RXADVANCE
2 Park Central Drive
Southborough, MA 01772

# NEW DRUG APPROVAL

| | |
|---|---|
| **Brand Name** | Detectnet™ |
| **Generic Name** | copper cu 64 dotatate |
| **Drug Manufacturer** | Curium US LLC |

## New Drug Approval

FDA Approval Date: September 3, 2020
Review Designation: Priority Orphan
Type of Review: Type 1 - New Molecular Entity
Dispensing Restrictions: None

## Place in Therapy

### DISEASE DESCRIPTION & EPIDEMIOLOGY

A neuroendocrine tumor (NET) is an uncommon cancer type that forms in neuroendocrine cells (Neuroendocrine tumors may also be called islet cell tumors, carcinoid cancer, or carcinoid tumors). NETs can occur almost anywhere in the body, but neuroendocrine tumors most commonly form in the gastrointestinal tract, lung, and pancreas. Neuroendocrine tumors form in neuroendocrine cell. Neuroendocrine cells can be found in many different organs. They carry messages from the nervous system to the endocrine system. In response to these messages, the endocrine system makes and releases hormones that control body functions like blood pressure, heart rate, digestion, breathing, and blood sugar. Some NETs release hormones, which can cause a lot of disruptive symptoms. When a NET produces hormones, it is called “functional.” neuroendocrine tumor. When a NET does not produce hormones, it is called “non-functional.”

Neuroendocrine tumors (NETs) arise from neuroendocrine cells in the endocrine and central nervous systems. NETs are responsible for approximately 0.5 % of all cancers. The incidence has gradually increased during the last three decades. The crude incidence is about 0.2/100,000. It increases with age and peaks between 50 and 70 years. Due to slowly growing nature of NETs, its prevalence is increasing. The prevalence has been estimated to be 35/100,000/year. Most NETs are diagnosed at advanced stages. The gastrointestinal tract is the most common location and is responsible for two-thirds of NETs. Most of them are diagnosed at the localized stage. However, NETs originating in the pancreas tend to be aggressive and about 60 % of these tumors are malignant at the time of diagnosis. The prognosis of NETs associates with their location, functional status, differentiation, and initial stages. The best survival rates are observed in patients with NETs arising in the rectum and appendix.

## Efficacy

The efficacy of Detectnet™ was established in two single-center, open-label studies. Study 1 prospectively evaluated a total of 63 subjects, including 42 patients with known or suspected NETs based on histology, conventional imaging, or clinical evaluations and 21 healthy volunteers. Of the 42 patients, 37 (88%) had a history of NETs at the time of Detectnet™ imaging. Among the total study population of 63 subjects, 28 (44%) were men and 35 (56%) were women with most subjects being white (86%). The mean age of the subjects was 54 years (range 25 to 82 years).

Detectnet™ images from each subject were interpreted as either positive or negative for NET by three independent readers who were blinded to clinical information and other imaging results. PET imaging results were compared to a composite reference standard consisting of a single oncologist’s blinded assessment of subject diagnosis based on available histopathology results, reports of conventional imaging (MRI, contrast CT, bone

scintigraphy, F 18 fludeoxyglucose PET/CT, F 18 sodium fluoride PET/CT, In 111 pentetreotide SPECT/CT, Ga 68 dotatate PET/CT) performed within 8 weeks prior to Detectnet™ imaging, and clinical and laboratory data including chromogranin A and serotonin levels. The proportion of subjects positive for disease per composite reference who were identified as positive by Detectnet™ imaging was used to quantify positive percent agreement. The proportion of subjects without disease per composite reference who were identified as negative by Detectnet™ imaging was used to quantify negative percent agreement.

## Safety

### ADVERSE EVENTS

Reported adverse reactions include nausea, vomiting, and flushing.

### WARNINGS & PRECAUTIONS

Radiation Risk: Ensure safe handling and preparation procedures to protect patients and health care workers from unintentional radiation exposure. Advise patients to hydrate before and after administration and to void frequently after administration.

Risk for Image Misinterpretation: Uptake of Detectnet™ can be seen in a variety of tumor types other than NETs, in other pathologic conditions, and as a normal physiologic variant (e.g., uncinate process of the pancreas).

### CONTRAINDICATIONS

N/A

## Clinical Pharmacology

### MECHANISMS OF ACTION

Copper Cu 64 dotatate binds to somatostatin receptors with highest affinity for subtype 2 receptors (SSTR2). It binds to cells that express somatostatin receptors including malignant neuroendocrine cells, which overexpress SSTR2 receptors. Copper Cu 64 is a positron (β+) emitting radionuclide with an emission yield that allows positron emission tomography (PET) imaging.

## Dose & Administration

### ADULTS

Recommended dose is 148 MBq (4 mCi) administered as an intravenous bolus injection.

### PEDIATRICS

The safety and effectiveness of Detectnet™ have not been established in pediatric patients.

### GERIATRICS

Clinical studies of Detectnet™ did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

### RENAL IMPAIRMENT

The effect of renal impairment on copper Cu 64 dotatate pharmacokinetics has not been studied.

# NEW DRUG APPROVAL

### HEPATIC IMPAIRMENT

The effect of hepatic impairment on copper Cu 64 dotatate pharmacokinetics has not been studied.

## Product Availability

### DOSAGE FORM(S) & STRENGTH(S)

Injection: 148 MBq (4 mCi) (37 MBq (1 mCi) per 1 mL) of copper Cu 64 dotatate in a single-dose vial.