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REMINDER: Musculoskeletal/Spine/Interventional Pain Management Clinical Guidelines

Highmark Blue Cross Blue Shield is providing a reminder to all providers.

The Musculoskeletal/Spine/Interventional Pain Management clinical guidelines will be updated and take effect February 14, 2020. This applies to both professional provider and facility claims.

At that time, clinical guidelines can be accessed utilizing the live link from the medical policy website.
**REMINDER: Cardiology & Radiology Imaging Clinical Guidelines**

Highmark Blue Cross Blue Shield is providing a reminder to all providers.

The Cardiology & Radiology Imaging clinical guidelines will be updated and take effect February 14, 2020. This applies to both professional provider and facility claims.

At that time, clinical guidelines can be accessed utilizing the live link from the medical policy website.

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**Coverage Guidelines Revised for Natalizumab (Tysabri)**

Highmark Blue Cross Blue Shield has added the following coverage criteria for natalizumab (Tysabri®). Natalizumab (Tysabri) may be considered medically necessary when prescribed by, or in consultation with, a neurologist or provider who specializes in the treatment of multiple sclerosis (MS), and the individual has a diagnosis of relapsing forms of MS as defined by an MRI of the brain showing abnormalities consistent with MS.

This medical policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-85, Natalizumab (Tysabri), for additional information.

**Place of Service: Outpatient**

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**Coverage Guidelines Revised for Irinotecan (Camptosar)**

Highmark Blue Cross Blue Shield has revised coverage criteria for Irinotecan (Camptosar®) to align with National Comprehensive Cancer Network (NCCN) Indications. The following updates will be made:

- Irinotecan (Camptosar) will be allowed as primary treatment for colon adenocarcinoma in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen when used as systemic therapy with panitumumab or cetuximab for unresectable synchronous liver and/or lung metastases if KRAS/NRAS/BRAF wild-type gene and left sided only tumors
- Irinotecan (Camptosar) will be allowed as primary treatment for colon adenocarcinoma in FOLFIRI regimen when therapy in FOLFIRI regimen, FOLFIRI with bevacizumab, cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene and left-sided tumors only) or in FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen with or without bevacizumab when:
  - Used as primary treatment for locally unresectable or medically inoperable disease; or
  - for unresectable synchronous liver and/or lung metastases that remain unresectable after primary systemic therapy; or
  - Used as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with imminent or existing obstruction; or
- Used as primary treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy; or
- Used for unresectable metachronous metastases that remain unresectable after primary treatment

- Irinotecan (Camptosar) in FOLFIRI (fluorouracil, leucovorin, and irinotecan) with bevacizumab, cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene and left-sided tumors only) or in FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen with or without bevacizumab for colon adenocarcinoma when:
  - Used as primary treatment for locally unresectable or medically inoperable disease; or
  - for unresectable synchronous liver and/or lung metastases that remain unresectable after primary systemic therapy; or
  - Used as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with imminent or existing obstruction; or
  - Used as primary treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy; or
  - Used for unresectable metachronous metastases that remain unresectable after primary treatment; or

- Subsequent therapy for unresectable advanced or metastatic colon adenocarcinoma when used in combination with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type only) if previously treated with oxaliplatin and/or irinotecan and if not previously treated with cetuximab or panitumumab

- Used as preoperative chemoradiation in combination with cisplatin as primary treatment for individuals who are medically fit for surgery and have non-cervical esophagus cT1bT2, N+ or cT4a, Any N squamous cell carcinoma or cT1b-cT2, N+ or cT3-cT4a, Any N esophageal and esophagogastric junction adenocarcinoma

- Palliative therapy for individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic esophageal and esophagogastric junction squamous cell carcinoma/adenocarcinoma and Karnofsky performance score greater than or equal to 60% or ECOG performance score less than or equal to two (2) as:
  - First-line therapy in combination with fluorouracil; or
  - Preferred second-line therapy in combination with fluorouracil (if regimen not previously used in first-line therapy) or as a single agent: or
  - Second-line therapy or subsequent therapy in combination with cisplatin or docetaxel

- Palliative therapy for locoregional gastric adenocarcinoma in individuals who are not surgical candidates, recurrent, or metastatic disease and with Karnofsky performance score greater than or equal to 60% or ECOG performance score less than or equal to 2 for:
  - first-line therapy in combination with fluorouracil or
  - preferred second-line or subsequent therapy in combination with fluorouracil (if regimen not previously used in first-line therapy) or as a single agent or
  - second-line therapy in combination with cisplatin or docetaxel

