

To estimate the **Potential Peak Sales** for pembrolizumab (Keytruda) in the indication of BCG-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) 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. This involves estimating the eligible patient population, treatment penetration rates, pricing, and market dynamics. Since exact data may not be publicly available, I will use reasonable assumptions based on epidemiology, market research, and available information about pembrolizumab and NMIBC.

Step 1: Define the Target Population

- **Indication:** BCG-unresponsive, high-risk NMIBC with CIS (with or without papillary tumors) who are ineligible for or elect not to undergo cystectomy.
- NMIBC accounts for ~75% of all bladder cancer cases, and high-risk NMIBC with CIS represents a subset of this population. BCG-unresponsive patients are a further subset, typically ~30-40% of high-risk patients who fail BCG therapy.
- Patients ineligible for or refusing cystectomy are a smaller group within this subset, as cystectomy (bladder removal) is a standard option for BCG-unresponsive cases.

Epidemiology of Bladder Cancer (Annual Incidence Estimates):

- **US:** ~80,000 new cases/year. NMIBC is ~75% (~60,000), high-risk NMIBC ~30% of NMIBC (~18,000), BCG-unresponsive ~30-40% (~5,400-7,200), and ineligible/refusing cystectomy ~50% of these (~2,700-3,600).
- **EU5:** ~120,000 new cases/year. NMIBC ~75% (~90,000), high-risk ~30% (~27,000), BCG-unresponsive ~30-40% (~8,100-10,800), ineligible/refusing cystectomy ~50% (~4,050-5,400).
- **China:** ~80,000 new cases/year. NMIBC ~75% (~60,000), high-risk ~30% (~18,000), BCG-unresponsive ~30-40% (~5,400-7,200), ineligible/refusing cystectomy ~50% (~2,700-3,600). (Note: Access to BCG therapy may be lower in China, potentially reducing the eligible population.)
- **Japan:** ~20,000 new cases/year. NMIBC ~75% (~15,000), high-risk ~30% (~4,500), BCG-unresponsive ~30-40% (~1,350-1,800), ineligible/refusing cystectomy ~50% (~675-900).

Total Eligible Patients (Midpoint Estimates):

- US: ~3,150
- EU5: ~4,725
- China: ~3,150
- Japan: ~788
- **Total across geographies:** ~11,813 patients/year.

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

- Pembrolizumab is a novel therapy for BCG-unresponsive NMIBC, approved by the FDA in January 2020 for this indication. Given the unmet need (limited options beyond cystectomy), a penetration rate of 20%-30% among eligible patients is reasonable during peak sales (likely 5-7 years post-launch, assuming no major competitors or patent cliffs).
- **Assumed penetration rate:** 25% (midpoint of 20%-30%).

Treated Patients at Peak (25% Penetration):

- US: $3,150 * 25\% = \sim 788$ patients/year
- EU5: $4,725 * 25\% = \sim 1,181$ patients/year
- China: $3,150 * 25\% = \sim 788$ patients/year
- Japan: $788 * 25\% = \sim 197$ patients/year
- **Total treated patients:** $\sim 2,954$ patients/year.

Step 3: Pricing of Pembrolizumab

- Pembrolizumab is a high-cost immunotherapy (PD-1 inhibitor). Pricing varies by region due to healthcare systems, reimbursement policies, and negotiations.
- **Annual Cost Estimates** (based on publicly available data for Keytruda in other indications, e.g., NSCLC or melanoma):
 - US: $\sim \$150,000$ /year per patient (list price before discounts).
 - EU5: $\sim \$100,000$ /year per patient (lower due to negotiations and universal healthcare systems).
 - China: $\sim \$50,000$ /year per patient (significant price reductions due to National Reimbursement Drug List negotiations and local competition).
 - Japan: $\sim \$120,000$ /year per patient (slightly lower than the US due to price controls).
- For NMIBC, treatment duration may differ (e.g., until disease progression or unacceptable toxicity), but for simplicity, assume a full year of treatment at peak.

Step 4: Calculate Potential Peak Sales**Peak Sales = Treated Patients * Annual Cost per Patient**

- US: $788 \text{ patients} * \$150,000 = \text{\$118.2 million}$
- EU5: $1,181 \text{ patients} * \$100,000 = \text{\$118.1 million}$
- China: $788 \text{ patients} * \$50,000 = \text{\$39.4 million}$
- Japan: $197 \text{ patients} * \$120,000 = \text{\$23.6 million}$
- **Total Peak Sales across geographies:** $\text{\$299.3 million/year}$

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

- First, calculate the total eligible patients and the value per patient (based on pricing).
- 1% of treated patients corresponds to 1% of the total eligible population being treated (since penetration rate is applied uniformly).

Eligible Patients (Total): 11,813

- 1% of eligible patients = 118.13 patients

Value of 1% Share (based on regional pricing):

- US: $(3,150/11,813) * 118.13 \text{ patients} * \$150,000 = \sim \$4.73 \text{ million}$
- EU5: $(4,725/11,813) * 118.13 \text{ patients} * \$100,000 = \sim \$4.73 \text{ million}$
- China: $(3,150/11,813) * 118.13 \text{ patients} * \$50,000 = \sim \$1.58 \text{ million}$
- Japan: $(788/11,813) * 118.13 \text{ patients} * \$120,000 = \sim \$0.95 \text{ million}$
- **Total \$ Value of 1% Share: \$11.99 million**

Alternatively, since peak sales are \$299.3 million at 25% penetration:

- 1% penetration (1/25th of 25%) of peak sales = $\$299.3 \text{ million} / 25 = \mathbf{\$11.97 \text{ million}}$ (matches closely with the above calculation).

Final Answers**1. Potential Peak Sales for Pembrolizumab in BCG-unresponsive NMIBC (CIS) at 20%-30% Penetration (using 25%):**

- US: \$118.2 million
- EU5: \$118.1 million
- China: \$39.4 million
- Japan: \$23.6 million
- **Total: \$299.3 million/year**

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

- US: \$4.73 million
- EU5: \$4.73 million
- China: \$1.58 million
- Japan: \$0.95 million
- **Total: \$11.97 million/year**

Caveats and Assumptions

- **Epidemiology:** Patient numbers are estimates based on general bladder cancer incidence and proportions for NMIBC, high-risk, BCG-unresponsive, and cystectomy ineligibility. Actual numbers may vary.

- **Penetration Rate:** 25% is an assumption; competition (e.g., other immunotherapies or intravesical therapies) or access barriers could impact this.

- **Pricing:** Costs are approximations and may differ based on discounts, reimbursement, or indication-specific pricing. Treatment duration in NMIBC may also be shorter or longer than assumed.

- **Market Dynamics:** Peak sales timing and uptake rates may differ by region due to regulatory approvals, reimbursement timelines, and healthcare system differences (e.g., slower adoption in

China).

If you have access to more specific data (e.g., exact patient numbers, pricing, or penetration forecasts), these calculations can be refined further.