Submitted by:
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NCCN Guidelines Panel: Pancreatic Adenocarcinoma

Dear Panel Members,

On behalf of United Healthcare, I respectfully request the NCCN Guideline Panel consider real world evidence (RWE) on treatment duration, hospitalizations and total cost of care associated with specific treatment regimens in their ratings of therapy for the NCCN Evidence Blocks and in their considerations for Categories of Preference.

Specific Changes: No specific changes requested.

FDA Clearance: Not applicable.

Data and Rationale: The NCCN Evidence Blocks include five components that help describe the value of the regimens recommended in the NCCN Guidelines®; these components are efficacy, safety, quality and quantity of evidence, consistency of evidence and affordability. The Evidence Blocks are an innovative way to help provide more transparency of treatment recommendations as well as potentially enable providers and patients to make more informed decisions based on patient's value system. However, the Evidence Blocks ratings are based on survey data based on panel members' knowledge of each component for each regimen recommendation. Therefore, the rationale for this submission is to provide panelists data on duration of therapy, hospitalizations during treatment and total cost of care drawn from UHC's data from our members who receive these treatments in real world setting. RWE takes into account patients who are not traditionally eligible for randomized clinical trials, for a variety of reasons, including comorbidities, which usually serve as exclusion criteria for the pivotal trials used for FDA approval. Additionally, data on hospitalizations and total cost of care are generally not available from published reports of clinical trials.

We are providing the RWE data on treatment duration, hospitalizations and total cost of care associated with specific treatment regimens for pancreatic cancer. Data to determine these components were available from a real world data asset consisting of patients' administrative data deterministically linked to clinical data and planned regimen requests collected via a web-based prior authorization (PA) tool for injectable chemotherapy utilized by UnitedHealth Care (UHC). Commercially insured patients were included, as long as they received at least their medical benefit from UHC and had claims data available in the Optum Research Database (ORD). Medicare Advantage patients were not included in the PA program until October 2019, and therefore this initial analysis is only among the commercially insured population. Patients with a PA request from June 1, 2015 to February 28, 2017 were identified and linked to their claims data for the same period. Patients who did not complete therapy or disenrolled

prior to February 28, 2017 were excluded. There were 1182 patients with completed treatment regimens for their initial episode of care for pancreatic cancer (neoadjuvant, adjuvant, or treatment for advanced disease), who were included in this analysis.

We have limited this first submission to the RWE for pancreatic cancer treatment regimens. We would appreciate feedback from the NCCN Guideline Panel as to whether this data provided additional information in their determinations of the ratings for NCCN Evidence Blocks and in their considerations for Categories of Preference. If this data does indeed provide additional information, then Optum and UHC will consider developing additional submissions of RWE for other cancer types.

Sincerely,

Jennifer Malin, MD, PhD
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Neoadjuvant (Resectable/Borderline Resectable)

Regimen	All-Cause inpatient stays (%)[a]	Median (Mean) duration of therapy[a]	Total Cost of Care (Average,SD)[a]
Fluorouracil + Leucovorin + Irinotecan + Oxaliplatin (FOLFIRINOX/ mFOLFIRINOX) 12C (q2w)	(N=116) 24%	71 (76) days	$68,443 ($57,712)
Gemcitabine + Albumin-bound Paclitaxel (G-nP) 4C (q4w)	(N = 54) 33%	86 (93) days	$89,192 ($78,852)

Adjuvant Therapy (Resectable)

Regimen	All-Cause inpatient stays (%)[a]	Median (Mean) duration of therapy[a]	Total Cost of Care (Average,SD)[a]
Gemcitabine + Capecitabine 6C (q 28 days)	(N = 37) 0%	197 (160) days	$105,211 ($78,212)
Fluorouracil + Leucovorin + Irinotecan + Oxaliplatin (mFOLFIRINOX) 12C (q2w)	(N = 9) 22%	89 (141) days	$91,372 ($64,620)
Gemcitabine 6C (q4w)	(N = 80) 15%	50 (80) days)	$24,800 ($29,024)
Fluorouracil (5-FU) + Leucovorin 6C (q4w)	(N = 11) 0%	49 (43)	$27,973 ($22,261)
Capecitabine 6C (q3w)	NR	NR	NR

NR = Not reported

Locally Advanced/Metastatic Pancreatic Cancer – 1st line therapy

Regimen	All-Cause inpatient stays (%)[a]	Median (Mean) duration of therapy[a]	Total Cost of Care (Average,SD)[a]
Fluorouracil + Leucovorin + Irinotecan + Oxaliplatin (FOLFIRINOX/mFOLFIRINOX)	(N = 360) 34%	85 (112) days	$87,971 ($92,818)
Gemcitabine + Albumin-bound paclitaxel (G-nP)	(N = 281) 37%	80 (101) days	$80,132 ($79,466)
Gemcitabine + Erlotinib	NR	NR	NR
Gemcitabine + Capecitabine	(N = 13) 23%	64 (92) days	$33,667 ($23,311)
Gemcitabine	(N = 55) 37%	44 (62) days	$35,083 ($43,358)
Fixed dose rate gemcitabine + docetaxel + Capecitabine (GTX)	NR	NR	NR
Gemcitabine + cisplatin	(N = 13) 23%	104 (100) days	$83,011 ($88,733)
Capecitabine	NR	NR	NR
5-FU/Leucovorin	(N = 4) 50%	37 (54) days	$26,012 ($28,320)

NR = Not reported

Notes (a)

- All-cause inpatient stays (%), Median duration of therapy, and total cost of care data is from eviCore and claims data. Not reported (NR) for some oral oncology medications due to coverage under pharmacy benefits.
- Total cost of care during therapy' is the average total cost of care during treatment for patients with a prior authorization request June 1, 2015, to February 28, 2017. Approximately 40% of patients do not have their pharmacy benefit costs captured in total cost of care.
- All-cause inpatient stays' is percent of patients with at least one inpatient stay for any reason during treatment for patients with a prior authorization request June 1, 2015, to February 28, 2017.
- Median duration of therapy is duration of treatment [median (25th percentile - 75th percentile)] for patients with a prior authorization request June 1, 2015 to February 28, 2017.