- Subsequent chemotherapy for individuals with small cell lung cancer and performance status 0-2 when used as a single agent, for relapse within 6 months following complete or partial response or stable disease with initial treatment
• Neoadjuvant therapy as a component of FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen or modified FOLFIRINOX regimen with or without subsequent chemoradiation when used for resectable pancreatic adenocarcinoma and ECOG performance status (PS) 0-1, particularly with high-risk features (ie, very highly elevated CA 19-9, large primary tumors, large regional lymph nodes, excessive weight loss, extreme pain)

• Therapy with (if not previously done) or without chemoradiation for local recurrence in the pancreatic operative bed after resection or for metastatic pancreatic adenocarcinoma with or without local recurrence if greater than or equal to 6 months from completion of primary therapy in individuals with good performance status (PS) when:
  o Used as a component of FOLFIRI (fluorouracil, leucovorin, irinotecan) regimen; or
  o Used as a component of FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) or modified FOLFIRINOX regimen if ECOG PS 0-1; or

• Primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable rectal adenocarcinoma if resection is contraindicated following neoadjuvant therapy when:
  o Used in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen; or
  o Used in FOLFIRI regimen with bevacizumab; or
  o Used in FOLFIRI regimen with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene only); or

• Therapy in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen, FOLFIRI with bevacizumab, FOLFIRI with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene only), or in FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen with or without bevacizumab when:
  o Used as adjuvant treatment (following resection and/or local therapy) for resectable metachronous metastases from rectal adenocarcinoma in individuals who have received previous chemotherapy or had growth on neoadjuvant chemotherapy; or
  o Used as adjuvant treatment for unresectable metachronous metastases that converted to resectable rectal adenocarcinoma after primary treatment; or

• Primary treatment with FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin and irinotecan) regimen with cetuximab or panitumumab for synchronous liver only and/or lung only metastases from rectal adenocarcinoma (KRAS/NRAS/BRAF wild-type gene only) that are unresectable or medically inoperable

• Subsequent therapy for progression of unresectable advanced or metastatic rectal adenocarcinoma when:
  o Used as a single agent or in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen with or without bevacizumab (preferred), ziv-ailibercept, or ramucirumab if previously treated with a fluoropyrimidine only or with oxaliplatin-based therapy without irinotecan; or
  o Used in FOLFIRI regimen with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene only) if previously treated with oxaliplatin-based regimens without irinotecan, cetuximab or panitumumab; or
  o Used in combination with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene only) if previously treated with oxaliplatin and/or irinotecan and if not previously treated with cetuximab or panitumumab; or
  o Used in combination with vemurafenib and cetuximab or panitumumab (if BRAF V600E mutation positive) if previously treated with oxaliplatin and/or irinotecan and if not previously treated with cetuximab or panitumumab; or
  o Used in combination with oxaliplatin with or without bevacizumab if previously treated with a fluoropyrimidine without irinotecan or oxaliplatin
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- Remove coverage as second-line therapy for locally advanced unresectable or metastatic pancreatic adenocarcinoma as fluoropyrimidine-based therapy for patients with good performance status and disease progression who were previously treated with gemcitabine-based therapy
- Remove coverage as a component of FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen if KPS greater than or equal to 70 for pancreatic adenocarcinoma
- Remove coverage when used for rectal adenocarcinoma in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen with or without bevacizumab or with or without cetuximab or panitumumab (KRAS/ NRAS/ BRAF wild-type gene only) or in FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen with or without bevacizumab as:
  - primary treatment for T3, N0, M0; any T, N1-2, M0; or T4 and/or locally unresectable or medically inoperable disease with no metastases if resection is contraindicated following neoadjuvant therapy; or
  - primary treatment for unresectable synchronous metastases or medically inoperable disease; or
  - systemic therapy following primary treatment with chemoradiation or local therapy for symptomatic unresectable synchronous metastases or medically inoperable disease; or
  - adjuvant treatment (following resection and/or local therapy) for resectable metachronous metastases in patients who have received previous chemotherapy or had growth on neoadjuvant chemotherapy; or
  - adjuvant treatment for unresectable metachronous metastases that converted to resectable disease
- Remove coverage when used in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen as neoadjuvant therapy for resectable synchronous metastases from rectal adenocarcinoma

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-109, Irinotecan (Camptosar), for additional information.

Place of Service: Outpatient

Coverage Guidelines Developed for Levoleucovorin (Khapzory)

Highmark Blue Cross Blue Shield has developed coverage criteria for levoleucovorin (Khapzory™) for the U.S. Food and Drug Administration (FDA) approved indications to include rescue after high-dose methotrexate in osteosarcoma, diminishing the toxicity associated with over dosage of folic acid antagonists or impaired methotrexate elimination, and treatment of individuals with metastatic colorectal cancer in combination with fluorouracil (5-fu).

The Medical Policy will apply to both professional provider and facility claims. The effective date was October 28, 2019.

Please refer to Medical Policy I-114, Levoleucovorin (Fusilev or Khapzory), for additional information.

