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

Submitted by: Dr. Debora Baton M.D. Head of Oncology

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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.


Sincerely,

Debora Barton, M.D.
Head of Oncology, Advanced Accelerator Applications