Velcade® (bortezomib)
(Intravenous/Subcutaneous)

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I. Length of Authorization [1,5,8,14,25,26,35-41]

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

- Initial treatment for Multiple Myeloma: Coverage will be provided for a total of 9 cycles (42-days per cycle).
- Re-treatment of Multiple Myeloma, initial treatment of Mantle Cell Lymphoma, & Adult T-Cell Leukemia/Lymphoma: Coverage will be provided for a total of 8 cycles (21-days per cycle).
- Systemic Light Chain Amyloidosis as a single agent or in combination with cyclophosphamide and/or dexamethasone: Coverage will be provided for a total of 8 cycles (35-days per cycle as a single agent; 21- or 28-days per cycle in combination with cyclophosphamide and/or dexamethasone).
- Systemic Light Chain Amyloidosis in combination with melphalan and dexamethasone: Coverage will be provided for a total of 9 cycles (21-days per cycle)
- Systemic Light Chain Amyloidosis in combination with lenalidomide and dexamethasone: Coverage will be provided for a total of 8 cycles (28-days per cycle).
- Systemic Light Chain Amyloidosis in combination with daratumumab and hyaluronidase-fihj, cyclophosphamide, and dexamethasone: Coverage will be provided for a total of 2 years.
- Waldenström's Macroglobulinemia in combination with rituximab and/or dexamethasone: Coverage will be provided for a total of 6 cycles (28-days per cycle) or 8 cycles (21-days per cycle).
- Pediatric Hodgkin Lymphoma: Coverage will be provided for a total of 4 cycles (21-days per cycle).

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II. Dosing Limits

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

- Velcade 3.5 mg powder for injection single-dose vial: 8 vials per 28 day supply

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

- **Multiple Myeloma & Systemic Light Chain Amyloidosis:**
  - 280 billable units every 35 days
- **Kaposi Sarcoma & Waldenström's Macroglobulinemia:**
  - 210 billable units every 28 days
- **Pediatric Hodgkin Lymphoma:**
  - 105 billable units every 21 days
- **All Other Indications:**
  - 140 billable units every 21 days

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]

- Will not be administered intrathecally; **AND**

Multiple Myeloma † Φ [1-4,6,13,15-20,24-26]

- Used in combination with a corticosteroid-containing regimen as primary therapy for symptomatic disease or for relapse (re-treatment) after 6 months following primary induction therapy with the same regimen; **OR**
- Used as maintenance therapy; **AND**
  - Used as a single agent; **OR**
  - Used in combination with lenalidomide (without dexamethasone); **OR**
  - Used in combination with lenalidomide and dexamethasone for transplant candidates; **OR**
- Used for relapsed or progressive disease in combination with a dexamethasone-containing regimen; **OR**
- Used in combination with dexamethasone in patients with a confirmed diagnosis of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome

Mantle Cell Lymphoma – B-Cell Lymphoma † Φ [1,2,12,21-23,27]

- Used as induction or additional therapy; **AND**
  - Used as a component of VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone); **OR**
- Used as subsequent therapy; **AND**

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- Used as a single agent; **OR**
- Used in combination with rituximab

Systemic Light Chain Amyloidosis ‡ [2,10]

- Patient has newly diagnosed disease OR used as repeat initial therapy if relapse-free for several years; **AND**
  - Used in combination with cyclophosphamide and dexamethasone; **OR**
  - Used as a single agent; **OR**
  - Used in combination with dexamethasone with or without melphalan or lenalidomide; **OR**
  - Used in combination with daratumumab and hyaluronidase-fihj, cyclophosphamide, and dexamethasone; **OR**
- Patient has relapsed or refractory disease; **AND**
  - Used as a single agent; **OR**
  - Used in combination with dexamethasone with or without melphalan

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL) ‡ [2,5,11,14,29]

- Used in combination with dexamethasone and rituximab; **OR**
- Used as a single agent; **OR**
- Used in combination with rituximab; **OR**
- Used in combination with dexamethasone

Multicentric Castleman's Disease – B-Cell Lymphoma ‡ [2,12]

- Used as subsequent therapy; **AND**
- Patient has progressed following treatment for relapsed/refractory or progressive disease; **AND**
- Used as a single agent or in combination with rituximab

Adult T-Cell Leukemia/Lymphoma ‡ [2,7,9]

- Used as a single agent; **AND**
- Used as subsequent therapy for non-responders to first-line therapy for acute disease or lymphoma subtypes

Acute Lymphoblastic Leukemia (ALL) – Adult* ‡ [3,9]

- Used in combination with chemotherapy; **AND**
- Patient has relapsed/refractory Philadelphia (Ph) chromosome negative T-cell disease (T-ALL)

**NCCN recommendations for ALL may be applicable to adolescent and young adult (AYA) patients within the age range of 15-39 years.*

Pediatric Acute Lymphoblastic Leukemia (ALL) ‡ [2,8,28]