Place of Service: Outpatient
Coverage Guidelines Revised for Alemtuzumab (Lemtrada)

Highmark Blue Cross Blue Shield has added the following coverage criteria for alemtuzumab (Lemtrada™).

Alemtuzumab (Lemtrada) may be considered medically necessary for the treatment of relapsing-remitting forms of multiple sclerosis (MS) when the following criteria are met:

- A diagnosis of relapsing forms of MS as defined by an MRI of the brain showing abnormalities consistent with MS; and
- Prescribed by or in consultation with a neurologist or provider who specializes in the treatment of MS; and
- Individual has had an inadequate response to two or more medications indicated for the treatment of MS; and
- Individual has HIV-negative status; and
- Alemtuzumab (Lemtrada) is not to be used in combination with other disease modifying therapies (DMTs); and
- Individual receives appropriate vaccinations, concomitant prophylaxis, and pre-infusion medications:
  - High dose corticosteroids prior to infusion and for first 3 days of each treatment course; and
  - Anti-viral prophylaxis for herpetic viral infections; and
  - Completion of any necessary immunizations at least 6 weeks prior to treatment with alemtuzumab (Lemtrada), with no live vaccines administered concurrent or within 6 weeks prior to treatment.

This medical policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-118, Alemtuzumab (Lemtrada), for additional information.

Place of Service: Outpatient

Coverage Guidelines Revised for Eribulin Mesylate (Halaven)

Highmark Blue Cross Blue Shield has revised coverage criteria for eribulin mesylate (Halaven ®) as follows:

Invasive breast cancer will be considered medically necessary for the following NCCN recommendations:

- Single agent (preferred regimen) for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER-2)-negative with EITHER of the following:
  - Hormone receptor-negative; or
  - Hormone receptor-positive with visceral crisis or endocrine therapy refractory; or
- Combination therapy with trastuzumab for recurrent or stage IV (M1) HER2-positive disease that is:
  - Hormone receptor-negative; or
  - Hormone receptor-positive with or without endocrine therapy.
Uterine neoplasms—uterine sarcoma will be considered medically necessary for the following NCCN recommendations:

- Used as single-agent therapy for recurrent or metastatic disease which has progressed following prior cytotoxic chemotherapy.

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-119, Eribulin Mesylate (Halaven), for additional information.

Place of Service: Outpatient

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**Coverage Guidelines Revised for Programmed Death Receptor (PD-1)/Programmed Death-Ligand (PD-L1) Blocking Antibodies**

Highmark Blue Cross Blue Shield has revised coverage criteria for Programmed Death Receptor (PD-1)/Programmed Death-Ligand (PD-L1) Blocking Antibodies per approved FDA indications and NCCN guidelines. The updated criteria will include the following updates:

- Avelumab (Bavencio®) as single agent subsequent systemic therapy for urothelial carcinoma of the prostate post-platinum will be limited to metastatic disease
- Removed coverage for nivolumab (Opdivo®) as a treatment for melanoma that is BRAF V600 wild type or mutation positive
- Nivolumab (Opdivo) as preferred adjuvant therapy as a single agent for stage II sentinel node positive cutaneous melanoma will be allowed during active nodal basin ultrasound surveillance or after complete lymph node dissection (CLND) and will be limited to resected disease
- Pembrolizumab (Keytruda®) as first-line, single agent for NSCLC expressing PD-L1 (Tumor Proportion Score (TPS) greater than or equal to 1%), with no EGFR or ALK genomic tumor aberrations will be limited to metastatic disease or stage III disease in individuals who are not candidates for surgical resection or definitive chemoradiation
- Pembrolizumab (Keytruda) for classic Hodgkin lymphoma will be updated to the following:
  - Treatment of Adult individuals aged 18 years and older as third-line or subsequent systemic therapy as a single agent for:
    - Disease that has relapsed or progressed after autologous hematopoietic stem cell transplant (HSCT) with or without brentuximab vedotin; or
    - Relapsed/refractory disease in individuals who are transplant-ineligible based on comorbidity or failure of second-line chemotherapy; or
    - Post-allogeneic transplant; or
  - Treatment of individuals greater than 60 years of age as palliative therapy as a single agent for:
    - Disease that has relapsed or progressed after autologous hematopoietic stem cell transplant (HSCT) ± brentuximab vedotin; or
    - Relapsed/refractory disease in individuals who are transplant-ineligible based on comorbidity or failure of second-line chemotherapy; or

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Post-allogeneic transplant

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-120, Programmed Death Receptor (PD-1)/ Programmed Death-Ligand (PD-L1) Blocking Antibodies, for additional information.

