Dasatinib:
Sprycel®; Phyrago Ψ
(Oral)

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I. Length of Authorization [1,5]

Coverage is provided for 6 months and may be renewed, unless otherwise specified.

- Treatment of newly diagnosed Pediatric Ph+ ALL can be authorized up to a maximum of 2 years of therapy.
- CML: For patients with possible TKI-resistant disease, coverage will be provided for 3 months and may be renewed for 6 months if the treatment response milestone criteria for TKI-sensitive disease is achieved *(Refer to Section IV for specific response criteria)*

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Sprycel 20 mg tablet: 2 tablets per day
- Sprycel 50 mg tablet: 2 tablets per day
- Sprycel 70 mg tablet: 2 tablets per day
- Sprycel 80 mg tablet: 1 tablet per day
- Sprycel 100 mg tablet: 2 tablets per day
- Sprycel 140 mg tablet: 1 tablet per day
- Phyrago 20 mg tablet: 2 tablets per day
- Phyrago 50 mg tablet: 2 tablets per day
- Phyrago 70 mg tablet: 2 tablets per day
- Phyrago 80 mg tablet: 1 tablet per day
- Phyrago 100 mg tablet: 2 tablets per day
- Phyrago 140 mg tablet: 1 tablet per day

B. Max Units (per dose and over time) [HCPCS Unit]:

Chronic Phase CML

- 100 mg per day

Bone Cancer

- 200 mg per day

Accelerated Phase CML, Myeloid or Lymphoid Blast Phase CML, Ph+ ALL, GIST, Cutaneous Melanoma, and Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes

- 140 mg per day

III. Initial Approval Criteria [1,2]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age, unless otherwise specified; **AND**

Universal Criteria [1,2]

- Patient will avoid concomitant therapy with all of the following:
  - Coadministration with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
  - Coadministration with strong CYP3A inhibitors (e.g., itraconazole, ketoconazole, clarithromycin, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
  - Coadministration with proton pump inhibitors and H_2 receptor antagonists, or if therapy is required, antacids may be used at staggered administration times; **AND**

Chronic Myelogenous Leukemia (CML) † Φ [1-3,5,14-18]

- Patient has Philadelphia chromosome-positive (Ph+) or *BCR::ABL1* positive disease; **AND**
- Patient does not have any of the following *BCR::ABL1* mutations: T315I/A, F317L/V/I/C, or V299L (****NOTE:** This does not apply to newly diagnosed chronic phase disease or continued therapy); **AND**
  - Patient has chronic phase disease and is at least 1 year of age †; **OR**
  - Patient is resistant, intolerant, or had an inadequate response to prior therapy consisting of a 3 month trial or longer with a tyrosine kinase inhibitor (e.g., imatinib, bosutinib, ponatinib, nilotinib, etc.); **AND**
    - Patient has chronic, accelerated, or blast phase disease †; **OR**
  - Used as primary treatment † ‡; **AND**
    - Used as single agent for newly diagnosed chronic phase disease; **OR**
    - Used as a single agent for accelerated phase disease; **OR**
    - Used as a single agent for myeloid blast phase disease if not a candidate for induction chemotherapy; **OR**
    - Used in combination with steroids for lymphoid blast phase disease if not a candidate for induction chemotherapy; **OR**
    - Used in combination with induction chemotherapy for disease in lymphoid blast phase or myeloid blast phase; **OR**

- Used as switch therapy ‡; **AND**
  - Patient received initial therapy with one of the following: imatinib, bosutinib or nilotinib; **AND**
  - Patient has *BCR::ABL1* transcript levels:
    - > 0.1% to 1% at 12 months (if treatment goal is treatment-free remission); **OR**
    - > 1% to 10% at 12 months; **OR**
    - > 10% at any response milestone; **OR**
- Used as continued therapy ‡; **AND**
  - Patient has *BCR::ABL1* transcript levels:
    - ≤ 10% at any response milestone; **OR**
    - > 10% at 3 months; **OR**
- Used post-allogeneic hematopoietic stem cell transplant (HCT) ‡; **AND**
  - Used for at least one year in patients with prior complete cytogenetic response (CCyR) for accelerated or blast phase disease; **OR**
  - Used as follow-up therapy in patients with molecular relapse (BCR::ABL1 transcript positive) following CCyR; **OR**
  - Used as follow-up therapy in patients with relapse or less than CCyR

