Epkinly[®] (epcoritamab-bysp) (Subcutaneous)

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Document Number: OHSU HEALTHSERVICES-0747

Date Reviewed: 09/2025Date of Origin: 06/04/2024

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I. Length of Authorization

Prior authorization validity will be provided for 6 months and may be renewed.

II. Dosing Limits

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

• 1200 billable units per 28 days

III. Initial Approval Criteria ¹

Prior authorization validity is provided in the following conditions:

Patient is at least 18 years of age; AND

Universal Criteria 1

- Prophylaxis for infection will be followed according to local guidelines (e.g., Pneumocystis
 jirovecii pneumonia (PJP), Herpes virus, etc.); AND
- Patient does not have a clinically significant active systemic infection; AND
- Patient does not have primary central nervous system (CNS) lymphoma or CNS involvement of disease; AND
- Used as a single agent; AND

B-Cell Lymphomas † ‡ 1-4,6,2e,4e

- Used after at least two prior lines of systemic therapies including at least one anti-CD20 antibody-containing regimen, unless contraindicated; AND
 - Patient has diffuse large B-cell Lymphoma (DLBCL) (including DLBCL, not otherwise specified), high-grade B-cell lymphoma, HIV-related B-cell lymphoma (i.e., HIV-related

DLBCL or HHV8-positive large B-cell lymphoma, not otherwise specified), or monomorphic post-transplant lymphoproliferative disorder (PTLD) (B-cell type); **AND**

- Used for partial response, progressive, relapsed, or refractory disease; OR
- Patient has follicular lymphoma (grade 1-3A) Φ; AND
 - Used for partial response, no response, progressive, relapsed, or refractory disease; AND
 - Prior therapy included an alkylating agent or lenalidomide (in addition to an anti-CD20 monoclonal antibody), unless contraindicated; AND
 - Use of epcoritamab-bysp will be restricted to patients with a contraindication or intolerance to mosunetuzumab-axgb; OR
- Patient has histologic transformation of an indolent lymphoma (follicular lymphoma or marginal zone lymphoma) to DLBCL; AND
 - Used for partial response, no response, progressive, relapsed, or refractory disease

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

Enhanced Oncology Value (EOV) Program – Redacted indications

Uses not listed above have inadequate data to support efficacy and are excluded from prior authorization validity.

Other treatment options including, but are not limited to, the following may be appropriate: radiation therapy, surgery, traditional chemotherapy (e.g., platinum, taxane), compassionate use/expanded access programs, clinical trials, supportive care, integrative and complementary therapies.

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

IV. Renewal Criteria ¹

Prior authorization validity may be renewed based upon the following criteria:

 Patient continues to meet the 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: serious infections, serious or life-threatening cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS), severe cytopenias (including neutropenia, anemia, and thrombocytopenia), etc.; AND
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration ^{1,7}

Indication	Dose
Follicular	Administer subcutaneously in 28-day cycles, until disease progression or unacceptable toxicity.
Lymphoma	 Cycle 1: Step-up dose one: 0.16 mg on day 1 Step-up dose two: 0.8 mg on day 8 Step-up dose three: 3 mg on day 15 First full dose: 48 mg on day 22 Cycles 2 and 3: 48 mg on days 1, 8, 15, 22 Cycles 4 to 9: 48 mg on days 1 and 15 Cycles 10 and beyond:
All other B-Cell	 48 mg on day 1 Administer subcutaneously in 28-day cycles, until disease progression or unacceptable toxicity.
Lymphoma Subtypes	 Cycle 1: Step-up dose one: 0.16 mg on day 1 Step-up dose two: 0.8 mg on day 8 First full dose: 48 mg on day 15 Patients should be hospitalized for 24 hours after administration of the first full 48 mg dose due to the risks of CRS and ICANS 48 mg on day 22 Cycles 2 and 3: 48 mg on days 1, 8, 15, 22 Cycles 4 to 9: 48 mg on days 1 and 15 Cycles 10 and beyond: 48 mg on day 1

Note

- Must be administered by a healthcare professional with appropriate medical support to manage severe reactions such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).
- Ensure adequate hydration before administering therapy. Premedicate before each dose in Cycle 1.

