

To estimate the **Potential Peak Sales** for pembrolizumab (Keytruda) in the indication of locally advanced or metastatic urothelial carcinoma (in combination with enfortumab vedotin) for patients ineligible for cisplatin-containing chemotherapy in the US, EU5 (France, Germany, Italy, Spain, UK), China, and Japan, as well as the **\$ value of a 1% share of treated patients**, we need to follow a structured approach. Since specific data such as exact patient numbers, pricing, and market penetration may not be publicly available in real-time, I will provide a framework based on reasonable assumptions and publicly available information up to October 2023. You can refine these numbers with more precise data if available.

Step 1: Define the Indication and Patient Population

- **Indication:** Locally advanced or metastatic urothelial carcinoma (mUC) in patients ineligible for cisplatin-containing chemotherapy, treated with pembrolizumab in combination with enfortumab vedotin.

- **Target Population:** Patients with mUC who cannot receive cisplatin due to comorbidities (e.g., renal impairment, hearing loss, or poor performance status). Literature suggests that approximately 40-50% of mUC patients are ineligible for cisplatin.

Step 2: Estimate the Eligible Patient Population

Using epidemiology data and cancer statistics, we can estimate the number of patients with mUC in the specified geographies. Below are approximate incidence rates for urothelial carcinoma (primarily bladder cancer, which accounts for most cases) and the proportion of advanced/metastatic cases.

- **US:** Bladder cancer incidence is ~80,000 new cases/year (American Cancer Society). About 15-20% are advanced/metastatic at diagnosis or progress to this stage (~12,000-16,000 patients). Of these, ~40-50% are cisplatin-ineligible (~5,000-8,000 patients).

- **EU5:** Incidence is ~150,000 new cases/year (European Cancer Information System). Advanced/metastatic cases are ~20-25% (~30,000-37,500 patients). Cisplatin-ineligible are ~40-50% (~12,000-18,750 patients).

- **China:** Incidence is ~80,000-100,000 new cases/year (Global Cancer Observatory). Advanced/metastatic cases are ~20-25% (~16,000-25,000 patients). Cisplatin-ineligible are ~40-50% (~6,400-12,500 patients).

- **Japan:** Incidence is ~20,000-25,000 new cases/year (Global Cancer Observatory). Advanced/metastatic cases are ~15-20% (~3,000-5,000 patients). Cisplatin-ineligible are ~40-50% (~1,200-2,500 patients).

Total Estimated Cisplatin-Ineligible mUC Patients (midpoint):

- US: ~6,500 patients

- EU5: ~15,375 patients

- China: ~9,450 patients

- Japan: ~1,850 patients

- **Total across geographies:** ~33,175 patients

Step 3: Assume Market Share for Pembrolizumab

The problem states a 20-30% share of treated patients for pembrolizumab in this indication. This accounts for competition from other therapies (e.g., other immune checkpoint inhibitors, chemotherapy regimens, or emerging treatments). Using the midpoint of 25% market share for calculations:

- Treated Patients with Pembrolizumab:

- US: $6,500 * 25\% = 1,625$ patients
- EU5: $15,375 * 25\% = 3,844$ patients
- China: $9,450 * 25\% = 2,363$ patients
- Japan: $1,850 * 25\% = 463$ patients
- **Total:** ~8,295 patients

Step 4: Estimate Annual Treatment Cost for Pembrolizumab

Pembrolizumab pricing varies by region due to differences in healthcare systems, negotiations, and discounts. Approximate annual costs per patient (based on standard dosing of 200 mg every 3 weeks or 400 mg every 6 weeks, roughly 17-18 cycles/year) are:

- **US:** ~\$150,000-\$180,000/year (list price before discounts).
- **EU5:** ~\$80,000-\$120,000/year (varies by country due to negotiated pricing).
- **China:** ~\$50,000-\$70,000/year (lower due to pricing controls and inclusion in National Reimbursement Drug List with discounts).
- **Japan:** ~\$100,000-\$130,000/year (based on reimbursed pricing).

Using midpoint estimates for simplicity:

- US: \$165,000/year
- EU5: \$100,000/year
- China: \$60,000/year
- Japan: \$115,000/year

Step 5: Calculate Potential Peak Sales

Peak Sales = Number of Treated Patients * Annual Cost per Patient

- **US:** 1,625 patients * \$165,000 = **\$268.1 million**
- **EU5:** 3,844 patients * \$100,000 = **\$384.4 million**
- **China:** 2,363 patients * \$60,000 = **\$141.8 million**
- **Japan:** 463 patients * \$115,000 = **\$53.2 million**
- **Total Potential Peak Sales:** **\$847.5 million**

This assumes 25% market share. For the range of 20-30%:

- At 20%: ~\$678 million
- At 30%: ~\$1,017 million

Step 6: Calculate \$ Value of 1% Share of Treated Patients

1% Share of Treated Patients = Total Eligible Patients * 1% * Annual Cost per Patient

- **US:** $6,500 * 1\% * \$165,000 = \10.7 million
- **EU5:** $15,375 * 1\% * \$100,000 = \15.4 million
- **China:** $9,450 * 1\% * \$60,000 = \5.7 million
- **Japan:** $1,850 * 1\% * \$115,000 = \2.1 million
- **Total Value of 1% Share:** **\$33.9 million**

Final Answer

- **Potential Peak Sales for Pembrolizumab** (at 20-30% market share):
- US: \$214.5M - \$321.8M
- EU5: \$307.5M - \$461.3M
- China: \$113.4M - \$170.1M
- Japan: \$42.6M - \$63.8M
- **Total: \$678M - \$1,017M** (midpoint ~\$847.5M at 25%)
- **\$ Value of 1% Share of Treated Patients:**
- US: \$10.7M
- EU5: \$15.4M
- China: \$5.7M
- Japan: \$2.1M
- **Total: \$33.9M**

Notes and Caveats

1. These estimates are based on approximations of patient populations, pricing, and market share. Real-world data may differ due to evolving treatment landscapes, payer negotiations, and access barriers.
2. Peak sales assume steady-state market penetration and do not account for patent cliffs or biosimilar competition.
3. Pricing in China and EU5 can vary significantly due to local reimbursement policies and discounts.
4. The combination therapy (with enfortumab vedotin) may influence market dynamics, as costs and access for the combination will impact adoption.

If you have access to more specific data (e.g., exact patient numbers, real-world pricing, or market research reports), these calculations can be refined further.