been approved by the US Food and Drug Administration (FDA) for this indication.

Several peritoneal lavage systems (FDA product code: LGZ) have been cleared for marketing by the FDA through the 510(k) process to provide “warmed, physiologically compatible sterile solution” (e.g., Performer HT perfusion system; RanD; Warrior Blood and Fluid Warmer; X-FLO Fluid Management System). None have received marketing approval or clearance to administer chemotherapy. The FDA has issued warnings to manufacturers of devices that are FDA-cleared for peritoneal lavage using sterile saline solutions when these devices are marketed for off-label use in HIPEC.

**Table 2. Hyperthermic Intraperitoneal Lavage Devices Cleared by the US Food and Drug Administration**

Device	Manufacturer	Date Cleared	510(k) No.	Indication
FluidSmart	THERMEDX LLC	9/5/2017	K172048	For irrigation, distention, fluid warming, and fluid volume/deficit measurements in endoscopic procedures within gynecology, urology, and orthopedic disciplines.
Hang&Go PAC	RanD S.r.l.	12/28/2016	K161613	To recirculate, filtrate and perfuse physiologically compatible sterile solution (i.e. saline solution) in the thoracic or abdominal cavity
The Belmont Hyperthermia Pump	BELMONT INSTRUMENT CORPORATION	9/2/2015	K152208	To raise the temperature of the thoracic or peritoneal cavity to the desired target temperature by continuously lavaging the



Device	Manufacturer	Date Cleared	510(k) No.	Indication
				cavity with circulating warmed sterile solution

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## History



Date	Comments
10/11/05	Add to Medicine section, Oncology subsection - New Policy
06/23/06	Update Scope and Disclaimer - No other changes.
07/10/07	Replace policy - Policy updated with literature review; references added. No change in policy statement.
10/9/07	Cross References Updated - No other changes.
07/08/08	Replace policy - Policy updated with literature search; no change to the policy statement. References added.
08/11/09	Replace policy - Policy updated with literature search; no change to the policy statement References added.
12/14/10	Replace policy - Policy updated with literature search; Rationale and Background sections revised extensively. Policy statement added that cytoreduction and hyperthermic intraperitoneal chemotherapy for the treatment of pseudomyxoma peritonei may be considered medically necessary; investigational policy statement clarified to specify that the indication considered is peritoneal carcinomatosis from colorectal cancer. The term, "pseudomyxoma peritonei" was added to the policy title. References 1-8, 10-12, and 17 added; reference 18 updated.
11/08/11	Replace policy – Policy updated with literature search. References 2, 4 and 20 added; references renumbered. Title changed to include peritoneal mesothelioma. Policy statement added that cytoreductive surgery and perioperative intraperitoneal chemotherapy for the treatment of peritoneal mesothelioma, previously not addressed, may be considered medically necessary. Use of the term "hyperthermic" changed to "perioperative" in the title and policy statements to include early postoperative intraperitoneal chemotherapy. Use of the term "cytoreduction" changed to "cytoreductive surgery" to be more specific. CPT codes added.
01/03/12	Deleted code 96445 removed.
12/19/12	Replace policy. Policy updated with literature search. No references added. No change to policy statements. ICD-10 codes are now effective 10/01/2014.
12/09/13	Replace policy. Policy updated with literature search through August 2013, references 18-22, 27, and 28 added; reference 26 updated. No change to policy statements.
03/11/14	Coding Update. Code 99.85 was removed per ICD-10 mapping project; this code is not utilized for adjudication of policy.
12/17/14	Annual Review. Policy updated with literature search; policy statements unchanged. ICD-9 diagnosis and ICD-10 diagnosis and procedure codes removed; these are not utilized in adjudication of the policy.
03/10/15	Annual Review. Policy updated with literature review through January 2, 2015 references 4-8, 10-14, 18-19, 24, 26-35, 43, 51-61, 63-80, and 83-85 added; references 14 and 23-24 deleted. Investigational policy statement for ovarian cancer, peritoneal carcinomatosis due to gastric cancer or endometrial cancer, and for all other indications added. Medically necessary policy statement unchanged. Clarification note



Date	Comments
	added to policy statement regarding perioperative Title changed to "Select Intra-Abdominal and Pelvic Malignancies" to include the additional indications. Clinical trials note added to Benefit Application.
10/01/16	Annual Review, approved September 13, 2016. Policy updated with literature review through June 10, 2016; references 73 and 86 added. Policy statements unchanged.
10/01/17	Annual Review, approved September 5, 2017. Policy updated with literature review through June 6, 2017; references 26 and 33 added. Policy statements unchanged.
10/01/18	Annual Review, approved September 20, 2018. Policy updated with literature review through August 2018; no references added. Policy statements unchanged. Removed CPT codes 77600, 77605, 77610, 77615, and 77620.
02/01/19	Interim Review, approved January 8, 2019. Policy updated with literature review through September 2018; reference 34 added; references 9-10 updated; some references removed. Hyperthermic intraperitoneal chemotherapy may be considered medically necessary for the treatment of newly diagnosed stage III ovarian cancer. Policy title changed from "Cytoreductive Surgery and Perioperative Intraperitoneal Chemotherapy for Select Intra-Abdominal and Pelvic Malignancies" to "Hyperthermic Intraperitoneal Chemotherapy for Select Intra-Abdominal and Pelvic Malignancies".
01/01/20	Annual Review, approved December 10, 2019. Policy updated with literature review through August 2019; references added; references on NCCN updated. Policy statements unchanged.
01/01/21	Annual Review, approved December 1, 2020. Policy updated with literature review through August 17, 2020; references added. Policy statements unchanged.
10/01/21	Annual Review, approved September 14, 2021. Policy updated with literature review through June 3, 2021; references added and updated. Policy statements unchanged.
10/01/22	Annual Review, approved September 26, 2022. Policy updated with literature review through May 25, 2022; references added and updated. Minor editorial refinements to policy statements; intent unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
10/01/23	Annual Review, approved September 11, 2023. Policy updated with literature review through June 15, 2023; references added and updated. Policy statements unchanged.
01/01/24	Coding update. Added new CPT code 96547.
10/01/24	Annual Review, approved September 23, 2024. Policy updated with literature review through June 5, 2024; references added; guideline references updated. Policy statements unchanged. Added CPT code 96548. Removed unlisted code 96549 as there are now specific CPT codes for HIPEC.
10/01/25	Annual Review, approved September 8, 2025. Policy updated with literature review through June 2, 2025; references added; guideline references updated. Policy statements unchanged.



Date	Comments
03/18/26	Minor update. Minor edits made for clarity only. Policy intent unchanged.

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2026 Premera All Rights Reserved.

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