

To estimate the **Potential Peak Sales** for margetuximab-cmkb (MARGENZA) in the indication of metastatic HER2-positive breast cancer in the US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan, as well as the **\$ value of a 1% share of treated patients** in these geographies, we need to follow a structured approach. Since specific data such as exact patient numbers, pricing, or market penetration might not be fully available, I will outline the methodology and provide a reasonable estimate based on publicly available information and assumptions. If you have access to specific data (e.g., patient population numbers or pricing), I can refine the calculations.

## **Step 1: Key Assumptions and Methodology**

1. **Indication and Patient Population:** Margetuximab-cmkb is approved for metastatic HER2-positive breast cancer in patients who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease. This is a third-line or later treatment setting, so the eligible patient population is a subset of the total HER2-positive breast cancer population.
2. **Market Share:** The question assumes a 20% to 30% share of treated patients for margetuximab-cmkb in this indication.
3. **Geographies:** US, EU5 (combined), China, and Japan.
4. **Pricing:** Pricing for margetuximab-cmkb varies by region. In the US, the wholesale acquisition cost (WAC) for MARGENZA is approximately \$2,200 per 250 mg vial (as per initial launch data). Assuming a typical regimen (e.g., 15 mg/kg every 3 weeks), annual treatment cost per patient can be estimated at ~\$100,000–\$150,000 in the US. Pricing in other regions is typically lower due to healthcare system differences (e.g., 50–70% of US pricing in EU5 and Japan, and significantly lower in China).
5. **Peak Sales:** Peak sales are typically achieved 5–7 years post-launch after maximum market penetration, assuming no major competitors or patent expiry within that timeframe.
6. **Patient Population:** We will estimate the number of eligible patients based on breast cancer incidence, HER2-positive prevalence (~15–20% of breast cancer cases), and the proportion in metastatic, third-line or later settings (~10–15% of HER2-positive cases).

## **Step 2: Estimate Eligible Patient Population**

### **#### 1. US**

- Total breast cancer incidence: ~280,000 new cases/year (American Cancer Society).
- HER2-positive: ~15–20% → ~42,000–56,000 patients.
- Metastatic HER2-positive (third-line or later): ~10–15% of HER2-positive → ~4,200–8,400 patients.
- **Assumption:** ~6,000 eligible patients annually.

### **#### 2. EU5 (Combined)**

- Total breast cancer incidence: ~350,000 new cases/year (ECIS - European Cancer Information System).
- HER2-positive: ~15–20% → ~52,500–70,000 patients.
- Metastatic HER2-positive (third-line or later): ~10–15% → ~5,250–10,500 patients.
- **Assumption:** ~7,500 eligible patients annually.

#### #### 3. China

- Total breast cancer incidence: ~420,000 new cases/year (Global Cancer Observatory).
- HER2-positive: ~15–20% → ~63,000–84,000 patients.
- Metastatic HER2-positive (third-line or later): ~10–15% → ~6,300–12,600 patients.
- **Assumption:** ~9,000 eligible patients annually (access to third-line therapies may be limited compared to US/EU).

#### #### 4. Japan

- Total breast cancer incidence: ~90,000 new cases/year (Global Cancer Observatory).
- HER2-positive: ~15–20% → ~13,500–18,000 patients.
- Metastatic HER2-positive (third-line or later): ~10–15% → ~1,350–2,700 patients.
- **Assumption:** ~2,000 eligible patients annually.

#### #### Total Eligible Patients Across Geographies

- US: 6,000
- EU5: 7,500
- China: 9,000
- Japan: 2,000
- **Total:** 24,500 patients annually.

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

- **US:** ~\$100,000–\$150,000 per patient/year (based on WAC and typical regimen).
- Assumption: \$125,000.
- **EU5:** ~60–70% of US pricing due to negotiated discounts.
- Assumption: \$80,000.
- **Japan:** Similar to EU5, ~\$80,000.
- **China:** Significantly lower due to pricing controls and generics/biosimilars competition.
- Assumption: \$30,000.

### **Step 4: Calculate Potential Peak Sales (20%–30% Market Share)**

#### #### 1. US

- Eligible patients: 6,000
- Market share: 20% = 1,200 patients; 30% = 1,800 patients
- Annual cost: \$125,000
- Peak Sales:

- 20% =  $1,200 \times \$125,000 = \$150 \text{ million}$

- 30% =  $1,800 \times \$125,000 = \$225 \text{ million}$

#### #### 2. EU5

- Eligible patients: 7,500

- Market share: 20% = 1,500 patients; 30% = 2,250 patients

- Annual cost: \$80,000

- Peak Sales:

- 20% =  $1,500 \times \$80,000 = \$120 \text{ million}$

- 30% =  $2,250 \times \$80,000 = \$180 \text{ million}$

#### #### 3. China

- Eligible patients: 9,000

- Market share: 20% = 1,800 patients; 30% = 2,700 patients

- Annual cost: \$30,000

- Peak Sales:

- 20% =  $1,800 \times \$30,000 = \$54 \text{ million}$

- 30% =  $2,700 \times \$30,000 = \$81 \text{ million}$

#### #### 4. Japan

- Eligible patients: 2,000

- Market share: 20% = 400 patients; 30% = 600 patients

- Annual cost: \$80,000

- Peak Sales:

- 20% =  $400 \times \$80,000 = \$32 \text{ million}$

- 30% =  $600 \times \$80,000 = \$48 \text{ million}$

#### #### Total Potential Peak Sales Across Geographies

- **20% Market Share:** \$150M (US) + \$120M (EU5) + \$54M (China) + \$32M (Japan) = **\$356 million**

- **30% Market Share:** \$225M (US) + \$180M (EU5) + \$81M (China) + \$48M (Japan) = **\$534 million**

**Potential Peak Sales Range: \$356 million to \$534 million annually.**

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

1% of treated patients corresponds to 1% of the eligible patient population treated with margetuximab-cmkb in each geography.

#### #### 1. US

- Eligible patients: 6,000
- 1% = 60 patients
- Annual cost: \$125,000
- Value of 1% share:  $60 \times \$125,000 = \$7.5 \text{ million}$

#### #### 2. EU5

- Eligible patients: 7,500
- 1% = 75 patients
- Annual cost: \$80,000
- Value of 1% share:  $75 \times \$80,000 = \$6.0 \text{ million}$

#### #### 3. China

- Eligible patients: 9,000
- 1% = 90 patients
- Annual cost: \$30,000
- Value of 1% share:  $90 \times \$30,000 = \$2.7 \text{ million}$

#### #### 4. Japan

- Eligible patients: 2,000
- 1% = 20 patients
- Annual cost: \$80,000
- Value of 1% share:  $20 \times \$80,000 = \$1.6 \text{ million}$

#### #### Total Value of 1% Share Across Geographies

- US: \$7.5M
- EU5: \$6.0M
- China: \$2.7M
- Japan: \$1.6M
- **Total: \$17.8 million**

### **Final Answer**

1. **Potential Peak Sales for margetuximab-cmkb** (assuming 20%–30% market share):

- **US:** \$150M–\$225M
- **EU5:** \$120M–\$180M

- **China:** \$54M–\$81M
- **Japan:** \$32M–\$48M
- **Total: \$356M–\$534M annually**

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

- **US:** \$7.5M
- **EU5:** \$6.0M
- **China:** \$2.7M
- **Japan:** \$1.6M
- **Total: \$17.8M**

## **Notes and Caveats**

- These estimates are based on assumptions for patient populations, pricing, and market penetration. Real-world data may vary due to competition (e.g., trastuzumab, pertuzumab, T-DM1, and other biosimilars), reimbursement policies, and access to treatment (especially in China).
- Peak sales could be influenced by clinical trial outcomes, label expansions, or adverse events.
- If you have access to more specific data (e.g., exact patient numbers or regional pricing), I can adjust the calculations accordingly.