**Place of Service: Outpatient**

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**Coverage Guidelines Revised for Proprotein Convertase Subtilisin Kexin 9 (PCSK9) Inhibitors**

Highmark Blue Cross Blue Shield has revised coverage criteria for Proprotein Convertase Subtilisin Kexin 9 (PCSK9) Inhibitors to align with national standards on the management of blood cholesterol. The criteria changes are as follows:

- Statin intolerant individuals will be required to meet ONE of the following criteria:
  - A trial of at least two chemically-distinct statins and documentation of severe and intolerable skeletal-muscle related symptoms with each of the two statins that resolved upon statin discontinuation; and
  - Documentation of ONE of the following during ANY course of statin therapy preventing high intensity dosing:
    - Creatinine kinase (CK) increase to 10 times upper limit of normal (ULN); or
    - Liver function tests (LFTs) increase to 3 times upper limit of normal (ULN); or
    - Hospitalization due to severe statin-related adverse event, such as rhabdomyolysis.
    - Documentation of myalgia (muscle symptoms without CK elevations) or
    - Documentation of myositis (muscle symptoms with CI elevations < 10 times upper limit of normal)

- The target LDL-C for Hypercholesterolemia with Atherosclerotic Cardiovascular Disease (ASCVD) will be reduced from 100mg/dl to 70mg/dl to align with national guidelines

- If individuals have less than or equal to a 20% decrease in LDL-C required to achieve target level after statin trials, they must try ezetimibe, fibrates, or bile acid sequestrants either alone (if intolerant) or in combination with a statin (if tolerated) for at least 8 continuous weeks, unless documented contraindication or intolerance

- The LCL-C for reauthorization criteria for Heterozygous Familial Hypercholesterolemia (HeFH) is being reduced from 160 mg/dl to 130 mg/dl and for Homozygous Familial Hypercholesterolemia (HoFH) it is being reduced from 100 mg/dl to 70 mg/dl

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-142, Proprotein Convertase Subtilisin Kexin 9 (PCSK9) Inhibitors, for additional information.

**Place of Service: Outpatient**
Testosterone Enanthate (Xyosted) Added to Clinical Guidelines

Highmark Blue Cross Blue Shield has added testosterone enanthate (Xyosted®) to the revised clinical criteria for Testosterone Androgens.

This new medical policy will apply to both professional provider and facility claims. The effective date is November 11, 2019.

Please refer to Medical Policy I-145, Testosterone Androgens, for additional information.

Place of Service: Inpatient/Outpatient

Coverage Guidelines Revised for Elotuzumab (Empliciti)

Highmark Blue Cross Blue Shield has revised coverage criteria for elotuzumab (Empliciti®) to align with the FDA recommended indications. The criteria changes indicate that elotuzumab (Empliciti) may only be used for individuals 18 years of age and older and bortezomib and dexamethasone will no longer be allowed in combination with elotuzumab (Empliciti) as an option for refractory multiple myeloma.

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-166, Elotuzumab (Empliciti), for additional information.

Place of Service: Outpatient

Coverage Guidelines Revised for Trabectedin (Yondelis)

Highmark Blue Cross Blue Shield has revised coverage criteria for trabectedin (Yondelis®) to align with the NCCN recommended indications. The criteria changes indicate that trabectedin (Yondelis) will no longer be covered as single agent therapy for uterine leiomyosarcoma that has been treated with a prior anthracycline-containing regimen for extrapelvic recurrence with no prior radiation therapy.

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-169, Trabectedin (Yondelis), for additional information.

Place of Service: Outpatient
Coverage Guidelines Revised for Ocrelizumab (Ocrevus)

Highmark Blue Cross Blue Shield has added the following coverage criteria for Ocrelizumab (Ocrevus®). Ocrelizumab (Ocrevus) may be considered medically necessary when prescribed by, or in consultation with, a neurologist or provider who specializes in the treatment of multiple sclerosis.

This medical policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-171, Ocrelizumab (Ocrevus), for additional information.

Place of Service: Outpatient

Coverage Criteria Revised for External Counterpulsation

Highmark Blue Cross Blue Shield has revised coverage criteria for M-52. This revised policy will apply to both professional and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy, M-52, External Counterpulsation for additional information.

Place of Service: Outpatient

Facility added to Artificial Hearts and Ventricular Assist Devices Diagnosis codes revised

Highmark Blue Cross Blue Shield has added Facility to the policy. This revised policy will apply to both professional and facility claims. The effective date is January 27, 2020. Diagnosis Codes have also been revised.

Please refer to Medical Policy S-60, Artificial Hearts and Ventricular Assist Devices for additional information.

Place of Service: Inpatient

Facility application added for Heart Transplantation

Facility has been added and this revised policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy S-122, Heart Transplantation, for additional information.

Place of Service: Inpatient
Facility application added for Heart/Lung Transplantation

Facility has been added and this revised policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy S-125, Heart/Lung Transplantation, for additional information.

