Mekinist® (trametinib)
(Oral)

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I. Length of Authorization [1,12]

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

- Adjuvant treatment of melanoma may be renewed for up to 1 year of therapy.

II. Dosing Limits

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

- Mekinist 0.5 mg tablet: 3 tablets per day
- Mekinist 2 mg tablet: 1 tablet per day
- Mekinist 4.7 mg (0.05 mg/1 mL) oral solution: 40 mL (2 mg) per day

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

- 2 mg daily

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age, unless otherwise specified; **AND**
- Patient has not received prior therapy with BRAF and/or MEK inhibitors (e.g., vemurafenib, encorafenib, cobimetinib, binimetinib, etc.) unless otherwise specified; **AND**

Universal Criteria [1]

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Patient does not have colorectal cancer; **AND**

Cutaneous Melanoma † ‡ Φ [1,7]

- Patient has BRAF V600 mutation-positive disease detected by an FDA approved or CLIA compliant test*; **AND**

- Used in combination with dabrafenib as adjuvant therapy; **AND**
  - Patient has lymph node involvement following complete resection, complete lymph node dissection (CLND), therapeutic lymph node dissection (TLND), or nodal basin ultrasound surveillance; **OR**
  - Patient has clinical satellite/in-transit metastases or local satellite/in-transit recurrence with no evidence of disease (NED) after complete excision to clear margins; **OR**
- Used as a single-agent therapy in BRAF-inhibitor treatment-naïve patients with unresectable or metastatic disease; **OR**
- Used in combination with dabrafenib in patients with unresectable or metastatic** disease; **AND**
  - Used as first-line or subsequent therapy; **OR**
  - Used as re-induction therapy for patients who experience disease control *(i.e., complete response, partial response, or stable disease)* from prior MEK inhibitor therapy, but subsequently have disease progression/relapse >3 months after treatment discontinuation; **OR**
- Patient has limited resectable disease; **AND**
  - Used as initial treatment in combination with dabrafenib; **AND**
    - Patient has stage III disease with clinical satellite/in-transit metastases; **OR**
    - Patient has local satellite/in-transit recurrence

***Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in transit metastases, as well as unresectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.*

Uveal Melanoma ‡ [7]

- Used as a single agent for treatment of distant metastatic disease

Anaplastic Thyroid Cancer (ATC) † Φ [1,7]

- Patient has BRAF V600E mutation-positive disease; **AND**
- Used in combination with dabrafenib; **AND**
  - Patient has locally advanced disease with no satisfactory locoregional treatment options; **OR**
  - Patient has metastatic disease

Non-Small Cell Lung Cancer (NSCLC) † Φ [1,7]

- Patient has BRAF V600E mutation-positive disease as detected by an FDA approved or CLIA compliant test*; **AND**

- Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
- Used in combination with dabrafenib

Adult Central Nervous System (CNS) Cancers ‡ [7]

- Patient has BRAF V600E mutation-positive disease; **AND**
- Used in combination with dabrafenib; **AND**
    - Used as adjuvant treatment for incomplete resection, biopsy, or surgically inaccessible location; **AND**
        - Patient has pilocytic astrocytoma OR pleomorphic xanthoastrocytoma (PXA) OR ganglioglioma; **OR**
    - Patient has Karnofsky Performance Status (KPS) ≥ 60; **AND**
        - Patient has recurrent or progressive WHO grade 2 oligodendroglioma (IDH-mutant, 1p19q codeleted) or IDH-mutant astrocytoma; **AND**
            - Patient has received prior fractionated external beam radiation therapy; **OR**
        - Patient has recurrent WHO grade 3 oligodendroglioma (IDH-mutant, 1p19q codeleted); **OR**
        - Patient has recurrent WHO grade 3 or 4 IDH-mutant astrocytoma; **OR**
    - Patient has recurrent glioblastoma; **OR**
    - Patient has recurrent or progressive WHO grade 1 glioma; **AND**
        - Patient has received prior fractionated external beam radiation therapy; **OR**
    - Used for brain metastases in patients with BRAF V600E mutation-positive melanoma; **AND**
        - Used as initial treatment in patients with small asymptomatic brain metastases; **OR**
        - Patient has recurrent limited brain metastases; **OR**
        - Used for relapsed disease in patients with limited brain metastases and either stable systemic disease or reasonable systemic treatment options; **OR**
        - Used for recurrent disease in patients with extensive brain metastases and stable systemic disease or reasonable systemic treatment options

