



# CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

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Coverage Policy Number ..... 4003

Subject **Imatinib (Gleevec®)**

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## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

**CIGNA covers imatinib (Gleevec®) as medically necessary for treatment of individuals with ANY of the following:**

- adult or pediatric Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) including recurrence of CML following stem cell transplantation (SCT)
- aggressive systemic mastocytosis
- dermatofibrosarcoma protuberans (DFSP)
- desmoid tumors (fibromatosis)
- gastrointestinal stromal tumor (GIST)
- hypereosinophilic syndrome/chronic eosinophilic leukemia (HES/CEL)
- myelodysplastic/myeloproliferative diseases (MDS/MPD)
- Ph+ acute lymphoblastic leukemia (ALL)
- Ph+ lymphoblastic lymphoma
- pigmented villonodular synovitis/Tenosynovial giant cell tumor (PVNS/TGCT)

## FDA Approved Indications

### Newly Diagnosed Philadelphia Positive Chronic Myeloid Leukemia (Ph+ CML)

Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia in chronic phase.

**Ph+ CML in Blast Crisis (BC), Accelerated Phase (AP) or Chronic Phase (CP) After Interferon-alpha (IFN) Therapy**

Patients with Philadelphia chromosome positive chronic myeloid leukemia in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

**Ph+ Acute Lymphoblastic Leukemia (ALL)**

Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia.

**Myelodysplastic/Myeloproliferative Diseases (MDS/MPD)**

Adult patients with myelodysplastic/ myeloproliferative diseases associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements.

**Aggressive Systemic Mastocytosis (ASM)**

Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation or with c-Kit mutational status unknown.

**Hypereosinophilic Syndrome (HES) and/or Chronic Eosinophilic Leukemia (CEL)**

Adult patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who have the FIP1L1-PDGFR $\alpha$  fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFR $\alpha$  fusion kinase negative or unknown.

**Dermatofibrosarcoma Protuberans (DFSP)**

Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans.

**Kit+ Gastrointestinal Stromal Tumors (GIST)**

Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors.

**Adjuvant Treatment of GIST**

Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST.

**FDA Recommended Dosing**

- Adults with Ph+ CML CP - 400 mg/day
- Adults with Ph+ CML AP or BC - 600 mg/day
- Pediatrics with Ph+ CML CP - 340 mg/m<sup>2</sup>/day
- Adults with Ph+ ALL - 600 mg/day
- Adults with MDS/MPD - 400 mg/day
- Adults with ASM - 100 mg/day or 400 mg/day
- Adults with HES/CEL - 100 mg/day or 400 mg/day
- Adults with DFSP - 800 mg/day
- Adults with metastatic and/or unresectable GIST - 400 mg/day
- Adjuvant treatment of adults with GIST - 400 mg/day

Doses of 400 mg or 600 mg should be administered once daily, whereas a dose of 800 mg should be administered as 400 mg twice a day. Daily dosing of 800 mg and above should be accomplished using the 400 mg tablet to reduce exposure to iron.

**Drug Availability**

Each film-coated tablet contains 100 mg or 400 mg of imatinib free base. 100 mg tablets are very dark yellow to brownish orange, film-coated tablets, round, biconvex with bevelled edges, debossed with "NVR" on one side and "SA" with score on the other side in bottles of 90 tablets. 400 mg tablets are very dark yellow to brownish orange, film-coated tablets, ovaloid, biconvex with bevelled edges, debossed with "400" on one side with score on the other side, and "SL" on each side of the score in bottles of 30 tablets.

## General Background

### Pharmacology

Imatinib, a protein-tyrosine kinase inhibitor, works by inhibiting the Bcr-Abl tyrosine kinase, the constitutive abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in chronic myeloid leukemia. Imatinib is also an inhibitor of the receptor tyrosine kinases for platelet-derived growth factor (PDGF) and stem cell factor (SCF), c-kit, and inhibits PDGF- and SCF-mediated cellular events. An in vitro study has shown that imatinib inhibits proliferation and induces apoptosis in gastrointestinal stromal tumor (GIST) cells, which express an activating c-kit mutation.

Imatinib is well absorbed after oral administration, with peak level obtained within two to four hours post-dose. Elimination half-lives of imatinib and its active metabolite, N-desmethyl derivative, are approximately 18 and 40 hours, respectively. Cytochrome P3A4 (CYP3A4) is the major enzyme responsible for metabolism of imatinib.

### Guidelines

The National Comprehensive Cancer Network (NCCN) recommends imatinib for the following

#### CML

##### Grade 1

Primary treatment for patients with newly diagnosed CML (Philadelphia chromosome or BCR-ABL positive).

##### Grade 2A

Initial-dose imatinib for follow-up therapy after primary treatment in patients with complete hematologic remission at 3 months; complete, partial, or minor cytogenetic response at 6 months; complete or partial cytogenetic response at 12 months; complete cytogenetic response at 18 months.

High-dose imatinib for follow-up therapy in patients with lack of acceptable response to standard-dose imatinib for minor cytogenetic response at 6 months or partial cytogenetic response or in cytogenetic relapse at 12 months.

Treatment of patients with disease progression as single agent for accelerated phase or single agent or in combination with induction chemotherapy for blast crisis. Acute lymphocytic leukemia-type induction chemotherapy is recommended for lymphoid blast crisis. Acute myeloid leukemia (AML)-type induction chemotherapy is recommended for myeloid blast crisis.

Posttransplant follow-up treatment in patients with molecular relapse (polymerase chain reaction positive) following complete cytogenetic remission or cytogenetic relapse or those who are not in cytogenetic remission.

Alternative treatment for patients with severe non-hematologic toxicity due to dasatinib therapy.

#### NHL (Lymphoblastic Lymphoma)

##### Grade 2A

Induction or reinduction therapy for Philadelphia chromosome-positive stage I-IV disease as a component of HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) regimen with rituximab in CD20-positive disease.

#### Non-Melanoma Skin Cancers - Dermatofibrosarcoma protuberans

##### Grade 2A

Used as adjuvant therapy in patients with positive surgical margins following excision; for recurrent disease if additional resection would lead to unacceptable functional or cosmetic outcomes; for metastatic disease. Tumors lacking the t(17;22) translocation may not respond to imatinib. Molecular analysis of a tumor using cytogenetics may be useful prior to the institution of imatinib therapy.

#### Soft Tissue Sarcoma

##### Grade 2A

- **Desmoid tumors (Fibromatosis)**

Initial treatment or treatment of recurrence for gross residual disease following surgery or unresectable disease for which surgery would be unacceptably morbid.

- **GIST**

Primary/preoperative treatment for patients with documented GIST that is marginally resectable; resectable with risk of significant morbidity; unresectable; recurrent metastatic disease.

Adjuvant treatment following complete resection of primary GIST; incomplete resection if imatinib not previously given; persistent gross residual disease (R2 resection) if imatinib previously given.

- **Pigmented villonodular synovitis/Tenosynovial giant cell tumor (PVNS/TGCT)**

Single-agent therapy for the treatment of PVNS/TGCT

### **Adverse Reactions**

The most frequently reported drug-related adverse events include: nausea, vomiting, diarrhea, edema, and muscle cramps. Edema was most frequently reported in lower limbs and was managed with diuretics, other supportive measures, or by reducing the dose. The frequency of severe superficial edema was 0.9–5%.

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## **Coding/Billing Information**

**Note:** This section is not in use.

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## **References**

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2. McEvoy GK, ed. AHFS 2011 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc. 2011.
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4. Novartis Pharmaceuticals Corporation. Gleevec® (imatinib) package insert. East Hanover, NJ : Novartis Pharmaceuticals Corporation. April 2011.
5. Ottmann OG, Wassmann B, Pfeifer H, Giagounidis A, Stelljes M, Dührsen U, Schmalzing M, Wunderle L, Binckebanck A, Hoelzer D; GMALL Study Group. Imatinib compared with chemotherapy as front-line treatment of elderly patients with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL). *Cancer*. 2007 May 15;109(10):2068-76.
6. Sawyers CL, Hochhaus A, Feldman E, et al. Imatinib induces hematologic and cytogenetic responses in patients with chronic myelogenous leukemia in myeloid blast crisis: results of a phase II study. *Blood* 2002;99:3530–9.
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## Policy History

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<b>Pre-Merger Organizations</b>	<b>Last Review Date</b>	<b>Policy Number</b>	<b>Title</b>
CIGNA HealthCare	5/15/2008	4003	Imatinib (Gleevec®)
Great-West Healthcare	8/2007	P.01.109.2	Gleevec

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