

To estimate the **Potential Peak Sales** for the drug **HEPZATO KIT** in the indication of uveal melanoma with unresectable hepatic metastases in the US, EU5 (Germany, France, Italy, Spain, and the 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 based on available data and reasonable assumptions. Since specific market data for HEPZATO KIT may not be publicly available, this analysis will rely on epidemiology data, pricing assumptions, and market penetration rates.

Step 1: Define the Target Population

Uveal melanoma is a rare cancer, and hepatic metastases occur in approximately 50% of patients with uveal melanoma. The indication for HEPZATO KIT specifies patients with unresectable hepatic metastases affecting less than 50% of the liver and limited or no extrahepatic disease. This further narrows the target population.

Incidence and Prevalence of Uveal Melanoma

- **US:** Incidence is ~5-6 per million annually (~1,500-2,000 new cases/year). About 50% develop hepatic metastases, so ~750-1,000 patients/year. Assuming ~30-40% meet the specific criteria for HEPZATO KIT (unresectable, limited liver involvement, limited extrahepatic disease), the eligible population is ~225-400 patients/year.
- **EU5:** Incidence is similar to the US (~5-6 per million). With a combined population of ~330 million, this translates to ~1,650-2,000 new cases/year. Hepatic metastases in 50% (~825-1,000), and ~30-40% eligible for HEPZATO KIT, results in ~250-400 patients/year.
- **China:** Incidence is lower in Asia (~1-2 per million). With a population of ~1.4 billion, this is ~1,400-2,800 new cases/year. Hepatic metastases in 50% (~700-1,400), and ~30-40% eligible, results in ~210-560 patients/year.
- **Japan:** Incidence is ~1-2 per million. With a population of ~125 million, this is ~125-250 new cases/year. Hepatic metastases in 50% (~60-125), and ~30-40% eligible, results in ~18-50 patients/year.

Since uveal melanoma is a chronic condition with a survival of 6-12 months for metastatic cases without treatment (and potentially longer with treatment), we will assume the **prevalent population** (patients eligible for treatment at any given time) is roughly 1.5-2x the annual incidence due to patients surviving into subsequent years.

Prevalent Eligible Population (Annual Treatable Patients)

- **US:** ~350-800 patients
- **EU5:** ~400-800 patients
- **China:** ~300-1,100 patients
- **Japan:** ~30-100 patients

Total Eligible Population Across Geographies: ~1,080-2,800 patients/year.

Step 2: Market Penetration (20%-30% Share of Treated Patients)

Assuming HEPZATO KIT achieves a market penetration of 20%-30% of eligible treated patients, the number of patients treated annually with HEPZATO KIT is:

- **US:** 20%-30% of 350-800 = ~70-240 patients
- **EU5:** 20%-30% of 400-800 = ~80-240 patients
- **China:** 20%-30% of 300-1,100 = ~60-330 patients
- **Japan:** 20%-30% of 30-100 = ~6-30 patients

Total Treated Patients Across Geographies: ~216-840 patients/year.

Step 3: Pricing Assumptions for HEPZATO KIT

HEPZATO KIT is a liver-directed therapy involving melphalan and a hepatic delivery system, positioning it as a high-cost specialty drug. Pricing for such therapies (e.g., orphan drugs or targeted oncology treatments) can vary significantly by region:

- **US:** Specialty oncology drugs for rare diseases often cost \$100,000-\$200,000 per treatment course. Assuming HEPZATO KIT requires multiple administrations or a single high-cost procedure, we estimate ~\$150,000 per patient per year.
- **EU5:** Pricing is typically 30%-50% lower than the US due to healthcare system negotiations. Assume ~\$75,000-\$100,000 per patient per year (average ~\$87,500).
- **China:** Pricing is significantly lower due to cost controls and local manufacturing or generics. Assume ~\$30,000-\$50,000 per patient per year (average ~\$40,000).
- **Japan:** Pricing is often aligned with the US or slightly lower. Assume ~\$100,000-\$120,000 per patient per year (average ~\$110,000).

Step 4: Calculate Potential Peak Sales

Peak sales are calculated as the number of treated patients multiplied by the annual cost per patient in each geography.

Peak Sales at 20% Market Penetration (Lower End)

- **US:** 70 patients x \$150,000 = **\$10.5 million**
- **EU5:** 80 patients x \$87,500 = **\$7.0 million**
- **China:** 60 patients x \$40,000 = **\$2.4 million**
- **Japan:** 6 patients x \$110,000 = **\$0.66 million**
- **Total Peak Sales (20%):** **\$20.56 million**

Peak Sales at 30% Market Penetration (Higher End)

- **US:** 240 patients x \$150,000 = **\$36.0 million**
- **EU5:** 240 patients x \$87,500 = **\$21.0 million**
- **China:** 330 patients x \$40,000 = **\$13.2 million**
- **Japan:** 30 patients x \$110,000 = **\$3.3 million**
- **Total Peak Sales (30%):** **\$73.5 million**

Range of Potential Peak Sales: \$20.6 million to \$73.5 million annually across the US, EU5, China, and Japan.

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

A 1% share of treated patients corresponds to 1% of the eligible population being treated with HEPZATO KIT. Using the midpoint of the eligible population for simplicity:

- **US:** 1% of 575 patients (midpoint of 350-800) = 5.75 patients x \$150,000 = **\$0.86 million**
- **EU5:** 1% of 600 patients (midpoint of 400-800) = 6 patients x \$87,500 = **\$0.53 million**
- **China:** 1% of 700 patients (midpoint of 300-1,100) = 7 patients x \$40,000 = **\$0.28 million**
- **Japan:** 1% of 65 patients (midpoint of 30-100) = 0.65 patients x \$110,000 = **\$0.07 million**
- **Total Value of 1% Share:** **\$1.74 million**

Final Answer

- **Potential Peak Sales for HEPZATO KIT** (assuming 20%-30% market penetration) in the US, EU5, China, and Japan: **\$20.6 million to \$73.5 million annually.**

- **\$ Value of 1% Share of Treated Patients** in these geographies: **\$1.74 million annually.**

Caveats and Assumptions

1. The eligible patient population is estimated based on limited data for uveal melanoma with hepatic metastases and specific criteria for HEPZATO KIT.
2. Pricing assumptions are based on comparable specialty oncology drugs and may vary based on reimbursement, competition, and market access.
3. Market penetration rates (20%-30%) are assumed based on the rarity of the disease and the specialized nature of the treatment. Actual penetration could be higher or lower depending on clinical outcomes, competition, and payer acceptance.
4. Peak sales assume steady-state market share and do not account for market entry delays, patent cliffs, or changes in treatment paradigms.

If more specific data on pricing, patient numbers, or market dynamics for HEPZATO KIT becomes available, these estimates can be refined.