VI. Billing Code/Availability Information

HCPCS Code:

• J9321 – Injection, epcoritamab-bysp, 0.16 mg; 1 billable unit = 0.16 mg

NDC(s):

• Epkinly 4 mg/0.8 mL single-dose vial: 82705-0002-xx

• Epkinly 48 mg/0.8 mL single-dose vial: 82705-0010-xx

VII. References (STANDARD)

- 1. Epkinly [package insert]. Plainsboro, NJ; Genmab US, Inc.; August 2024. Accessed September 2025.
- Hutchings M, Mous R, Clausen MR, et al. Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: an open-label, phase 1/2 study. Lancet. 2021 Sep 25;398(10306):1157-1169. Doi: 10.1016/S0140-6736(21)00889-8. Epub 2021 Sep 8.
- 3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) epcoritamab. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2025.
- 4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas, Version 3.2025. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed September 2025.
- 5. Thieblemont C, Phillips T, Ghesquieres H, et al. Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell-Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial. J Clin Oncol. 2023 Apr 20;41(12):2238-2247. doi: 10.1200/JCO.22.01725. Epub 2022 Dec 22. PMID: 36548927; PMCID: PMC10115554.
- Linton KM, Vitolo U, Jurczak W, et al. Epcoritamab monotherapy in patients with relapsed or refractory follicular lymphoma (EPCORE NHL-1): a phase 2 cohort of a single-arm, multicentre study. Lancet Haematol. 2024 Jun 13:S2352-3026(24)00166-2. doi: 10.1016/S2352-3026(24)00166-2.
- 7. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Epcoritamab-bysp: Diffuse Large B-Cell Lymphoma Chemotherapy Order Template, DBL85. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2024.

8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Epcoritamab-bysp: Classic Follicular Lymphoma Chemotherapy Order Template, FOL35. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed August 2024.

VIII. References (ENHANCED)

- 1e. Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma. *N Engl J Med*. 2022;387(24):2220-2231. doi:10.1056/NEJMoa2206913.
- 2e. Thieblemont C, Phillips T, Ghesquieres H, et al. Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell–Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial. Journal of Clinical Oncology. Published online December 22, 2022. doi:https://doi.org/10.1200/jco.22.01725
- 3e. Columvi [package insert]. South San Francisco, CA; Genetech, Inc; June 2023. Accessed April 2024.
- 4e. Bartlett NL, Sehn LH, Matasar MJ, et al. Mosunetuzumab Monotherapy Demonstrates Durable Efficacy with a Manageable Safety Profile in Patients with Relapsed/Refractory Follicular Lymphoma Who Received ≥2 Prior Therapies: Updated Results from a Pivotal Phase II Study [abstract]. Blood 2022;140:1467-1470.
- 5e. Prime Therapeutics Management. Epkinly Clinical Literature Review Analysis. Last updated September 2025. Accessed September 2025.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C82.00	Follicular lymphoma grade I, unspecified site
C82.01	Follicular lymphoma grade I, lymph nodes of head, face and neck
C82.02	Follicular lymphoma, grade I, intrathoracic lymph nodes
C82.03	Follicular lymphoma grade I, intra-abdominal lymph nodes
C82.04	Follicular lymphoma grade I, lymph nodes of axilla and upper limb
C82.05	Follicular lymphoma grade I, lymph nodes of inguinal regional and lower limb
C82.06	Follicular lymphoma grade I, intrapelvic lymph nodes
C82.07	Follicular lymphoma grade I, spleen
C82.08	Follicular lymphoma grade I, lymph nodes of multiple sites
C82.09	Follicular lymphoma grade I, extranodal and solid organ sites
C82.10	Follicular lymphoma grade II, unspecified site
C82.11	Follicular lymphoma grade II, lymph nodes of head, face and neck
C82.12	Follicular lymphoma, grade II, intrathoracic lymph nodes

