

**NCCN NET submission cover letter**

Date: November 14, 2012

Submission Request c/o Joan McClure  
National Comprehensive Cancer Network  
500 Old York Road, Suite 250  
Jenkintown, PA 19046

**RE: Clinical Evidence in Support of Lanreotide in Neuroendocrine Tumors**

Name: Kathleen Graham Lomax, MD  
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Date of request: November 1, 2012  
NCCN Guidelines Panel: Neuroendocrine Tumors

Dear Guidelines Panel

On behalf of Ipsen Biopharmaceuticals, Inc., we respectfully request the NCCN Neuroendocrine Tumors Guideline Panel to review the enclosed data for the use of lanreotide (Somatuline® Depot) in the treatment of patients with neuroendocrine tumors. This information is provided in response to your verbal request which followed our original submission.

**Specific changes:** As a result of the information provided in this letter and the accompanying documentation, you may conclude it is appropriate to change the terminology from “octreotide” to “somatostatin analogs” in several places within the NCCN Guidelines for Neuroendocrine Tumors as noted in the accompanying table. You may also choose to include the recommended dosing schedule for lanreotide.

**FDA status:** Somatuline® Depot (lanreotide) has not been approved in the United States for use in patients with neuroendocrine tumors (NETs).

**Rationale for recommended changes:**

The efficacy of lanreotide in patients with functional NETs has been demonstrated in several published studies. Furthermore, the comparable mechanisms of action and clinical activity of lanreotide and octreotide have been acknowledged in several articles that review current management strategies for patients with NETs and carcinoid syndrome.

**Data to support the use of lanreotide in neuroendocrine tumors:**

This request to amend the NCCN NET guidelines to broaden the terminology to “somatostatin analogs” to reflect inclusion of lanreotide is based on several key studies that are briefly described in the accompanying synopsis.

#### **Excerpt from Supporting Literature:**

The following articles are submitted in support of the proposed changes (the full list of supporting articles is in the synopsis document). Of note, many articles refer to Somatuline Autogel. “Autogel” is the name used ex-US and it refers to the same formulation called “Depot” in the US.

Khan MS, El-Khouly F, Davies P, Toumpanakis C, Caplin ME. Long-term results of treatment of malignant carcinoid syndrome with prolonged release Lanreotide (Somatuline Autogel). *Aliment Pharmacol Ther*. 2011; 34(2):235-42.

O’Toole D, Ducreux M, Bommelaer G, et al. Treatment of carcinoid syndrome: a prospective crossover evaluation of lanreotide versus octreotide in terms of efficacy, patient acceptability, and tolerance. *Cancer*. 2000;88(4):770-6.

Ruszniewski P, Ish-Shalom S, Wymenga M, et al. Rapid and sustained relief from the symptoms of carcinoid syndrome: results from an open 6-month study of the 28-day prolonged-release formulation of lanreotide. *Neuroendocrinology*. 2004;80(4):244-51.

Tartaglia A, Vezzadini C, Bianchini S, Vezzadini P. Gastrinoma of the stomach: a case report. *Int J Gastrointest Cancer*. 2005; 35(3):211-6.

Tomassetti P. Treatment of type II gastric carcinoid tumors with somatostatin analogues. *N Engl J Med*. 2000; 343(8):551-4.

Wymenga AN, Eriksson B, Salmela PI, et al. Efficacy and safety of prolonged-release lanreotide in patients with gastrointestinal neuroendocrine tumors and hormone-related symptoms. *J Clin Oncol*. 1999;17(4):1111.

#### **Reviews**

Oberg K. Management of neuroendocrine tumours. 2004;15(Suppl 4); iv293-1v298.

Modlin IM, Pavel M, Kidd M, et al. Somatostatin analogues in the treatment of gastroenteropancreatic neuroendocrine (carcinoid) tumours. *Aliment Pharmacol Ther* 2009; 31:169-88.

We appreciate the opportunity to provide this additional information for consideration by the NCCN Neuroendocrine Tumors Panel. If you have any questions or require additional information, please do

not hesitate to contact me at 908-275-6042 or via e-mail at kathleen.lomax@Ipsen.com. Thank you for your time and consideration.

Sincerely,

Kathleen Graham Lomax, MD

Enclosures:

Table of proposed changes

Synopsis

References