Place of Service: Inpatient

Facility application added for Pancreas/Kidney Transplantation

Facility has been added and this revised policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy S-126, Pancreas/Kidney Transplantation, for additional information.

Place of Service: Inpatient

Coverage Guidelines Developed for Rhinomanometry

Highmark Blue Cross Blue Shield has developed coverage criteria for the use of rhinomanometry as an evaluation tool for cleft palate surgery. Rhinomanometry may be considered medically necessary when nasendoscopy is not available and it is not considered a replacement for nasendoscopy.

All other indications will remain not medically necessary.

The Medical Policy will apply to both professional provider and facility claims. The effective date is November 18, 2019.

Please refer to Medical Policy M-84-001 for additional information.

Place of Service: Outpatient
Coverage Criteria Revised for Irinotecan (Camptosar)

Highmark’s Medicare Advantage products have revised coverage criteria for Irinotecan (Camptosar®) to align with National Comprehensive Cancer Network (NCCN) Indications. The following updates will be made:

- Irinotecan (Camptosar) will be allowed as primary treatment for colon adenocarcinoma in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen when used as systemic therapy with panitumumab or cetuximab for unresectable synchronous liver and/or lung metastases if KRAS/NRAS/BRAF wild-type gene and left sided only tumors

- Irinotecan (Camptosar) will be allowed as primary treatment for colon adenocarcinoma in FOLFIRI regimen when therapy in FOLFIRI regimen, FOLFIRI with bevacizumab, cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene and left-sided tumors only) or in FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen with or without bevacizumab when:
  - Used as primary treatment for locally unresectable or medically inoperable disease; or
  - for unresectable synchronous liver and/or lung metastases that remain unresectable after primary systemic therapy; or
  - Used as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with imminent or existing obstruction; or
  - Used as primary treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy; or
  - Used for unresectable metachronous metastases that remain unresectable after primary treatment