Adult Acute Lymphoblastic Leukemia (ALL) † Φ [1-4,6]

- Patient does not have any of the following *BCR::ABL1* mutations: T315I/A, F317L/V/I/C, or V299L; **AND**
  - Patient has Philadelphia chromosome-positive (Ph+) disease; **AND**
    - Patient is resistant, intolerant, or had an inadequate response to prior therapy, consisting of a 3 month trial or longer, with any of the following: imatinib, bosutinib, ponatinib, nilotinib, etc. †; **OR**
  - Patient has Ph+ B-ALL ‡; **AND**
    - Used for relapsed or refractory disease; **AND**
      - Used as a single agent; **OR**
      - Used in combination with inotuzumab ozogamicin; **OR**
      - Used in combination with blinatumomab; **OR**
    - Used as maintenance therapy; **AND**
      - Used in combination with POMP regimen (vincristine and prednisone with or without methotrexate and mercaptopurine); **AND**
        - ➢ Used following consolidation therapy for patients with negative minimal residual disease (if not already included in a multi-part regimen); **OR**
      - Used as single agent therapy; **AND**
        - ➢ Used post-hematopoietic stem cell transplant; **OR**

        - Used in patients unfit for additional therapies; **OR**
    - Used as induction therapy; **AND**
        - Used as frontline therapy OR for relapsed/refractory disease (if not previously given); **AND**
            - Used in combination with a corticosteroid; **OR**
            - Used in combination with vincristine and dexamethasone; **OR**
            - Used as a component of a multiagent chemotherapy regimen *(Note: May be used in patients at least 15 years of age)*; **OR**
    - Used as consolidation therapy; **AND**
        - Used for relapsed/refractory disease (if not previously given); **AND**
            - Used as a component of a multiagent chemotherapy regimen *(Note: May be used in patients at least 15 years of age)*; **OR**
        - Used as frontline therapy; **AND**
            - Used as a component of a multiagent chemotherapy regimen *(Note: May be used in patients at least 15 years of age)*; **OR**
            - Used as a single agent in patients unfit for additional therapies; **OR**
            - Used in combination with blinatumomab; **AND**
                - Used for persistent/rising minimal residual disease after complete response to induction therapy; **OR**
                - Used for negative minimal residual disease after complete response to induction therapy if patient is not a candidate for multiagent therapy

Pediatric Acute Lymphoblastic Leukemia (ALL) † ‡ Φ [1-3,10]

- Patient is at least 1 year of age to <18 years of age**; **AND**
    - Philadelphia chromosome-positive (Ph+) disease; **AND**
        - Used in combination with chemotherapy for newly diagnosed disease †; **OR**
    - Patient has Ph-like B-ALL with ABL class kinase fusion; **AND**
        - Used as part of a cytotoxic chemotherapy regimen; **AND**
        - Used as induction or consolidation therapy; **OR**
    - Patient has Ph+ B-ALL; **AND**
        - Used as part of a cytotoxic chemotherapy regimen; **AND**
            - Used as induction or consolidation therapy; **OR**
            - Used for relapsed or refractory disease; **OR**
    - Patient has T-ALL with ABL-class translocation; **AND**
        - Used as part of a TKI-based regimen for relapsed or refractory disease

***The pediatric ALL panel considers "pediatric" to include any patient aged 18 years and younger, and certain adolescent and young adult (AYA) patients up to 30 years of age when treated in a pediatric oncology setting.*

Gastrointestinal Stromal Tumors (GIST) ‡ [3,7,12,21]

- Used as a single agent; **AND**
- Patient has gross residual (R2 resection), unresectable primary, recurrent, or metastatic disease OR tumor rupture; **AND**
- Used as second-line therapy for generalized (widespread, systemic) disease progression; **AND**
- Used after prior treatment with avapritinib; **AND**
- Patient has PDGFRA exon 18 mutations that are insensitive to imatinib (including the PDGFRA D842V mutation)

Bone Cancer (Chondrosarcoma and Chordoma) ‡ [3,8,9,13]

