CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
2Q17 July – August

BRAND NAME
Imfinzi®

GENERIC NAME
Durvalumab

MANUFACTURER
AstraZeneca

DATE OF APPROVAL
May 1, 2017

PRODUCT LAUNCH DATE
Currently commercially available

REVIEW TYPE

☐ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

☒ Review type 5 (RT5): Abbreviated Review for Intravenous Chemotherapy Agents
Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit

FDA APPROVED INDICATION(S)
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.

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OFF-LABEL USES
Not applicable

CLINICAL EFFICACY[1,2]
Urothelial cancer is a type of bladder cancer that starts with urothelial cells that line the bladder. These cells are transitional cells, which can change shape and stretch when the bladder is full. Bladder cancer represents 4.7% of all new cancer cases with a 5 year survival rate of 77.3% (2007 to 2013). Standard treatment strategies include surgery, radiation, chemotherapy and immune therapy.

The safety and efficacy of Imfinzi was evaluated in a multicenter, multi-cohort, open-label clinical trial. A total of 182 patients with locally advanced or metastatic urothelial carcinoma who had progressed while on or after a platinum-based therapy were enrolled. Enrolled patients had to initiate Imfinzi therapy at least 13 weeks prior to the data cut-off date. All patients received Imfinzi 10mg/kg via intravenous infusion every 2 weeks for up to 12 months or until unacceptable toxicity or disease progression. Assessments of tumors were performed at Weeks 6, 12 and 16, then every 8 weeks for the first year and every 12 weeks thereafter.

Efficacy outcome measures were confirmed Objective Response Rate (ORR) and duration of response (DoR). Results are summarized in Table 1. The median follow-up was 5.6 months. Among the total 31 responding patients, 14 patients (45%) had ongoing responses of 6 months or longer and 5 patients (16%) had ongoing responses of 12 months or longer.

Table 1: Efficacy Results of Imfinzi therapy

	All Patients N=182	PD-L1 High N=95	PD-L1 Low/Negative N=73	PD-L1 NE N=14
ORR n (%) (95% CI)	31 (17.0%) (11.9, 23.3)	25 (26.3%) (17.8, 36.4)	3 (4.1%) (0.9, 11.5)	3 (21.4%) (4.7, 50.8)
Complete response	5	3	1	1
Partial response	26	22	2	2
Median duration of response	NR (0.9+, 19.9+)	NR (0.9+, 19.9+)	12.3 (1.9+, 12.3)	NR (2.3+, 2.6+)

PD-L1=Programmed cell death ligand-1; NE=not evaluable; NR=not reached

Expression of PD-L1 can be induced by inflammatory signals and can be expressed on both tumor cells and tumor-associated immune cells in the tumor microenvironment.

CONTRAINDICATIONS
None

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BLACK BOX WARNINGS
None

DRUG INTERACTIONS
Drug interactions are not reported in the package labeling.

ADVERSE REACTIONS
Thirty-one percent of patients studied had a drug delay or interruption in therapy due to adverse reaction. The most common (>2%) were liver injury (4.9%), urinary tract infection (3.3%), acute kidney injury (3.3%) and musculoskeletal pain (2.7%).

The most common adverse events (reported in ≥ 15% of patients) were fatigue (39%), musculoskeletal pain (24%), constipation (21%), decreased appetite (19%), nausea (16%), peripheral edema (15%), and urinary tract infection (15%).

Eight patients (4.4%) who were treated with Imfinzi experienced Grade 5 adverse events of cardiorespiratory arrest, general physical health deterioration, sepsis, ileus, pneumonitis, or immune-mediated hepatitis. The drug was discontinued for adverse reactions in 3.3% of patients.

The following immune-mediated precautions and warnings apply: pneumonitis (1 death), hepatitis (1 death), colitis, and endocrinopathies.

DOSAGE AND ADMINISTRATION
10 mg/kg as an intravenous infusion over 60 minutes every 2 weeks
Dose adjustments or drug discontinuation may be required based on severity of adverse drug reactions.

PRODUCT AVAILABILITY
Injection: 500 mg/10 mL and 120 mg/2.4 mL solution in a single-dose vial

THERAPEUTIC ALTERNATIVES[3,4]

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
Bavencio® (avelumab)	10 mg/kg IV infusion over 60 minutes every 2 weeks	Has additional FDA indications
Keytruda® (pembrolizumab)	200 mg IV infusion over 30 minutes every 3 weeks	Has additional FDA indications
Opdivo® (nivolumab)	240 mg IV infusion over 60 minutes	Has additional FDA indications

	every 2 weeks until disease progression or unacceptable toxicity	
Tecentriq® (atezolizumab)	1,200 mg IV over 60 minutes every 3 weeks	Has additional FDA indications

Utilization Management Recommendation
• There is significant potential for inappropriate use and utilization management should be considered for the following reason(s): o To ensure appropriate use of medications that have a significant potential for use that may lead to inferior or unpredictable outcome i. Imfinzi is approved for second-line therapy after prior trial of a platinum-containing chemotherapy ii. Recommended utilization management tool(s): (check all that apply) (1) ☒ Prior authorization (2) ☐ Quantity limits (3) ☐ Provider newsletter (4) ☐ Hard block (plan exclusion) (5) ☐ Messaging (6) ☐ Electronic step therapy (7) ☐ Clinical program
Product Comparison
• Not applicable

[1] Imfinzi [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; May 2017.
[2] National Cancer Institute. Available at: https://www.cancer.gov/types/bladder. Accessed May 9, 2017.
[3] Clinical Pharmacology. Available at: http://www.clinicalpharmacology-ip.com/Default.aspx. Accessed May 9, 2017.
[4] National Comprehensive Cancer Network. Bladder Cancer. Version 5.2017. Accessed from https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf, June 1, 2017.