Pediatric Central Nervous System (CNS) Cancers † ‡ [1,7,17,26]

- Patient has BRAF V600E mutation-positive disease; **AND**
- Used in in combination with dabrafenib; **AND**
    - Patient has low-grade glioma †; **AND**
        - Patient is ≥ 1 year of age and < 18 years of age; **AND**

        - Patient requires systemic therapy; **OR**
    - Patient has diffuse high-grade glioma ‡; **AND**
        - Used as adjuvant therapy *(excluding diffuse midline glioma, H3 K27-altered or pontine location)*; **AND**
            - Patient is < 3 years of age; **OR**
            - Patient is ≥ 3 years of age and ≤ 18 years of age; **AND**
                - Used following standard brain radiation therapy (RT) with or without concurrent temozolomide; **OR**
        - Used for recurrent or progressive disease *(excluding oligodendroglioma, IDH-mutant and 1p/19q co-deleted or astrocytoma IDH-mutant)*; **AND**
            - Patient is ≤ 18 years of age

Ovarian Cancer (Epithelial Ovarian /Fallopian Tube /Primary Peritoneal) ‡ [7]

- Used in combination with dabrafenib; **AND**
    - Patient has BRAF V600E mutation-positive persistent or recurrent disease; **AND**
    - Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); **OR**
- Used as a single agent; **AND**
    - Patient has recurrent low-grade serous carcinoma

Histiocytic Neoplasms ‡ [7]

- Used as single agent therapy; **AND**
- Patient has a mitogen-activated protein (MAP) kinase pathway mutation, or no detectable mutation, or testing not available; **AND**
- Patient has one of the following:
    - Relapsed/refractory or symptomatic Erdheim-Chester Disease (ECD); **OR**
    - Rosai-Dorfman Disease; **AND**
        - Patient has symptomatic unresectable (bulky/site of disease) unifocal disease; **OR**
        - Patient has symptomatic multifocal disease; **OR**
        - Patient has relapsed or refractory disease; **OR**
    - Langerhans Cell Histiocytosis (LCH); **AND**
        - Patient has multisystem disease with symptomatic or impending organ dysfunction; **OR**
        - Patient has single-system lung disease; **OR**
        - Patient has multifocal single system bone disease not responsive to treatment with a bisphosphonate and >2 lesions; **OR**
        - Patient has CNS lesions; **OR**

- Patient has relapsed or refractory disease

Solid Tumors with *BRAF V600E* mutation † [1,14,15]

- Patient is at least 6 years of age; **AND**
- Patient has BRAF V600E mutation-positive solid tumors; **AND**
- Patient has unresectable or metastatic disease that has progressed following prior treatment; **AND**
- Patient has no satisfactory alternative treatment options; **AND**
- Used in combination with dabrafenib; **AND**
- Patient has one of the following solid tumors **¥**:
  - Anaplastic thyroid cancer
  - Biliary tract cancer
  - Adenocarcinoma of small intestine
  - High or Low Grade Glioma
  - Low grade serous ovarian carcinoma

***¥** Note: Solid tumors not listed, that are BRAF V600E mutation-positive, will be reviewed on a case-by-case basis and considered medically necessary when all other relevant medication and indication specific criteria are met.*

