I. PURPOSE
To define and describe the accepted indications for Imfinzi (durvalumab) usage in the treatment of cancer.

II. DEFINITIONS

Imfinzi (durvalumab): is a human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that blocks the interaction of PD-L1 with PD-1 and CD80 (B7.1). Blockade of PD-L1/PD-1 and PD-L1/CD80 interactions releases the inhibition of immune responses, without inducing antibody dependent cell-mediated cytotoxicity (ADCC).

Imfinzi (durvalumab) is FDA approved for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. Recently in 2018, Imfinzi received FDA approval for unresectable stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

Imfinzi (durvalumab) is available in 120 mg and 500 mg single dose vials.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Imfinzi (durvalumab) may be considered medically necessary when any of the following selection criteria is met:

1. Urothelial Carcinoma
   a. The member has locally advanced, metastatic, or recurrent urothelial carcinoma and Imfinzi (durvalumab) is being used as a single agent for the following:
      i. Disease progression during or following platinum-containing chemotherapy OR
      ii. Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy AND
      iii. Has a ECOG PS 0-1.

2. Non-Small Cell Lung Cancer (NSCLC)
a. Imfinzi (durvalumab) is being used as consolidation therapy in members with unresectable stage III disease, performance status (PS) 0-1, and no disease progression after 2 or more cycles of definitive chemoradiation.

**Exclusion Criteria:** Imfinzi (durvalumab) is not considered medically necessary when any of the following selection criteria is met:

1. Imfinzi (durvalumab) is being used after disease progression with the same regimen or prior anti-PD-1 or PD-L1 inhibitor.
2. Concurrent use with other anticancer treatments, steroids, or immunosuppressive agents.
3. Dosing exceeds single dose limit of Imfinzi (durvalumab) 10mg/kg or maximum duration of 12 months for NSCLC consolidation therapy.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

**IV. PROCEDURE**

Requests for Imfinzi (durvalumab) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:**
   
a. Urothelial Carcinoma: 10 mg/kg IV infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity.
   
b. Stage III NSCLC: 10 mg/kg IV infusion over 60 minutes every 2 weeks until disease progression, unacceptable toxicity, or a MAX of 12 months.

2. **Dosage Adjustments:**
   
a. Nephritis (Grade 2, creatinine greater than 1.5 to 3 times ULN): Withhold dose and administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Resume treatment when adverse reaction returns to Grade 1 and the corticosteroid dose has been reduced to less than 10 mg prednisone or equivalent per day.
   
b. Nephritis (Grade 3, creatinine greater than 3 to 6 times ULN; Grade 4, creatinine greater than 6 times ULN): Permanently discontinue. Administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper.
   
c. Hepatitis (Grade 2, ALT or AST greater than 3 to 8 times ULN or total bilirubin greater than 1.5 to 5 times ULN): Withhold dose and administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Resume treatment when adverse reaction returns to Grade 1 and the corticosteroid dose has been reduced to less than 10 mg prednisone or equivalent per day.
   
d. Hepatitis (Grade 3, ALT or AST greater than 8 times ULN or total bilirubin greater than 5 times ULN): Permanently discontinue. Administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Hepatitis (Concurrent ALT or AST greater than 3 times ULN and total bilirubin greater than 2 times ULN with no other cause): Permanently discontinue. Administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Adrenal insufficiency (hypophysitis/hypopituitarism, Grade 2 to 4): Withhold dose until clinically stable. Administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper and hormone replacement as clinically indicated.
e. Adverse reaction, inability to taper corticosteroid to 10 mg/day or less prednisone or equivalent per day within 12 weeks after last durvalumab dose: Permanently discontinue.

f. Adverse reaction, persistent (Grade 2 or 3; excluding endocrinopathies), not recovering to Grade 0 or 1 within 12 weeks after last dose: Permanently discontinue.

g. Any Grade 3 adverse effect: Withhold dose and administer corticosteroids 1 to 4 mg/kg/day of prednisone or equivalent, followed by taper. Resume treatment when adverse reaction returns to Grade 1 and the corticosteroid dose has been reduced to less than 10 mg prednisone or equivalent per day.

h. Any Grade 4 adverse effect: Permanently discontinue. Consider administering 1 to 4 mg/kg/day of prednisone or equivalent followed by taper.

i. Colitis or diarrhea (Grade 2): Withhold dose and administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Resume treatment when adverse reaction returns to Grade 1 and the corticosteroid dose has been reduced to less than 10 mg prednisone or equivalent per day.

j. Colitis or diarrhea (Grade 3 or 4): Permanently discontinue. Administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Hyperthyroidism (Grade 2 to 4): Withhold dose until clinically stable and administer symptomatic treatment.

k. Infection (Grade 3 or 4): Withhold dose and administer symptomatic treatment. Treat with anti-infective for suspected or confirmed infections.

l. Infusion-related reactions (Grade 1 to 2): Interrupt or slow rate of infusion; consider premedications with subsequent doses.

m. Infusion-related reactions (Grade 3 to 4): Permanently discontinue

n. Pneumonitis (Grade 2): Withhold dose and administer 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Resume treatment when adverse reaction returns to Grade 1 and the corticosteroid dose has been reduced to less than 10 mg prednisone or equivalent per day.

o. Pneumonitis (Grade 3 or 4): Permanently discontinue. Administer 1 to 4 mg/kg/day prednisone or equivalent followed by taper. Rash or dermatitis (Grade 2, for greater than 1 week; Grade 3): Withhold dose and consider administering 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Resume treatment when adverse reaction returns to Grade 1 and the corticosteroid dose has been reduced to less than 10 mg prednisone or equivalent per day.

p. Rash or dermatitis (Grade 4): Permanently discontinue. Consider administering 1 to 2 mg/kg/day prednisone or equivalent followed by taper. Type 1 diabetes mellitus (Grade 2 to 4): Withhold dose until clinically stable. Initiate treatment with insulin as clinically indicated.

3. Monitoring

a. Tumor response indicates efficacy

b. Liver function: During each treatment cycle

c. Thyroid function: Prior to initiation and periodically throughout treatment

d. Blood glucose: During treatment

e. Renal function: Prior to and during each treatment cycle

f. Signs or symptoms of endocrinopathies

g. Signs or symptoms of adrenal insufficiency
h. Signs or symptoms of diabetes
i. Signs or symptoms of hypophysitis or hypopituitarism
j. Signs or symptoms of immune thrombotic thrombocytopenia
k. Signs and symptoms of infusion-related reactions.

V. APPROVAL AUTHORITY
1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS
VII. REFERENCES