- Irinotecan (Camptosar) in FOLFIRI (fluorouracil, leucovorin, and irinotecan) with bevacizumab, cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene and left-sided tumors only) or in FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen with or without bevacizumab for colon adenocarcinoma when:
  - Used as primary treatment for locally unresectable or medically inoperable disease; or
  - for unresectable synchronous liver and/or lung metastases that remain unresectable after primary systemic therapy; or
  - Used as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with imminent or existing obstruction; or
  - Used as primary treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy; or
  - Used for unresectable metachronous metastases that remain unresectable after primary treatment; or
- Subsequent therapy for unresectable advanced or metastatic colon adenocarcinoma when used in combination with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type only) if previously treated with oxaliplatin and/or irinotecan and if not previously treated with cetuximab or panitumumab.
- Used as preoperative chemoradiation in combination with cisplatin as primary treatment for individuals who are medically fit for surgery and have non-cervical esophagus cT1bT2, N+ or cT4a; Any N squamous cell carcinoma or cT1b-cT2, N+ or cT3-cT4a, Any N esophageal and esophagogastric junction adenocarcinoma.
- Palliative therapy for individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic esophageal and esophagogastric junction squamous cell carcinoma/adenocarcinoma and Karnofsky performance score greater than or equal to 60% or ECOG performance score less than or equal to two (2) as:
  - First-line therapy in combination with fluorouracil; or
  - Preferred second-line therapy in combination with fluorouracil (if regimen not previously used in first-line therapy) or as a single agent: or
  - Second-line therapy or subsequent therapy in combination with cisplatin or docetaxel.
- Palliative therapy for locoregional gastric adenocarcinoma in individuals who are not surgical candidates, recurrent, or metastatic disease and with Karnofsky performance score greater than or equal to 60% or ECOG performance score less than or equal to 2 for:
  - First-line therapy in combination with fluorouracil or
  - Preferred second-line or subsequent therapy in combination with fluorouracil (if regimen not previously used in first-line therapy) or as a single agent: or
  - Second-line therapy in combination with cisplatin or docetaxel.
- Subsequent chemotherapy for individuals with small cell lung cancer and performance status 0-2 when used as a single agent, for relapse within 6 months following complete or partial response or stable disease with initial treatment.
- Neoadjuvant therapy as a component of FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen or modified FOLFIRINOX regimen with or without subsequent chemoradiation when used for resectable pancreatic adenocarcinoma and ECOG performance status (PS) 0-1, particularly with high-risk features (ie, very highly elevated CA 19-9, large primary tumors, large regional lymph nodes, excessive weight loss, extreme pain).
- Therapy with (if not previously done) or without chemoradiation for local recurrence in the pancreatic operative bed after resection or for metastatic pancreatic adenocarcinoma with or without local recurrence if greater than or equal to 6 months from completion of primary therapy in individuals with good performance status (PS) when:
  - Used as a component of FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen; or
  - Used as a component of FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) or modified FOLFIRINOX regimen if ECOG PS 0-1; or
- Primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable rectal adenocarcinoma if resection is contraindicated following neoadjuvant therapy when:
  - Used in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen; or
  - Used in FOLFIRI regimen with bevacizumab; or
  - Used in FOLFIRI regimen with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene only); or
- Therapy in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen, FOLFIRI with bevacizumab, FOLFIRI with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-
type gene only), or in FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen with or without bevacizumab when:
  o Used as adjuvant treatment (following resection and/or local therapy) for resectable metachronous metastases from rectal adenocarcinoma in individuals who have received previous chemotherapy or had growth on neoadjuvant chemotherapy; or
  o Used as adjuvant treatment for unresectable metachronous metastases that converted to resectable rectal adenocarcinoma after primary treatment; or
  • Primary treatment with FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin and irinotecan) regimen with cetuximab or panitumumab for synchronous liver only and/or lung only metastases from rectal adenocarcinoma (KRAS/NRAS/BRAF wild-type gene only) that are unresectable or medically inoperable
  • Subsequent therapy for progression of unresectable advanced or metastatic rectal adenocarcinoma when:
    o Used as a single agent or in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen with or without bevacizumab (preferred), ziv-aflibercept, or ramucirumab if previously treated with a fluoropyrimidine only or with oxaliplatin-based therapy without irinotecan; or
    o Used in FOLFIRI regimen with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene only) if previously treated with oxaliplatin-based regimens without irinotecan, cetuximab or panitumumab; or
    o Used in combination with cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene only) if previously treated with oxaliplatin and/or irinotecan and if not previously treated with cetuximab or panitumumab; or
    o Used in combination with vemurafenib and cetuximab or panitumumab (if BRAF V600E mutation positive) if previously treated with oxaliplatin and/or irinotecan and if not previously treated with cetuximab or panitumumab; or
    o Used in combination with oxaliplatin with or without bevacizumab if previously treated with a fluoropyrimidine without irinotecan or oxaliplatin
  • Remove coverage as second-line therapy for locally advanced unresectable or metastatic pancreatic adenocarcinoma as fluoropyrimidine-based therapy for patients with good performance status and disease progression who were previously treated with gemcitabine-based therapy
  • Remove coverage as a component of FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen if KPS greater than or equal to 70 for pancreatic adenocarcinoma
  • Remove coverage when used for rectal adenocarcinoma in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen with or without bevacizumab or with or without cetuximab or panitumumab (KRAS/NRAS/BRAF wild-type gene only) or in FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen with or without bevacizumab as:
    o primary treatment for T3, N0, M0; any T, N1-2, M0; or T4 and/or locally unresectable or medically inoperable disease with no metastases if resection is contraindicated following neoadjuvant therapy; or
    o primary treatment for unresectable synchronous metastases or medically inoperable disease; or
    o systemic therapy following primary treatment with chemoradiation or local therapy for symptomatic unresectable synchronous metastases or medically inoperable disease; or
    o adjuvant treatment (following resection and/or local therapy) for resectable metachronous metastases in patients who have received previous chemotherapy or had growth on neoadjuvant chemotherapy; or
    o adjuvant treatment for unresectable metachronous metastases that converted to resectable disease
• Remove coverage when used in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen as neoadjuvant therapy for resectable synchronous metastases from rectal adenocarcinoma

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-24, Irinotecan (Camptosar), for additional information.

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**Clinical Guidelines Established for Pegloticase (Krystexxa)**

Highmark’s Medicare Advantage products have established coverage guidelines for pegloticase (Krystexxa™).

Pegloticase (Krystexxa) may be considered medically necessary for the treatment of chronic gout in individuals 18 years of age and older who have failed to normalize serum uric acid, and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

The use of pegloticase for any other indication is considered not medically necessary.

This new medical policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-29, Pegloticase (Krystexxa) for additional information.

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**Clinical Guidelines Revised for Natalizumab (Tysabri)**

Highmark’s Medicare Advantage products have revised coverage guidelines for natalizumab (Tysabri®).

Natalizumab (Tysabri) may be considered medically necessary when the individual has a diagnosis of relapsing forms of multiple sclerosis (MS) as defined by an MRI of the brain showing abnormalities consistent with MS.

This new medical policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-85, Natalizumab (Tysabri), for additional information.
Coverage Criteria Revised for Developed for Levoleucovorin (Khapzory)

Highmark’s Medicare Advantage products have developed coverage criteria for levoleucovorin (Khapzory™) for the U.S. Food and Drug Administration (FDA) approved indications to include rescue after high-dose methotrexate in osteosarcoma, diminishing the toxicity associated with over dosage of folic acid antagonists or impaired methotrexate elimination, and treatment of individuals with metastatic colorectal cancer in combination with fluorouracil (5-fu).