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- Patient is at least 1 year of age**; **AND**
  - Patient has relapsed or refractory disease; **AND**
  - Used as a component of the COG AALL07P1 regimen (bortezomib, vincristine, doxorubicin, pegaspargase, prednisone); **AND**
    - Patient has Philadelphia (Ph) chromosome negative B-cell disease (B-ALL); **OR**
    - Used in combination with dasatinib or imatinib for Philadelphia (Ph) chromosome positive B-cell disease (B-ALL); **OR**
  - Patient has relapsed or refractory T-cell disease (T-ALL); **AND**
    - Used in combination with a corticosteroid (e.g., prednisone or dexamethasone), vincristine, doxorubicin, and pegaspargase

***NCCN recommendations for Pediatric ALL may be applicable to certain adolescent and young adult (AYA) patients up to 31 years of age.*

Kaposi Sarcoma ‡ [2,41]

- Used as subsequent therapy for relapsed or refractory disease; **AND**
- Patient has advanced cutaneous, oral, visceral, or nodal disease; **AND**
- Patient has progressed on or not responded to first-line therapy; **AND**
- Patient has progressed on alternate first-line therapy; **AND**
  - Used as a single-agent in patients without human immunodeficiency virus (HIV); **OR**
  - Used in combination with antiretroviral therapy (ART) for patients with HIV

Pediatric Hodgkin Lymphoma ‡ [3,45]

- Patient age is 18 years and under***; **AND**
- Used for relapsed or refractory disease in combination with ifosfamide and vinorelbine

****Pediatric Hodgkin Lymphoma patients may include certain adolescent and young adult (AYA) patients up to 39 years of age.*

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

IV. Renewal Criteria [1,2,6]

Coverage can be renewed based upon the following criteria:

- 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**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Example of unacceptable toxicity include: peripheral neuropathy, hypotension, cardiac toxicity, pulmonary toxicity, posterior reversible encephalopathy syndrome (PRES), gastrointestinal toxicity, thrombocytopenia, neutropenia, tumor lysis syndrome, hepatic toxicity, thrombotic microangiopathy, etc.

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V. Dosage/Administration [1,5,6,8,14,25,26,30,35-43]

Indication	Dose
Multiple Myeloma – initial treatment	1.3 mg/m² intravenously (IV)/subcutaneously (SC) in combination with oral melphalan and oral prednisone for nine 6-week treatment cycles. In cycles 1-4, Velcade is given twice weekly (days 1, 4, 8, 11, 22, 25, 29, and 32). In cycles 5-9, Velcade is given once weekly (days 1, 8, 22, and 29).
Multiple Myeloma – maintenance therapy	Following primary therapy with a bortezomib-containing regimen for transplant-ineligible patients: 1.3 mg/m² IV/SC every two weeks or 1.6 mg/m² IV/SC weekly (days 1, 8, 15, and 22) every 35 days until disease progression or unacceptable toxicity Following autologous stem cell transplant: 1.3 mg/m² IV/SC every two weeks until disease progression or unacceptable toxicity
Multiple Myeloma – re-treatment	1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) followed by a 10-day rest period (days 12-21) for up to 8 cycles
Mantle Cell Lymphoma – previously untreated	1.3 mg/m² IV/SC in combination with rituximab, cyclophosphamide, doxorubicin, and oral prednisone for six 3-week treatment cycles. Velcade is given twice weekly (days 1, 4, 8, and 11) followed by a 10-day rest period on days 12-21. For patients with a response first documented at cycle 6, two additional cycles are recommended.
Multiple Myeloma & Mantle Cell Lymphoma – relapsed	1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) followed by a 10-day rest period (days 12-21). • For extended therapy of more than 8 cycles, Velcade may be administered on the standard schedule or, for relapsed multiple myeloma, on a maintenance schedule of once weekly for 4 weeks (days 1, 8, 15, and 22), followed by a 13-day rest period (days 23 to 35).
Systemic Light Chain Amyloidosis	Single agent: 1.6 mg/m² IV/SC weekly (days 1, 8, 15, and 22) every 35 days or 1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 21 days for up to 8 cycles In combination with cyclophosphamide and/or dexamethasone: 1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 21 or 28 days for up to 8 cycles In combination with melphalan and dexamethasone: 1.3mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 28 days for up to 9 cycles In combination with lenalidomide and dexamethasone: 1.3mg/m² IV/SC twice weekly (days 1, 8, and 15) every 28 days for up to 8 cycles In combination with daratumumab and hyaluronidase-fihj, cyclophosphamide, and dexamethasone: 1.3mg/m² IV/SC weekly (days 1, 8, 15, and 22) every 28 days for up to 2 years

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Waldenström's macroglobulinemia	Single agent: • 1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 21 days, until disease progression or unacceptable toxicity In combination with rituximab and/or dexamethasone: • 1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 21 days for 4 continuous cycles, followed by a 12-week rest period, then up to 4 additional cycles given every 12 weeks • 1.6 mg/m² IV/SC weekly (days 1, 8, and 15) every 28 days for up to 6 cycles
Adult T-Cell Leukemia/ Lymphoma	1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 21 days for up to 8 cycles
Kaposi Sarcoma	1.6 mg/m² IV weekly (days 1, 8, and 15) every 28 days
Pediatric Hodgkin Lymphoma	1.2 mg/m² IV/SC on days 1, 4, and 8 every 21 days for up to 4 cycles
All Other Indications	1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) for 2 weeks of a 21 day cycle
Reconstituted concentration varies by route of administration: • *1 mg/mL intravenously* • *2.5 mg/mL subcutaneously*	