***** If confirmed using an immunotherapy assay-http://www.fda.gov/CcompanionDiagnostics*

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

IV. Renewal Criteria [1]

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. Examples of unacceptable toxicity include: interstitial lung disease/pneumonitis, cardiomyopathy, new primary malignancies, severe hemorrhagic events, colitis/gastrointestinal perforation, venous thromboembolic events (e.g., deep vein thrombosis [DVT], pulmonary embolism [PE], etc.), ocular toxicities (e.g., persistent retinal pigment epithelial detachment [RPED], retinal vein occlusion [RVO], etc.), serious skin toxicities (e.g., Stevens-Johnson syndrome [SJS], drug reaction with eosinophilia and systemic symptoms [DRESS], etc.), serious febrile reactions, hyperglycemia, etc.; **AND**
- Left ventricular ejection fraction (LVEF) has not had an absolute decrease of ≥ 10% from baseline and is not below the lower limit of normal (LLN) *(LVEF results must be within the previous 3 months)*; **AND**

Adjuvant treatment of Cutaneous Melanoma [1,12]

- Treatment has not exceeded 1 year of therapy

Cutaneous Melanoma (re-induction therapy) [7]

- *Refer to Section III for criteria (see Cutaneous Melanoma – Used as re-induction therapy)*

V. Dosage/Administration [1,9-12,15,17-24]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Cutaneous Melanoma, Uveal Melanoma, ATC, NSCLC, Adult CNS Cancers, Ovarian Cancer, Histiocytic Neoplasms</td><td>Administer 2 mg orally once daily until disease progression/recurrence or unacceptable toxicity
(Note: for adjuvant treatment of melanoma, treat until disease recurrence or unacceptable toxicity for up to 1 year).</td></tr>
<tr><td>Solid Tumors with BRAF V600E mutation</td><td><u>Adult Patients</u>
Administer 2 mg orally once daily until disease progression/recurrence or unacceptable toxicity

<u>Pediatric Patients</u>
– Tablets (for use in patients weighing at least 26 kg):
<table>
<tr><th>Body weight</th><th>Recommended dosage</th></tr>
<tr><td>26 to 37 kg</td><td>1 mg orally once daily</td></tr>
<tr><td>38 to 50 kg</td><td>1.5 mg orally once daily</td></tr>
<tr><td>51 kg or greater</td><td>2 mg orally once daily</td></tr>
</table>
– Oral Solution:
<table>
<tr><th>Body weight</th><th>Recommended dosage total volume of oral solution once daily (trametinib content)</th></tr>
<tr><td>8 kg</td><td>6 mL (0.3 mg)</td></tr>
<tr><td>9 kg</td><td>7 mL (0.35 mg)</td></tr>
<tr><td>10 kg</td><td>7 mL (0.35 mg)</td></tr>
<tr><td>11 kg</td><td>8 mL (0.4 mg)</td></tr>
<tr><td>12 to 13 kg</td><td>9 mL (0.45 mg)</td></tr>
<tr><td>14 to 17 kg</td><td>11 mL (0.55 mg)</td></tr>
<tr><td>18 to 21 kg</td><td>14 mL (0.7 mg)</td></tr>
<tr><td>22 to 25 kg</td><td>17 mL (0.85 mg)</td></tr>
<tr><td>26 to 29 kg</td><td>18 mL (0.9 mg)</td></tr>
<tr><td>30 to 33 kg</td><td>20 mL (1 mg)</td></tr>
<tr><td>34 to 37 kg</td><td>23 mL (1.15 mg)</td></tr>
<tr><td>38 to 41 kg</td><td>25 mL (1.25 mg)</td></tr>
<tr><td>42 to 45 kg</td><td>28 mL (1.4 mg)</td></tr>
<tr><td>46 to 50kg</td><td>32 mL (1.6 mg)</td></tr>
<tr><td>≥ 51 kg</td><td>40 mL (2 mg)</td></tr>
</table>
***Administer until disease progression or unacceptable toxicity</td></tr>
<tr><td>Pediatric CNS Cancers</td><td><u>Low-Grade Glioma</u>
– Tablets:
<table>
<tr><th>Body weight</th><th>Recommended dosage</th></tr>
<tr><td>26 to 37 kg</td><td>1 mg orally once daily</td></tr>
</table></td></tr>
</table>