The Medical Policy will apply to both professional provider and facility claims. The effective date was October 28, 2019.

Please refer to Medical Policy I-114, Levoleucovorin (Fusilev or Khapzory), for additional information.

Clinical Guidelines Revised for Alemtuzumab (Lemtrada)

Highmark’s Medicare Advantage products have revised coverage guidelines for alemtuzumab (Lemtrada™).

Alemtuzumab (Lemtrada) may be considered medically necessary for the treatment of relapsing-remitting forms of MS in individuals who have had an inadequate response to two or more medications indicated for the treatment of MS and when ALL of the following criteria are met:

- A diagnosis of relapsing forms of MS as defined by an MRI of the brain showing abnormalities consistent with MS; and
- Individual has HIV-negative status; and
- Alemtuzumab (Lemtrada) is not to be used in combination with other disease modifying therapies (DMTs); and
- Individual receives appropriate vaccinations, concomitant prophylaxis, and pre-infusion medications:
  - High dose corticosteroids prior to infusion and for first 3 days of each treatment course; and
  - Anti-viral prophylaxis for herpetic viral infections; and
  - Completion of any necessary immunizations at least 6 weeks prior to treatment with alemtuzumab (Lemtrada), with no live vaccines administered concurrent or within 6 weeks prior to treatment.

This new medical policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-118, Alemtuzumab (Lemtrada), for additional information.
Coverage Criteria Revised for Eribulin Mesylate (Halaven)

Highmark’s Medicare Advantage products have revised coverage criteria for eribulin mesylate (Halaven ®) as follows:

Invasive breast cancer will be considered medically necessary for the following NCCN recommendations:

- Single agent (preferred regimen) for recurrent or stage IV (M1) human epidermal growth factor receptor 2 (HER-2)-negative with EITHER of the following:
  - Hormone receptor-negative; or
  - Hormone receptor-positive with visceral crisis or endocrine therapy refractory; or
- Combination therapy with trastuzumab for recurrent or stage IV (M1) HER2-positive disease that is:
  - Hormone receptor-negative; or
  - Hormone receptor-positive with or without endocrine therapy.

Uterine neoplasms-uterine sarcoma will be considered medically necessary for the following NCCN recommendations:

- Used as single-agent therapy for recurrent or metastatic disease which has progressed following prior cytotoxic chemotherapy.

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-119, Eribulin Mesylate (Halaven), for additional information.

Coverage Criteria Revised for Programmed Death Receptor (PD-1)/Programmed Death-Ligand (PD-L1) Blocking Antibodies

Highmark’s Medicare Advantage products have revised coverage criteria for Programmed Death Receptor (PD-1)/Programmed Death-Ligand (PD-L1) Blocking Antibodies per approved Food and Drug Administration (FDA) indications and National Comprehensive Cancer Network (NCCN) guidelines. The updated criteria will include the following updates:

- Avelumab (Bavencio®) as single agent subsequent systemic therapy for urothelial carcinoma of the prostate post-platinum will be limited to metastatic disease
- Removed coverage for nivolumab (Opdivo®) as a treatment for melanoma that is BRAF V600 wild type or mutation positive
- Nivolumab (Opdivo) as preferred adjuvant therapy as a single agent for stage II sentinel node positive cutaneous melanoma will be allowed during active nodal basin ultrasound surveillance or after complete lymph node dissection (CLND) and will be limited to resected disease
- Pembrolizumab (Keytruda®) as first-line, single agent for NSCLC expressing PD-L1 (Tumor Proportion Score (TPS) greater than or equal to 1%), with no EGFR or ALK genomic tumor aberrations will be limited to metastatic disease or stage III disease in individuals who are not candidates for surgical resection or definitive chemoradiation
• Pembrolizumab (Keytruda) for classic Hodgkin lymphoma will be updated to the following:
  o Treatment of Adult individuals aged 18 years and older as third-line or subsequent systemic therapy as a single agent for:
    ▪ Disease that has relapsed or progressed after autologous hematopoietic stem cell transplant (HSCT) with or without brentuximab vedotin; or
    ▪ Relapsed/refractory disease in individuals who are transplant-ineligible based on comorbidity or failure of second-line chemotherapy; or
    ▪ Post-allogeneic transplant; or
  o Treatment of individuals greater than 60 years of age as palliative therapy as a single agent for:
    ▪ Disease that has relapsed or progressed after autologous hematopoietic stem cell transplant (HSCT) ± brentuximab vedotin; or
    ▪ Relapsed/refractory disease in individuals who are transplant-ineligible based on comorbidity or failure of second-line chemotherapy; or
    ▪ Post-allogeneic transplant

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-120, Programmed Death Receptor (PD-1)/ Programmed Death-Ligand (PD-L1) Blocking Antibodies, for additional information.