VI. Billing Code/Availability Information

HCPCS Code:

- J9041– Injection, bortezomib (Velcade), 0.1 mg; 1 billable unit = 0.1 mg

NDC:

- Velcade 3.5 mg single-dose vial powder for injection: 63020-0049-xx

VII. References

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C46.0	Kaposi's sarcoma of skin
C46.1	Kaposi's sarcoma of soft tissue
C46.2	Kaposi's sarcoma of palate
C46.3	Kaposi's sarcoma of lymph nodes

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ICD-10	ICD-10 Description
C46.4	Kaposi's sarcoma of gastrointestinal sites
C46.50	Kaposi's sarcoma of unspecified lung
C46.51	Kaposi's sarcoma of right lung
C46.52	Kaposi's sarcoma of left lung
C46.7	Kaposi's sarcoma of other sites
C46.9	Kaposi's sarcoma, unspecified
C81.10	Nodular sclerosis Hodgkin lymphoma, unspecified site
C81.11	Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.12	Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.13	Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes
C81.14	Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.15	Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.16	Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes
C81.17	Nodular sclerosis Hodgkin lymphoma, spleen
C81.18	Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites
C81.19	Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites
C81.20	Mixed cellularity Hodgkin lymphoma, unspecified site
C81.21	Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.23	Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes
C81.24	Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.25	Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.26	Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes
C81.27	Mixed cellularity Hodgkin lymphoma, spleen
C81.28	Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites
C81.29	Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites
C81.30	Lymphocyte depleted Hodgkin lymphoma, unspecified site
C81.31	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.33	Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes
C81.34	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.35	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.36	Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes
C81.37	Lymphocyte depleted Hodgkin lymphoma, spleen

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ICD-10	ICD-10 Description
C81.38	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites
C81.39	Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites
C81.40	Lymphocyte-rich Hodgkin lymphoma, unspecified site
C81.41	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.43	Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes
C81.44	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.45	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.46	Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes
C81.47	Lymphocyte-rich Hodgkin lymphoma, spleen
C81.48	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites
C81.49	Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites
C81.70	Other Hodgkin lymphoma unspecified site
C81.71	Other Hodgkin lymphoma lymph nodes of head, face, and neck
C81.72	Other Hodgkin lymphoma intrathoracic lymph nodes
C81.73	Other Hodgkin lymphoma intra-abdominal lymph nodes
C81.74	Other Hodgkin lymphoma lymph nodes of axilla and upper limb
C81.75	Other Hodgkin lymphoma lymph nodes of inguinal region and lower limb
C81.76	Other Hodgkin lymphoma intrapelvic lymph nodes
C81.77	Other Hodgkin lymphoma spleen
C81.78	Other Hodgkin lymphoma lymph nodes of multiple sites
C81.79	Other Hodgkin lymphoma extranodal and solid organ sites
C81.90	Hodgkin lymphoma, unspecified, unspecified site
C81.91	Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck
C81.92	Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
C81.93	Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
C81.94	Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
C81.95	Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C81.96	Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
C81.97	Hodgkin lymphoma, unspecified, spleen
C81.98	Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
C81.99	Hodgkin lymphoma, unspecified, extranodal and solid organ sites
C83.10	Mantle cell lymphoma, unspecified site
C83.11	Mantle cell lymphoma, lymph nodes of head, face and neck

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ICD-10	ICD-10 Description
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes
C83.13	Mantle cell lymphoma, intra-abdominal lymph nodes
C83.14	Mantle cell lymphoma, lymph nodes of axilla and upper limb
C83.15	Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
C83.16	Mantle cell lymphoma, intrapelvic lymph nodes
C83.17	Mantle cell lymphoma, spleen
C83.18	Mantle cell lymphoma, lymph nodes of multiple sites
C83.19	Mantle cell lymphoma, extranodal and solid organ sites
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
C88.0	Waldenstrom macroglobulinemia
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma, in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse
C91.50	Adult T-cell lymphoma/leukemia (HTLV-1-associated) not having achieved remission
C91.52	Adult T-cell lymphoma/leukemia (HTLV-1-associated), in relapse
D47.9	Neoplasm of uncertain behavior of lymphoid, hematopoietic and related tissue, unspecified

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ICD-10	ICD-10 Description
D47.Z2	Castleman disease
E31.9	Polyglandular dysfunction, unspecified
E85.81	Light chain (AL) amyloidosis
E85.89	Other amyloidosis
E85.9	Amyloidosis, unspecified
G62.9	Polyneuropathy, unspecified
G90.0	Idiopathic peripheral autonomic neuropathy
L89.9	Pressure ulcer of unspecified site
Z85.71	Personal history of Hodgkin Lymphoma
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

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

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 Determination (NCD, Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

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

Jurisdiction(s): 6, K	**NCD/LCD/LCA Document (s):** A52371
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a52371&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

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

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Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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

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