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C82.13	Follicular lymphoma grade II, intra-abdominal lymph nodes
C82.14	Follicular lymphoma grade II, lymph nodes of axilla and upper limb
C82.14	Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb
C82.16	Follicular lymphoma grade II, intrapelvic lymph nodes
C82.17	Follicular lymphoma grade II, spleen
C82.18	Follicular lymphoma grade II, lymph nodes of multiple sites
C82.19	Follicular lymphoma grade II, extranodal and solid organ sites
C82.20	Follicular lymphoma grade III, unspecified, unspecified site
C82.21	Follicular lymphoma grade III, unspecified, lymph nodes of head, face and neck
C82.22	Follicular lymphoma, grade III, unspecified, intrathoracic lymph nodes
C82.23	Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes
C82.24	Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb
C82.25	Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb
C82.26	Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes
C82.27	Follicular lymphoma grade III, unspecified, spleen
C82.28	Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites
C82.29	Follicular lymphoma grade III, unspecified, extranodal and solid organ sites
C82.30	Follicular lymphoma grade IIIa, unspecified site
C82.31	Follicular lymphoma grade IIIa, lymph nodes of head, face and neck
C82.32	Follicular lymphoma, grade IIIa, intrathoracic lymph nodes
C82.33	Follicular lymphoma grade IIIa, intra-abdominal lymph nodes
C82.34	Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb
C82.35	Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb
C82.36	Follicular lymphoma grade IIIa, intrapelvic lymph nodes
C82.37	Follicular lymphoma grade IIIa, spleen
C82.38	Follicular lymphoma grade IIIa, lymph nodes of multiple sites
C82.39	Follicular lymphoma grade IIIa, extranodal and solid organ sites
C82.40	Follicular lymphoma grade IIIb, unspecified site
C82.41	Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck
C82.42	Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C82.43	Follicular lymphoma grade IIIb, intra-abdominal lymph nodes
C82.44	Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb
C82.45	Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb
C82.46	Follicular lymphoma grade IIIb, intrapelvic lymph nodes
C82.47	Follicular lymphoma grade IIIb, spleen
C82.48	Follicular lymphoma grade IIIb, lymph nodes of multiple sites
C82.49	Follicular lymphoma grade IIIb, extranodal and solid organ sites
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C82.50	Diffuse follicle center lymphoma, unspecified site
C82.51	Diffuse follicle center lymphoma, lymph nodes of head, face and neck
C82.52	Diffuse follicle center lymphoma, intrathoracic lymph nodes
C82.53	Diffuse follicle center lymphoma, intra-abdominal lymph nodes
C82.54	Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb
C82.55	Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.56	Diffuse follicle center lymphoma, intrapelvic lymph nodes
C82.57	Diffuse follicle center lymphoma, spleen
C82.58	Diffuse follicle center lymphoma, lymph nodes of multiple sites
C82.59	Diffuse follicle center lymphoma, extranodal and solid organ sites
C82.60	Cutaneous follicle center lymphoma, unspecified site
C82.61	Cutaneous follicle center lymphoma, lymph nodes of head, face and neck
C82.62	Cutaneous follicle center lymphoma, intrathoracic lymph nodes
C82.63	Cutaneous follicle center lymphoma, intra-abdominal lymph nodes
C82.64	Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb
C82.65	Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.66	Cutaneous follicle center lymphoma, intrapelvic lymph nodes
C82.67	Cutaneous follicle center lymphoma, spleen
C82.68	Cutaneous follicle center lymphoma, lymph nodes of multiple sites
C82.69	Cutaneous follicle center lymphoma, extranodal and solid organ sites
C82.80	Other types of follicular lymphoma, unspecified site
C82.81	Other types of follicular lymphoma, lymph nodes of head, face and neck
C82.82	Other types of follicular lymphoma, intrathoracic lymph nodes
C82.83	Other types of follicular lymphoma, intra-abdominal lymph nodes
C82.84	Other types of follicular lymphoma, lymph nodes of axilla and upper limb
C82.85	Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb
C82.86	Other types of follicular lymphoma, intrapelvic lymph nodes
C82.87	Other types of follicular lymphoma, spleen
C82.88	Other types of follicular lymphoma, lymph nodes of multiple sites
C82.89	Other types of follicular lymphoma, extranodal and solid organ sites
C82.90	Follicular lymphoma, unspecified, unspecified site
C82.91	Follicular lymphoma, unspecified, lymph nodes of head, face and neck
C82.92	Follicular lymphoma, unspecified, intrathoracic lymph nodes
C82.93	Follicular lymphoma, unspecified, intra-abdominal lymph nodes
C82.94	Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb
C82.95	Follicular lymphoma, unspecified lymph nodes of inguinal region and lower limb
C82.96	Follicular lymphoma, unspecified, intrapelvic lymph nodes