Place of Service: Outpatient

Coverage Criteria Revised for Proprotein Convertase Subtilisin Kexin 9 (PCSK9) Inhibitors

Highmark’s Medicare Advantage products have revised coverage criteria for Proprotein Convertase Subtilisin Kexin 9 (PCSK9) Inhibitors to align with national standards on the management of blood cholesterol. The criteria changes are as follows:

• Statin intolerant individuals will be required to meet ONE of the following criteria:
  o A trial of at least two chemically-distinct statins and documentation of severe and intolerable skeletal-muscle related symptoms with each of the two statins that resolved upon statin discontinuation; and
  o Documentation of ONE of the following during ANY course of statin therapy preventing high intensity dosing:
    ▪ Creatinine kinase (CK) increase to 10 times upper limit of normal (ULN); or
    ▪ Liver function tests (LFTs) increase to 3 times upper limit of normal (ULN); or
    ▪ Hospitalization due to severe statin-related adverse event, such as rhabdomyolysis.
    ▪ Documentation of myalgia (muscle symptoms without CK elevations) or
    ▪ Documentation of myositis (muscle symptoms with CI elevations < 10 times upper limit of normal)
- The target LDL-C for Hypercholesterolemia with Atherosclerotic Cardiovascular Disease (ASCVD) will be reduced from 100mg/dl to 70mg/dl to align with national guidelines.
- If individuals have less than or equal to a 20% decrease in LDL-C required to achieve target level after statin trials, they must try ezetimibe, fibrates, or bile acid sequestrants either alone (if intolerant) or in combination with a statin (if tolerated) for at least 8 continuous weeks, unless documented contraindication or intolerance.
- The LCL-C for reauthorization criteria for Heterozygous Familial Hypercholesterolemia (HeFH) is being reduced from 160 mg/dl to 130 mg/dl and for Homozygous Familial Hypercholesterolemia (HoFH) it is being reduced from 100 mg/dl to 70 mg/dl.

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-142, Proprotein Convertase Subtilisin Kexin 9 (PCSK9) Inhibitors, for additional information.

### Coverage Criteria Revised for Elotuzumab (Empliciti)

Highmark’s Medicare Advantage products have revised coverage criteria for elotuzumab (Empliciti®) to align with the U.S. Food and Drug Administration (FDA) recommended indications. The criteria changes indicate that elotuzumab (Empliciti) may only be used for individuals 18 years of age and older and bortezomib and dexamethasone will no longer be allowed in combination with elotuzumab (Empliciti) as an option for refractory multiple myeloma.

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-166, Elotuzumab (Empliciti), for additional information.

### Coverage Criteria Revised for Trabectedin (Yondelis)

Highmark’s Medicare Advantage products have revised coverage criteria for trabectedin (Yondelis®) to align with the National Comprehensive Cancer Network (NCCN) recommended indications. The criteria changes indicate that trabectedin (Yondelis) will no longer be covered as single agent therapy for uterine leiomyosarcoma that has been treated with a prior anthracycline-containing regimen for extrapelvic recurrence with no prior radiation therapy.

The Medical Policy will apply to both professional provider and facility claims. The effective date is January 27, 2020.

Please refer to Medical Policy I-169, Trabectedin (Yondelis), for additional information.
Comments on these new medical policies?
We want to know what you think about our new medical policy changes. Send us an email with any questions or comments that you may have on the new medical policies in this edition of Medical Policy Update.

Write to us at medicalpolicy@highmark.com.

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About this newsletter

*Medical Policy Update* is the monthly newsletter for most health care professionals (and office staff) and facilities who participate in our networks and submit claims to Highmark using the 837P HIPAA transaction or the CMS 1500 form, or the 837I HIPAA transaction.

*Medical Policy Update* focuses only on medical policy and claims administration updates, including coding guidelines and procedure code revisions, and is the sole source for this information. For all other news, information and updates, be sure to read *Provider News*, available on the Provider Resource Center at [www.highmarkbcbs.com](http://www.highmarkbcbs.com).

Inquiries about Eligibility, Benefits, Claims Status or Authorizations

For inquiries about eligibility, benefits, claim status or authorizations, Highmark Blue Cross Blue Shield encourages providers to use the electronic resources available to them - Navinet® and the applicable HIPAA transactions – prior to placing a telephone call to the Provider Service Center at 1-800-242-0514.

Acknowledgement

The five-digit numeric codes that appear in *Medical Policy Update* were obtained from the *Current Procedural Terminology (CPT)*, as contained in CPT-2019, Copyright 2018, by the American Medical Association. *Medical Policy Update* includes CPT descriptive terms and numeric procedure codes and modifiers that are copyrighted by the American Medical Association. These procedure codes and modifiers are used for reporting medical services and procedures.