

To estimate the **Potential Peak Sales** for cabozantinib (Cabometyx) in the indication of locally advanced or metastatic differentiated thyroid cancer (DTC) in the US, EU5 (France, Germany, Italy, Spain, UK), China, and Japan, as well as the **\$ value of a 1% share of treated patients** in these geographies, we need to make several assumptions and follow a structured approach. Since specific data such as exact patient numbers, pricing, or market penetration may not be publicly available in real-time, I will outline the methodology and use reasonable estimates based on available data and industry norms.

The indication is for adult and pediatric patients (12 years and older) with locally advanced or metastatic DTC that has progressed following prior VEGFR-targeted therapy and who are ineligible or refractory to radioactive iodine. This is a niche indication with a relatively small patient population, as DTC is less common than other cancers, and the subset of patients meeting these specific criteria is even smaller.

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## **Step 1: Estimate the Target Patient Population**

Differentiated thyroid cancer (DTC) accounts for the majority of thyroid cancer cases. However, only a small percentage of DTC patients progress to locally advanced or metastatic stages and fail prior VEGFR-targeted therapies while being ineligible for radioactive iodine. Below are rough estimates of the target population:

### **1. US:**

- Thyroid cancer incidence: ~44,000 new cases per year (American Cancer Society).
- DTC accounts for ~90% of cases: ~40,000 cases.
- Advanced/metastatic DTC: ~10-15% of DTC cases (~4,000-6,000 patients).
- Subset ineligible for radioactive iodine and failing VEGFR therapy: ~10-20% of advanced cases (~400-1,200 patients annually).
- Prevalent pool (considering multi-year treatment): ~1,000-3,000 patients.

### **2. EU5 (France, Germany, Italy, Spain, UK):**

- Combined population is roughly similar to the US (~330 million).
- Incidence and prevalence of thyroid cancer are comparable, adjusted for population.
- Target patient pool: ~1,000-3,000 patients (prevalent).

### **3. China:**

- Population: ~1.4 billion (4x US population).
- Thyroid cancer incidence is lower per capita due to differences in screening and risk factors, but total cases are higher.
- Target patient pool (prevalent): ~2,000-6,000 patients.

### **4. Japan:**

- Population: ~125 million (~1/3 of US).
- High screening rates, leading to higher thyroid cancer detection.
- Target patient pool (prevalent): ~500-1,500 patients.

#### **Total Target Patient Pool (Prevalent):**

- US: 1,000-3,000
- EU5: 1,000-3,000
- China: 2,000-6,000
- Japan: 500-1,500
- **Total:** ~4,500-13,500 patients.

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### **Step 2: Estimate the Share of Treated Patients**

The problem states a **20% to 30% share of treated patients** for cabozantinib. This means that of the eligible patients, 20-30% are assumed to be treated with cabozantinib due to factors like physician preference, reimbursement, competition, and patient access.

- **Low-end (20%):**  $0.2 * (4,500 \text{ to } 13,500) = 900 \text{ to } 2,700 \text{ patients treated.}$
- **High-end (30%):**  $0.3 * (4,500 \text{ to } 13,500) = 1,350 \text{ to } 4,050 \text{ patients treated.}$

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### **Step 3: Estimate Annual Cost of Treatment per Patient**

Cabozantinib (Cabometyx) is a high-cost targeted therapy. Pricing varies by region due to differences in healthcare systems and reimbursement structures:

- **US:** Annual cost ~\$150,000-\$200,000 per patient (based on pricing for other indications like renal cell carcinoma or hepatocellular carcinoma).
- **EU5:** Annual cost ~\$80,000-\$120,000 per patient (lower due to price negotiations and discounts).
- **China:** Annual cost ~\$30,000-\$50,000 per patient (lower pricing due to market access agreements and generics competition).
- **Japan:** Annual cost ~\$80,000-\$120,000 per patient (similar to EU5).

For simplicity, let's assume an average cost per patient:

- US: \$175,000
- EU5: \$100,000
- China: \$40,000
- Japan: \$100,000

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## **Step 4: Calculate Potential Peak Sales**

Peak sales are calculated as: **Number of treated patients \* Annual cost per patient**. We will distribute the patient pool proportionally based on the estimates above and calculate for the low-end (20% share) and high-end (30% share).

#### Low-End (20% Share)

- **US:**  $(1,000-3,000) * 0.2 = 200-600$  patients \* \$175,000 = **\$35M-\$105M**
- **EU5:**  $(1,000-3,000) * 0.2 = 200-600$  patients \* \$100,000 = **\$20M-\$60M**
- **China:**  $(2,000-6,000) * 0.2 = 400-1,200$  patients \* \$40,000 = **\$16M-\$48M**
- **Japan:**  $(500-1,500) * 0.2 = 100-300$  patients \* \$100,000 = **\$10M-\$30M**
- **Total Peak Sales (Low-End): \$81M-\$243M**

#### High-End (30% Share)

- **US:**  $(1,000-3,000) * 0.3 = 300-900$  patients \* \$175,000 = **\$52.5M-\$157.5M**
- **EU5:**  $(1,000-3,000) * 0.3 = 300-900$  patients \* \$100,000 = **\$30M-\$90M**
- **China:**  $(2,000-6,000) * 0.3 = 600-1,800$  patients \* \$40,000 = **\$24M-\$72M**
- **Japan:**  $(500-1,500) * 0.3 = 150-450$  patients \* \$100,000 = **\$15M-\$45M**
- **Total Peak Sales (High-End): \$121.5M-\$364.5M**

**Potential Peak Sales Range: \$81M to \$364.5M annually** across the US, EU5, China, and Japan, assuming a 20%-30% share of treated patients.

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## **Step 5: Calculate \$ Value of 1% Share of Treated Patients**

A 1% share of treated patients corresponds to 1% of the total target patient pool (4,500-13,500), i.e., **45-135 patients**.

- **US:**  $(1,000-3,000) * 0.01 = 10-30$  patients \* \$175,000 = **\$1.75M-\$5.25M**
- **EU5:**  $(1,000-3,000) * 0.01 = 10-30$  patients \* \$100,000 = **\$1M-\$3M**
- **China:**  $(2,000-6,000) * 0.01 = 20-60$  patients \* \$40,000 = **\$0.8M-\$2.4M**
- **Japan:**  $(500-1,500) * 0.01 = 5-15$  patients \* \$100,000 = **\$0.5M-\$1.5M**
- **Total \$ Value of 1% Share: \$4.05M-\$12.15M**

**\$ Value of 1% Share of Treated Patients: \$4M to \$12M annually** across the specified geographies.

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## **Summary of Results**

### **1. Potential Peak Sales for Cabozantinib (20%-30% Share):**

- US: \$35M-\$157.5M
- EU5: \$20M-\$90M
- China: \$16M-\$72M
- Japan: \$10M-\$45M
- **Total: \$81M to \$364.5M annually**

### **2. \$ Value of 1% Share of Treated Patients:**

- US: \$1.75M-\$5.25M
- EU5: \$1M-\$3M
- China: \$0.8M-\$2.4M
- Japan: \$0.5M-\$1.5M
- **Total: \$4M to \$12M annually**

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## **Caveats and Assumptions**

- **Patient Population:** The estimates for the target patient pool are based on rough percentages and may vary based on real-world data, regional differences in diagnosis, and treatment patterns.

- **Pricing:** Drug pricing is assumed based on typical costs for targeted therapies in oncology and may differ due to local negotiations, insurance coverage, or generics.

- **Market Share:** The 20%-30% share assumes competition from other therapies (e.g., other TKIs like lenvatinib or sorafenib) and barriers to access.

- **Treatment Duration:** Assumes patients are treated for one year on average; actual duration may vary based on progression-free survival or overall survival data for cabozantinib in this indication.

For more precise estimates, real-world data on patient numbers, market access, and competitive landscape would be required. However, this analysis provides a reasonable range based on available information and industry standards.