Name of Policy:
Imfinzi (durvalumab)

Policy #: 673      Effective Date: August 8, 2017
Category: Pharmacy      Last Review Date: June 2017

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**Description of Procedure or Service:**

Imfinzi (durvalumab) is a human monoclonal programmed death ligand 1 (PD-L1) blocking antibody. Durvalumab works by blocking the interaction of programmed cell death ligand 1 (PD-L1) with the PD-1 and CD80 (B7.1) molecules. This interaction releases the inhibitory effects of PD-L1 on the immune response resulting in the restoration of immune responses, including anti-tumor immune responses.

**Policy:**

**Imfinzi (durvalumab) meets** Blue Cross Blue Shield of Alabama’s medical criteria for coverage when used as a **single agent** for the treatment of **locally advanced or metastatic urothelial carcinoma** when all of the following criteria are met:

A. Inoperable or metastatic transitional-cell urothelial carcinoma histologically or cytologically confirmed; and

B. One of the following:
   1. Disease has progressed during or following platinum-containing therapy; or
   2. Disease has progressed within 12 months of neoadjuvant or adjuvant treatment with platinum-containing therapy; and

C. Current Eastern Cooperative Oncology Group (ECOG) performance status of 0-1; and

D. Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; and

E. Does not have **any** of the following:
   1. History of immunodeficiency; or
   2. History of severe autoimmune disease; or
   3. Require systemic immunosuppression; or
   4. Active immune-mediated disease; or
   5. Severe or life-threatening infection; or
   6. Untreated central nervous system (CNS) metastases.

*Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.*

**Key Points:**

Urothelial bladder cancers arise from the epithelium of the bladder and are the sixth most common form of cancer in the US. It is estimated that in 2017, approximately 79,030 Americans will be diagnosed with bladder cancer, and an estimated 16.870 will die from this disease.

In an open-label, phase 1/2 study by Massard and colleagues, the safety and efficacy of durvalumab was investigated. A total of 61 participants with inoperable or metastatic solid tumors were treated with durvalumab every 2 weeks for up to 12 months. The majority of
participants (93.4%) had received one or more prior systemic therapies and 31.1% had received three or more prior systemic therapies. The primary endpoint was safety and the secondary endpoint was objective response rate. Median duration of follow-up was 4.3 months. A total of 63.9% (39/61) individuals reported a treatment related adverse event (AE). The most common AEs were low grade and included fatigue, diarrhea, and decreased appetite. There were 3 participants who experienced grade 3 AEs and there were no reported grade 4 or 5 events. In 42 participants, the objective response rate was 31.0% (95% confidence interval [CI], 17.6 to 47.1) and 46.4% (95% CI, 27.5 to 66.1) in the PD-L1-positive subgroup, and 0% (95% CI, 0.0 to 23.2) in the PD-L1-negative subgroup.

A 2017 update on this study (N=103) showed a 29.5% ORR for PD-L1 disease and a 7.7% ORR for PD-L1 low or negative disease. O at 6 months was 68.4% for the PD-L1 high group and 44.7% for the PD-L1 low/negative group. Median duration of response was not yet reached at time of data cutoff. Grade 3 or 4 treatment-related AEs occurred in 5.2% of treated patients and 3 patients had a grade 3 or 4 immune-mediated AE.

The National Comprehensive Cancer Network (NCCN) Bladder Cancer Guidelines (V5. 2017) has a 2A recommendation for the use of durvalumab as subsequent systemic therapy for locally advanced or metastatic disease after platinum-based therapy.

**Key Words:**
Imfinzi, durvalumab, urothelial carcinoma, bladder cancer

**Approved by Governing Bodies:**
On May 1, 2017, the U.S. Food and Drug Administration (FDA) approved durvalumab for the treatment of individuals 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. This indication was approved under an accelerated process and is based on tumor response rate and duration of response. The FDA also included a contingency that continued approval may be based upon verification and description of clinical benefit in confirmatory trials.

**Benefit Application:**
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply.
FEP: Special benefit consideration may apply. Refer to member’s benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.
Current Coding:
CPT Codes: J9999 Not otherwise classified, antineoplastic drugs [when specified as durvalumab]

References:

Policy History:
Medical Policy Group, June 2017 (2): New policy created.
Medical Policy Administration Committee, July 2017

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date of the policy.
hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.