- Used as single agent; **AND**
  - Patient has metastatic and widespread chondrosarcoma; **AND**
    - Patient has metastatic disease at presentation; **OR**
    - Patient has systemic recurrence of high grade (grade II or III), clear cell, or extracompartmental disease; **OR**
  - Patient has recurrent conventional or chondroid chordoma

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes ‡ [3,19,20]

- Patient has eosinophilia and ABL1 rearrangement; **AND**
  - Patient has chronic or blast phase myeloid or lymphoid neoplasms; **AND**
    - Used as a single agent; **OR**
  - Patient has blast phase lymphoid, myeloid, or mixed lineage neoplasms; **AND**
    - Used in combination with ALL- or AML-type induction chemotherapy followed by allogeneic HCT (if eligible)

Cutaneous Melanoma ‡ [3]

- Used as subsequent therapy as a single agent; **AND**
- Patient has metastatic or unresectable disease with activating mutations of KIT; **AND**
- Used for disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-5,10,11,13,19,21]

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: pulmonary arterial hypertension, severe myelosuppression (neutropenia, anemia,

thrombocytopenia), fluid retention, cardiovascular toxicity (ischemia, cardiac-related fluid retention, conduction system abnormalities, arrhythmia/palpitations), QT prolongation, severe dermatologic reactions, tumor lysis syndrome, serious bleeding-related events, hepatotoxicity, etc.; **AND**

Adult Acute Lymphoblastic Leukemia (ALL)

- Treatment response or stabilization of disease as indicated by CBC, bone marrow cytogenic analysis, QPCR, or FISH

Pediatric Acute Lymphoblastic Leukemia (ALL)

- Treatment response or stabilization of disease as indicated by CBC, bone marrow cytogenic analysis, QPCR, or FISH; **AND**
- Patient's with newly diagnosed Ph+ ALL have not exceeded a maximum of 2 years of therapy

Chronic Myelogenous Leukemia (CML)

- Treatment response as indicated by one of the following:
  - Patient has TKI-sensitive disease as confirmed by one of the following *BCR::ABL1* (IS) transcript levels:
    - ≤ 10% at 3 months or 6 months; **OR**
    - > 0.1% to 1% at 12 months and beyond (if treatment goal is long-term survival); **OR**
    - ≤ 0.1% at 12 months and beyond (if treatment goal is treatment-free remission); **OR**
  - Patient has <u>possible</u> TKI resistant disease as confirmed by a > 50% reduction in *BCR::ABL1* (IS) transcript levels compared to pretreatment baseline OR minimally above the 10% cutoff; **AND**
    - Treatment can be continued for an additional 3 months; **AND**
    - Follow-up *BCR::ABL1* (IS) transcript levels will be drawn after the 3 month extended treatment period to determine if continued treatment is warranted (i.e., patient meets the treatment response milestone criteria for TKI-sensitive disease as noted above)

  <u>*Note:*</u> cytogenetic assessment of response may be used if quantitative RT-PCR (QPCR) using International Scale (IS) for *BCR::ABL1* is not available
- Patients meeting all of the following criteria may be candidates for discontinuation provided they received counseling on, and have consented to, the risks (including TKI withdrawal) and benefits of stopping TKI therapy:
  - Patient is at least 18 years of age; **AND**
  - Patient has received TKI therapy for ≥ 3 years; **AND**
  - Patient has no history of accelerated or blast phase CML (i.e. chronic phase only); **AND**
  - Patient had a stable molecular response (MR4; *BCR::ABL1* ≤0.01% IS) for ≥ 2 years (as documented on ≥ 4 tests performed ≥ 3 months apart); **AND**
  - Patient has quantifiable *BCR::ABL1* transcripts; **AND**

- Patient has access to a reliable qPCR test with a sensitivity of detection of at least MR4.5 (*BCR::ABL1* ≤ 0.0032% IS) and that provides results within 2 weeks; **AND**
- Patient can meet the ongoing monitoring requirements after discontinuation

Gastrointestinal Stromal Tumors (GIST)

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

Bone Cancer (Chondrosarcoma and Chordoma)

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes

- Disease response as evidenced by at least one of the following:
  - Decrease in spleen size or improvements in other myelofibrosis symptoms (such as weakness, fatigue, cough, dyspnea, myalgias, angioedema, rash, fever, rhinitis, etc.)
  - Stabilization or improvement as evidenced by a complete response [CR] (i.e. morphologic, cytogenetic or molecular complete response CR), complete hematologic response, or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