38 to 50 kg	1.5 mg orally once daily
51 kg or greater	2 mg orally once daily

- **Oral solution:**

Body weight	Recommended dosage total volume of oral solution once daily (trametinib content)
8 kg	6 mL (0.3 mg)
9 kg	7 mL (0.35 mg)
10 kg	7 mL (0.35 mg)
11 kg	8 mL (0.4 mg)
12 to 13 kg	9 mL (0.45 mg)
14 to 17 kg	11 mL (0.55 mg)
18 to 21 kg	14 mL (0.7 mg)
22 to 25 kg	17 mL (0.85 mg)
26 to 29 kg	18 mL (0.9 mg)
30 to 33 kg	20 mL (1 mg)
34 to 37 kg	23 mL (1.15 mg)
38 to 41 kg	25 mL (1.25 mg)
42 to 45 kg	28 mL (1.4 mg)
46 to 50kg	32 mL (1.6 mg)
≥ 51 kg	40 mL (2 mg)

***Administer until disease progression or unacceptable toxicity.

High-Grade Glioma
Administer up to 2 mg orally once daily until disease progression/recurrence or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug oral, chemotherapeutic, Not Otherwise Specified

NDC(s):

- Mekinist 0.5 mg tablet: 00078-0666-xx
- Mekinist 0.5 mg tablet: 00078-1105-xx
- Mekinist 2 mg tablet: 00078-0668-xx
- Mekinist 2 mg tablet: 00078-1112-xx
- Mekinist 4.7 mg (0.05 mg/1 mL) oral solution: 00078-1161-xx

VII. References

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7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) trametinib. National Comprehensive Cancer Network, 2023. 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 March 2023.
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26. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Pediatric Central Nervous System Cancers. Version 2.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C22.1	Intrahepatic bile duct carcinoma
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C43.0	Malignant melanoma of lip

ICD-10	ICD-10 Description
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.11	Malignant melanoma of right eyelid, including canthus
C43.12	Malignant melanoma of left eyelid, including canthus
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of left 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
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube

ICD-10	ICD-10 Description
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified
C69.30	Malignant neoplasm of unspecified choroid
C69.31	Malignant neoplasm of right choroid
C69.32	Malignant neoplasm of left choroid
C69.40	Malignant neoplasm of unspecified ciliary body
C69.41	Malignant neoplasm of right ciliary body
C69.42	Malignant neoplasm of left ciliary body
C69.60	Malignant neoplasm of unspecified orbit
C69.61	Malignant neoplasm of right orbit
C69.62	Malignant neoplasm of left orbit
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified
C72.0	Malignant neoplasm of spinal cord
C72.9	Malignant neoplasm of central nervous system, unspecified
C73	Malignant neoplasm of thyroid gland

ICD-10	ICD-10 Description
C79.31	Secondary malignant neoplasm of brain
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.2	Malignant mast cell neoplasm
C96.5	Multifocal and unisystemic Langerhans-cell histiocytosis
C96.6	Unifocal Langerhans-cell histiocytosis
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D43.0	Neoplasm of uncertain behavior of brain, supratentorial
D43.1	Neoplasm of uncertain behavior of brain, infratentorial
D43.2	Neoplasm of uncertain behavior of brain, unspecified
D43.4	Neoplasm of uncertain behavior of spinal cord
D43.9	Neoplasm of uncertain behavior of central nervous system, unspecified
D76.3	Other histiocytosis syndromes
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.43	Personal history of malignant neoplasm of ovary
Z85.820	Personal history of malignant melanoma of skin
Z85.841	Personal history of malignant neoplasm of brain

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): 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.

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