January 30, 2018

Submission Request

National Comprehensive Cancer Network

RE: Clinical Evidence in Support of LUTATHERA® (lutetium Lu 177 dotatate) in treatment of somatostatin receptor-positive GEP-NETs in adults

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Date of Request	January 30, 2018
NCCN Guidelines Panel:	Neuroendocrine Tumors

To Whom It May Concern:

On behalf of Advanced Accelerator Applications, a Novartis Company, I respectfully request the NCCN Neuroendocrine Panel to review the enclosed data for inclusion of Lutathera® (lutetium Lu 177 dotatate) for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

Specific Changes: Recommend Lutathera® as a treatment option for Gastrointestinal Tract NET and Pancreatic NET.

FDA Clearance: The FDA approved Lutathera in January 26th, 2018 for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

Rationale: In support of the proposed change, data from the NETTER-1 phase 3 clinical trial in patients with advanced midgut neuroendocrine tumors showed statistically significant and clinically relevant prolongation of progression-free survival (primary endpoint) with ^{177}Lu-Dotatate versus high-dose octreotide LAR, as well as a significantly higher response rate. Preliminary evidence of overall survival benefit is seen in the pre-defined per protocol interim analysis [(1)].

Furthermore, the study conducted in the Erasmus Medical Center (Netherlands) included patients with gastroenteropancreatic and bronchial neuroendocrine tumors, and published a median follow up of 78 months [(2)]. Efficacy results were supportive of NETTER-1, and robust safety data was presented for 610 patients, showing a favorable safety profile.

The following articles are submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

1. Strosberg et al. Phase 3 trial of 177Lu-Dotatate for midgut neuroendocrine tumors. N Engl J Med. 2017;376:125-135.

2. Brabander T, van der Zwan WA, Teunissen JJM, et al. Long-term efficacy, survival, and safety of [177Lu-DOTA0,Tyr3]octreotate in patients with gastroenteropancreatic and bronchial neuroendocrine tumors. Clin Cancer Res. 2017;23(16):4617-4624.

Sincerely,

Debora Barton

Debora Barton, M.D.

Head of Oncology, Advanced Accelerator Applications