Cutaneous Melanoma

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration [1,2,7-9,20,22]

Indication	Dose
Accelerated Phase CML and Myeloid or Lymphoid Blast Phase CML	140 mg by mouth once daily
Chronic Phase CML	Adult 100 mg by mouth once daily Pediatric ➢ 10 – <20 kg : 40 mg once daily ➢ 20 – <30 kg : 60 mg once daily ➢ 30 – <45 kg : 70 mg once daily ➢ ≥ 45 kg: 100 mg once daily
Philadelphia chromosome-positive (Ph+) Acute Lymphocytic Leukemia (ALL)	Adult 140 mg by mouth once daily Pediatric ➢ 10 – <20 kg : 40 mg once daily ➢ 20 – <30 kg : 60 mg once daily ➢ 30 – <45 kg : 70 mg once daily ➢ ≥ 45 kg: 100 mg once daily
Gastrointestinal Stromal Tumors (GIST)	70 mg by mouth twice daily

Bone Cancer (Chondrosarcoma and Chordoma)	50-100 mg by mouth twice daily
Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes	Up to 140 mg by mouth once daily
Cutaneous Melanoma	70 mg by mouth twice daily

VI. Billing Code/Availability Information

HCPCS Code:

- J8999: Prescription drug, oral, chemotherapeutic, NOS

NDC(s):

- Sprycel 20 mg tablet: 00003-0527-xx
- Sprycel 50 mg tablet: 00003-0528-xx
- Sprycel 70 mg tablet: 00003-0524-xx
- Sprycel 80 mg tablet: 00003-0855-xx
- Sprycel 100 mg tablet: 00003-0852-xx
- Sprycel 140 mg tablet: 00003-0857-xx
- Phyrago 20 mg tablet Ψ: N/A
- Phyrago 50 mg tablet Ψ: N/A
- Phyrago 70 mg tablet Ψ: N/A
- Phyrago 80 mg tablet Ψ: N/A
- Phyrago 100 mg tablet Ψ: N/A
- Phyrago 140 mg tablet Ψ: N/A

Ψ *Designated products approved by the FDA as a 505(b)(2) NDA of the innovator product. These products are not rated as therapeutically equivalent to their reference listed drug in the Food and Drug Administration's (FDA) Orange Book and are therefore considered single source products based on the statutory definition of "single source drug" in section 1847A(c)(6) of the Act. For a complete list of all approved 505(b)(2) NDA products please reference the latest edition of the Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations / Orange Book / FDA*

VII. References

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C40.00	Malignant neoplasm of scapula and long bones of unspecified upper limb
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.20	Malignant neoplasm of long bones of unspecified lower limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.30	Malignant neoplasm of short bones of unspecified lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.80	Malignant neoplasm of overlapping sites of bone and articular cartilage of unspecified limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.90	Malignant neoplasm of unspecified bones and articular cartilage of unspecified limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of pelvic bones, sacrum and coccyx
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast

C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C49.A0	Gastrointestinal stromal tumor unspecified site
C49.A1	Gastrointestinal stromal tumor of esophagus
C49.A2	Gastrointestinal stromal tumor of stomach
C49.A3	Gastrointestinal stromal tumor of small intestine
C49.A4	Gastrointestinal stromal tumor of large intestine
C49.A5	Gastrointestinal stromal tumor of rectum
C49.A9	Gastrointestinal stromal tumor of other sites
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C83.50	Lymphoblastic (diffuse) lymphoma, unspecified site
C83.51	Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56	Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma, spleen
C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse
C94.8	Other specified leukemias
C94.80	Other specified leukemias not having achieved remission

C94.81	Other specified leukemias, in remission
C94.82	Other specified leukemias, in relapse
C95.1	Chronic leukemia of unspecified cell type
C95.10	Chronic leukemia of unspecified cell type not having achieved remission
C95.11	Chronic leukemia of unspecified cell type, in remission
C95.12	Chronic leukemia of unspecified cell type, in relapse
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
Z85.820	Personal history of malignant melanoma of skin
Z85.831	Personal history of malignant neoplasm of soft tissue
Z85.830	Personal history of malignant neoplasm of bone

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC