Select Oral Oncology Drugs

Policy # 00642
Original Effective Date: 01/01/2019
Current Effective Date: 01/01/2019

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider cabozantinib (Cabometyx™)‡, brand and generic imatinib (Gleevec®)‡, palbociclib (Ibrance®)‡, lenalidomide (Revlimid®)‡, dasatinib (Sprycel®)‡, sunitinib (Sutent®)‡, and enzalutamide (Xtandi®)‡ for the treatment of cancer to be **eligible for coverage.**

Patient Selection Criteria
Coverage eligibility for cabozantinib (Cabometyx), brand and generic imatinib (Gleevec), palbociclib (Ibrance), lenalidomide (Revlimid), dasatinib (Sprycel), sunitinib (Sutent), and enzalutamide (Xtandi) will be considered when the following criteria are met for the requested drug:

- For Cabometyx requests
  - Patient has a diagnosis of advanced renal cell carcinoma (RCC); OR
  - Patient has a diagnosis of non-small cell lung cancer (NSCLC) with rearranged during transfection (RET) gene rearrangements
- For Gleevec and generic imatinib requests
  - Patient has a diagnosis of acute lymphoblastic leukemia (ALL) that is Philadelphia chromosome positive (Ph+); OR
  - Patient has a diagnosis of chronic myeloid leukemia (CML) that is Philadelphia chromosome positive (Ph+); OR
  - Patient has a diagnosis of dermatofibrosarcoma protuberans (DFSP); OR
  - Patient has a diagnosis of gastrointestinal stromal tumor (GIST); OR
  - Patient has a diagnosis of hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL); OR
  - Patient has a diagnosis of aggressive systemic mastocytosis (ASM); OR
  - Patient has a diagnosis of myelodysplastic/myeloproliferative disease (MDS/MPD) [e.g. polycythemia vera, myelofibrosis]; AND
    - The condition is associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements; OR
  - Patient has a diagnosis of chordoma; OR
  - Patient has a diagnosis of unresectable or advanced fibromatosis (Desmoid tumors); OR
  - Patient has a diagnosis of chronic graft versus host disease (GVHD) AND
  - Patient has tried at least one conventional systemic treatment for GVHD (e.g. corticosteroids, cyclosporine, tacrolimus, mycophenolate); OR
  - Patient has a diagnosis of metastatic melanoma; AND

- Patient has c-Kit-positive advanced/recurrent or metastatic melanoma; OR
- Patient has a diagnosis of pigmented villonodular synovitis/tenosynovial giant cell tumor (PVNS/TGCT)
- If the request is for brand Gleevec: the patient has tried and failed (e.g. intolerance or inadequate response) GENERIC imatinib unless there is clinical evidence or patient history that suggests the use of GENERIC imatinib will be ineffective or cause an adverse reaction to the patient (e.g. difference in dyes, fillers, or preservatives).
- *(Note: this specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- For Ibrance requests
  - Patient is a postmenopausal female with a diagnosis of breast cancer and meets all of the following criteria
    - Patient has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive (ER+) and/or progesterone receptor positive (PR+)] disease; AND
    - Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
    - Patient meets ONE of the following criteria
      - Ibrance will be used as first-line (initial) endocrine based therapy in combination with anastrozole, exemestane, or letrozole; OR
      - Patient meets both of the following conditions:
        - Patient has relapsed or progressed during prior endocrine therapy with at least one of the following: anastrozole, exemestane, letrozole, tamoxifen, toremifene (Fareston®)‡, exemestane plus everolimus (Afinitor®)‡, fulvestrant (Faslodex®)‡, Afinitor plus Faslodex or tamoxifen, megestrol, fluoxymesterone, ethinyl estradiol; AND
        - Ibrance will be used in combination with Faslodex; AND
    - Patient has not had disease progression while on Ibrance, ribociclib (Kisqali®)‡, or abemaciclib (Verzenio®)‡; OR
  - Patient is a pre/perimenopausal female with a diagnosis of breast cancer and meets all of the following criteria:
    - Patient has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive (ER+) and/or progesterone receptor positive (PR+)] disease; AND
    - Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
    - Patient is receiving ovarian suppression/ablation with a gonadotropin-releasing hormone (GnRH) agonist (e.g., leuprolide [Leupron®]‡, triptorelin [Trelstar®]‡, goserelin [Zoladex®]‡), or has had surgical bilateral oophorectomy or ovarian irradiation; AND
    - Patient meets ONE of the following conditions:

- □ Ibrance will be used as first-line (initial) endocrine based therapy in combination with anastrozole, exemestane, or letrozole; OR
- □ Patient meets BOTH of the following criteria:
  - ▸ Patient has relapsed or progressed during prior endocrine therapy with at least one of the following: anastrozole, exemestane, letrozole, tamoxifen, Fareston, exemestane plus Afinitor, Faslodex, Afinitor plus Faslodex or tamoxifen, megestrol acetate, fluoxymesterone, ethinyl estradiol; AND
  - ▸ Ibrance will be used in combination with Faslodex; AND

- Patient has not had disease progression while on Ibrance, Kisqali, or Verzenio; OR

- Patient is a male with a diagnosis of breast cancer and meets all of the following criteria
  - Patient has advanced or metastatic hormone receptor positive (HR+) (i.e. estrogen receptor positive [ER+] and/or progesterone receptor positive [PR+]) disease; AND
  - Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - Patient meets ONE of the following criteria:
    - Patient meets BOTH of the following criteria:
      - Patient is receiving a GnRH agonist (e.g. Lupron, Trelstar, Zoladex); AND
      - Ibrance will be used as first-line (initial) endocrine based therapy in combination with anastrozole, exemestane, or letrozole; OR
    - Patient meets BOTH of the following criteria:
      - Patient has relapsed or progressed during prior endocrine therapy with at least one of the following: anastrozole, exemestane, letrozole, tamoxifen, Fareston, exemestane plus Afinitor, Faslodex, Afinitor plus Faslodex or tamoxifen, megestrol acetate, fluoxymesterone, ethinyl estradiol; AND
      - Ibrance will be used in combination with Faslodex; AND
  - Patient has not had disease progression while on Ibrance, Kisqali, or Verzenio; OR
- Patient has a diagnosis of well-differentiated/dedifferentiated liposarcoma.

- For Revlimid requests
  - Patient has a diagnosis of mantle cell lymphoma (MCL) and ONE of the following:
    - Patient has tried TWO prior therapies or therapeutic regimens (e.g., HyperCVAD [cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine]+rituximab; the NORDIC regimen [dose-intensified induction immunochemotherapy with rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone alternating with rituximab and high-dose cytarabine]; RDHAP [rituximab, dexamethasone, cytarabine, cisplatin]; RCHOP [rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone]; bendamustine [Treanda®]‡ plus rituximab; bortezomib (Velcade®)‡ ± rituximab; Velcade; ibrutinib [Imbruvica®]‡; or acalabrutinib [Calquence®]‡); OR

        - Patient has tried one prior therapy or therapeutic regimen (examples listed above) and cannot take Velcade according to the prescribing physician; OR
    - Patient has a diagnosis of multiple myeloma (MM); OR
    - Patient has a diagnosis of myelodysplastic syndrome (MDS) and meets ONE of the following
        - Patient has symptomatic anemia; OR
        - Patient has transfusion-dependent anemia; OR
        - Patient has anemia that is not controlled with an erythroid stimulating agent (e.g. epoetin [Epogen®‡/Procrit®]‡ or darbepoetin [Aranesp®]‡); OR
    - Patient has a diagnosis of refractory or progressive Castleman's Disease; OR
    - Patient has a diagnosis of diffuse large B cell lymphoma (DLBCL); AND
        - Patient has tried at least one other medication treatment regimen (e.g., RCHOP, dose-adjusted EPOCH [etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin] + rituximab, RCEPP [rituximab, cyclophosphamide, etoposide, prednisone, procarbazine], DHAP [dexamethasone, cisplatin, cytarabine] ± rituximab, and Treanda ± rituximab); OR
    - Patient has a diagnosis of follicular lymphoma; OR
    - Patient has a diagnosis of relapsed or refractory classical Hodgkin lymphoma (i.e. nodular sclerosis, mixed cellularity, lymphocyte depleted, and lymphocyte-rich subtypes of Hodgkin lymphoma); OR
    - Patient has a diagnosis of myelofibrosis; AND
        - Patient has tried at least one other therapy (e.g., ruxolitinib [Jakafi®]‡, androgens [e.g. nandrolone, oxymetholone], Epogen, Procrit, Aranesp, prednisone, danazol, thalidomide, melphalan, Myleran® [busulfan], alpha interferons, and hydroxyurea); OR
    - Patient has a diagnosis of systemic light chain amyloidosis.
- For Sprycel requests
    - Patient has a diagnosis of acute lymphoblastic leukemia (ALL) that is Philadelphia chromosome positive (Ph+); OR
    - Patient has a diagnosis of chronic myeloid leukemia (CML) that is Philadelphia chromosome positive (Ph+); OR
    - Patient has a diagnosis of gastrointestinal stromal tumor (GIST) and all of the following:
        - Patient has tried imatinib (Gleevec); AND
        - Patient has tried sunitinib (Sutent); AND
        - Patient has tried regorafenib (Stivarga®)‡
- For Sutent requests
    - Patient has a diagnosis of gastrointestinal stromal tumor (GIST) AND one of the following
        - Sutent will be used as a single agent AND the patient has tried imatinib (Gleevec); OR
        - Sutent will be used in combination with everolimus (Afinitor®)‡ ; AND the patient meets all of the following criteria:
            - □ Patient has tried imatinib (Gleevec); AND

- □ Patient has tried Sutent monotherapy; AND
- □ Patient has tried Stivarga; OR

- Patient has a diagnosis of renal cell carcinoma (RCC) AND one of the following:
  - Patient is at high risk of recurrent RCC following nephrectomy and Sutent is used for adjuvant therapy; OR
  - The patient has advanced RCC; OR
- Patient has a diagnosis of advanced, unresectable neuroendocrine tumor; OR
- Patient has a diagnosis of alveolar soft part sarcoma (ASPS); OR
- Patient has a diagnosis of angiosarcoma; OR
- Patient has a diagnosis of recurrent chordoma; OR
- Patient has a diagnosis of differentiated (i.e. papillary, follicular, and Hürthle cell) thyroid carcinoma that is refractory to radioactive iodine therapy; OR
- Patient has a diagnosis of medullary thyroid carcinoma that is refractory to vandetanib (Caprelsa®)‡, or cabozantinib (Cometriq®)‡ treatment; OR
- Patient has a diagnosis of recurrent or progressive meningioma; OR
- Patient has a diagnosis of solitary fibrous tumor/hemangiopericytoma; OR
- Patient has a diagnosis of thymic carcinoma that is refractory to chemotherapy (e.g., carboplatin/paclitaxel) or radiation therapy

- For Xtandi requests
  - Patient has a diagnosis of castration-resistant prostate cancer (CRPC)

When Services Are Considered Not Medically Necessary
The use of brand Gleevec when the patient has not tried and failed (e.g. intolerance or inadequate response) generic imatinib is considered to be **not medically necessary.****

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of cabozantinib (Cabometyx), brand and generic imatinib (Gleevec), palbociclib (Ibrance), lenalidomide (Revlimid), dasatinib (Sprycel), sunitinib (Sutent), and enzalutamide (Xtandi) when patient selection criteria are not met for the requested drug (except those designated not medically necessary**) to be **investigational.***

Background/Overview

Many cancers can be treated with oral therapies in addition to or instead of traditional intravenous chemotherapy infusions. These oral treatments are typically administered daily until disease progression or unacceptable toxicity and can be associated with increased life expectancy and quality of life in patients with cancer. Dosing information as well as descriptions of possible adverse drug reactions can be found in the FDA-approved package insert for the respective drug. Many of these drugs are commonly used for oncology indications beyond those approved by the FDA. The National Comprehensive Cancer Network

(NCCN) provides evidence-based guidelines regarding the appropriate treatment options for each type of cancer.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Cabometyx is FDA-approved for the treatment of patients with advanced renal cell carcinoma.

Gleevec is FDA-approved for the treatment of newly diagnosed Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML); Ph+ CML in blast crisis, accelerated phase, or chronic phase after interferon-alpha therapy; adult patients with relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL); pediatric patients with newly diagnosed Ph+ ALL; adult patients with myelodysplastic/myeloproliferative diseases associated with PDGFR gene re-arrangements; adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation or with c-Kit mutational status unknown; adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL); adult patients with unresectable, recurrent, and/or metastatic dermatofibrosarcoma protuberans, patients with Kit positive unresectable and/or metastatic gastrointestinal stromal tumor (GIST); and adjuvant treatment of adult patients following complete gross resection of Kit positive GIST.

Ibrance is FDA approved for the treatment of HR+, HER2 negative advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in combination with fulvestrant in women with disease progression following endocrine therapy.

Revlimid is FDA approved for treatment of multiple myeloma in combination with dexamethasone; as maintenance therapy in patients with multiple myeloma following autologous hematopoietic stem cell transplantation; for treatment of patients with transfusion-dependent anemia due to low or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities; and for the treatment of patients with mantle cell lymphoma whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

Sprycel is FDA approved for the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase; for the treatment of chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib; for treatment of Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy; and for the treatment of pediatric patients with Ph+ CML in chronic phase.

Sutent is FDA approved for the treatment of gastrointestinal stromal tumors (GIST) after disease progression on or intolerance to imatinib; for the treatment of advanced renal cell carcinoma; for the adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma following nephrectomy; and for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.

Xtandi is FDA approved for the treatment of patients with castration-resistant prostate cancer.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The criteria in this policy are based on FDA approved indications for each included drug as well as evidence based recommendations from the NCCN and are designed to ensure the most appropriate therapy for each patient.

References

1. Cabometyx [package insert]. Exelixis, Inc. South San Francisco, CA. December 2017.
2. Gleevec [package insert]. Novartis. East Hanover, NJ. July 2018.
3. Ibrance [package insert]. Pfizer. New York, NY. February 2018.
4. Revlimid [package insert]. Celgene. Summit, NJ. December 2017.
5. Sprycel [package insert]. Bristol Myers Squibb. Princeton, NJ. January 2018.
6. Sutent [package insert]. Pfizer. New York, NY. November 2017.
7. Xtandi [package insert]. Astellas Pharma US, Inc. Northbrook, IL. July 2018.
8. Oncology—Cabometyx Prior Authorization Policy. Express Scripts. January 2018.
9. Oncology—Gleevec Prior Authorization Policy. Express Scripts. March 2018.
10. Oncology—Ibrance Prior Authorization Policy. Express Scripts. September 2018.
11. Oncology—Revlimid Prior Authorization Policy. Express Scripts. March 2018.
12. Oncology—Sprycel Prior Authorization Policy. Express Scripts. March 2018.
13. Oncology—Sutent Prior Authorization Policy. Express Scripts. April 2018.
14. Oncology—Xtandi Prior Authorization Policy. Express Scripts. July 2018.

Policy History

Original Effective Date: 01/01/2019
Current Effective Date: 01/01/2019
10/04/2018 Medical Policy Committee review
10/17/2018 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 10/2019

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);

2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.