C02.07	Follicular lymphoma, unspecified, spleen			
C82.97				
C82.98	Follicular lymphoma, unspecified, lymph nodes of multiple sites			
C82.99	Follicular lymphoma, unspecified, extranodal and solid organ sites			
C83.30	Diffuse large B-cell lymphoma unspecified site			
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck			
C83.32	Diffuse large B-cell lymphoma intrathoracic lymph nodes			
C83.33	Diffuse large B-cell lymphoma intra-abdominal lymph nodes			
C83.34	Diffuse large B-cell lymphoma lymph nodes of axilla and upper limb			
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb			
C83.36	Diffuse large B-cell lymphoma intrapelvic lymph nodes			
C83.37	Diffuse large B-cell lymphoma, spleen			
C83.38	Diffuse large B-cell lymphoma lymph nodes of multiple sites			
C83.39	Diffuse large B-cell lymphoma extranodal and solid organ sites			
C83.80	Other non-follicular lymphoma, unspecified site			
C83.81	Other non-follicular lymphoma, lymph nodes of head, face, and neck			
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes			
C83.83	Other non-follicular lymphoma, intra-abdominal lymph nodes			
C83.84	Other non-follicular lymphoma, lymph nodes of axilla and upper limb			
C83.85	Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb			
C83.86	Other non-follicular lymphoma, intrapelvic lymph nodes			
C83.87	Other non-follicular lymphoma, spleen			
C83.88	Other non-follicular lymphoma, lymph nodes of multiple sites			
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites			
C83.90	Non-follicular (diffuse) lymphoma, unspecified site			
C83.91	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of head, face, and neck			
C83.92	Non-follicular (diffuse) lymphoma, unspecified intrathoracic lymph nodes			
C83.93	Non-follicular (diffuse) lymphoma, unspecified intra-abdominal lymph nodes			
C83.94	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of axilla and upper limb			
C83.95	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of inguinal region and lower limb			
C83.96	Non-follicular (diffuse) lymphoma, unspecified intrapelvic lymph nodes			
C83.97	Non-follicular (diffuse) lymphoma, unspecified spleen			
C83.98	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of multiple sites			
C83.99	Non-follicular (diffuse) lymphoma, unspecified extranodal and solid organ sites			
C85.10	Unspecified B-cell lymphoma, unspecified site			
C85.11	Unspecified B-cell lymphoma, lymph nodes of head, face, and neck			
C85.12	Unspecified B-cell lymphoma, intrathoracic lymph nodes			
C85.13	Unspecified B-cell lymphoma, intra-abdominal lymph nodes			

C85.14	Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb			
C85.15	Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb			
C85.16	Unspecified B-cell lymphoma, intrapelvic lymph nodes			
C85.17	Unspecified B-cell lymphoma, spleen			
C85.18	Unspecified B-cell lymphoma, lymph nodes of multiple sites			
C85.19	Unspecified B-cell lymphoma, extranodal and solid organ sites			
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site			
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face and neck			
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes			
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes			
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb			
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb			
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes			
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen			
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites			
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites			
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site			
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck			
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes			
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes			
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb			
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb			
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes			
C85.87	Other specified types of non-Hodgkin lymphoma, spleen			
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites			
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites			
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)			

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		
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA		
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	ку, он	CGS Administrators, LLC		