

To estimate the **Potential Peak Sales** for pembrolizumab (KEYTRUDA) in the indication of unresectable or metastatic tumor mutational burden-high (TMB-H) solid tumors (≥ 10 mutations/megabase) 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 making reasonable assumptions based on available data about the patient population, treatment rates, market share, pricing, and other factors. Since specific data for this exact indication and geographies might not be publicly available in real-time, I will outline the methodology and provide illustrative calculations based on general oncology market data and assumptions.

****Step 1: Define the Indication and Patient Population****

- **Indication:** Pembrolizumab is approved for TMB-H (≥ 10 mut/Mb) solid tumors in patients with unresectable or metastatic disease who have progressed following prior treatment and have no satisfactory alternative options.

- **Patient Population:** TMB-H solid tumors are a subset of advanced solid tumors. Studies suggest that approximately 5-10% of advanced solid tumors across various cancer types have TMB-H (≥ 10 mut/Mb). The most common cancers with TMB-H include non-small cell lung cancer (NSCLC), melanoma, and bladder cancer, among others.

- **Geographies:** US, EU5, China, Japan.

Estimated Incidence of Advanced Solid Tumors and TMB-H Subset

- **US:** Annual incidence of advanced/metastatic solid tumors is ~500,000 patients. Assuming 5-10% are TMB-H, this translates to **25,000-50,000 eligible patients**.

- **EU5:** Annual incidence of advanced solid tumors is ~400,000. Assuming 5-10% are TMB-H, this translates to **20,000-40,000 eligible patients**.

- **China:** Annual incidence of advanced solid tumors is ~1,000,000 (due to larger population and higher cancer incidence). Assuming 5-10% are TMB-H, this translates to **50,000-100,000 eligible patients**.

- **Japan:** Annual incidence of advanced solid tumors is ~150,000. Assuming 5-10% are TMB-H, this translates to **7,500-15,000 eligible patients**.

Total eligible TMB-H patients across geographies: **102,500-205,000 patients annually**.

Treatment Rate

Not all eligible patients will receive treatment due to factors like access to testing, reimbursement, or clinical ineligibility. Assuming a **treatment rate of 50-70%**, the treated patient population is:

- US: 12,500-35,000

- EU5: 10,000-28,000

- China: 25,000-70,000

- Japan: 3,750-10,500

- Total: **51,250-143,500 treated patients annually**.

****Step 2: Market Share Assumption****

The query assumes a **20-30% share of treated patients** for pembrolizumab in this indication. This is reasonable given that pembrolizumab (KEYTRUDA) is a leading PD-1 inhibitor, but it faces competition from other immunotherapies (e.g., nivolumab) and emerging therapies. Applying this share:

- Total treated patients with pembrolizumab: **10,250-43,050 patients annually** (20-30% of 51,250-143,500).

Breakdown by Geography (Midpoint of Ranges for Simplicity)

Using midpoint of treated patients and 25% market share for simplicity:

- US: 23,750 treated patients x 25% = **5,938 patients**.
- EU5: 19,000 treated patients x 25% = **4,750 patients**.
- China: 47,500 treated patients x 25% = **11,875 patients**.
- Japan: 7,125 treated patients x 25% = **1,781 patients**.
- Total: **24,344 patients annually**.

****Step 3: Pricing of Pembrolizumab****

Pembrolizumab pricing varies by geography due to differences in healthcare systems, reimbursement, and market access. Average annual cost per patient (based on typical dosing for advanced cancer, often 200 mg every 3 weeks) is approximated as follows (in USD):

- US: ~\$150,000 per patient per year.
- EU5: ~\$100,000 per patient per year (lower due to negotiated pricing).
- China: ~\$50,000 per patient per year (lower due to pricing controls and generics/biosimilars).
- Japan: ~\$120,000 per patient per year (similar to EU but with some premium pricing).

Duration of Treatment

Patients with advanced solid tumors on pembrolizumab typically receive treatment for **6-12 months** on average (due to progression, toxicity, or other factors). For simplicity, assume an average of **9 months of treatment**, or 75% of the annual cost.

Adjusted cost per patient:

- US: \$150,000 x 0.75 = **\$112,500**.
- EU5: \$100,000 x 0.75 = **\$75,000**.
- China: \$50,000 x 0.75 = **\$37,500**.
- Japan: \$120,000 x 0.75 = **\$90,000**.

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

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

- **US:** 5,938 patients x \$112,500 = **\$668 million**.
- **EU5:** 4,750 patients x \$75,000 = **\$356 million**.
- **China:** 11,875 patients x \$37,500 = **\$445 million**.
- **Japan:** 1,781 patients x \$90,000 = **\$160 million**.
- **Total Peak Sales:** \$668M + \$356M + \$445M + \$160M = **\$1,629 million (~\$1.63 billion)**.

Using the range of market share (20-30%) and patient estimates, peak sales could range from **\$1.3 billion to \$2.0 billion annually** across these geographies.

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

First, calculate the total number of treated patients (midpoint for simplicity): 97,375 (sum of midpoints: 23,750 US + 19,000 EU5 + 47,500 China + 7,125 Japan).

- 1% of treated patients = 974 patients.

Now calculate revenue per 1% share by geography:

- **US:** 1% of 23,750 = 238 patients x \$112,500 = **\$26.8 million**.
- **EU5:** 1% of 19,000 = 190 patients x \$75,000 = **\$14.3 million**.
- **China:** 1% of 47,500 = 475 patients x \$37,500 = **\$17.8 million**.
- **Japan:** 1% of 7,125 = 71 patients x \$90,000 = **\$6.4 million**.
- **Total \$ Value of 1% Share:** \$26.8M + \$14.3M + \$17.8M + \$6.4M = **\$65.3 million**.

****Final Answer****

- **Potential Peak Sales for Pembrolizumab in TMB-H Solid Tumors (20-30% Market Share):**

- US: \$535M - \$802M (average ~\$668M)
- EU5: \$285M - \$427M (average ~\$356M)
- China: \$356M - \$534M (average ~\$445M)
- Japan: \$128M - \$192M (average ~\$160M)
- **Total: \$1.3 billion - \$2.0 billion annually** (average ~\$1.63 billion).

- **\$ Value of 1% Share of Treated Patients:**

- US: \$26.8 million
- EU5: \$14.3 million
- China: \$17.8 million
- Japan: \$6.4 million
- **Total: \$65.3 million.**

****Caveats and Assumptions****

1. **Patient Population:** Estimates of TMB-H prevalence and treatment rates are based on general oncology data and may vary by specific tumor type or testing adoption.
2. **Pricing:** Drug pricing is approximate and subject to change based on reimbursement policies, discounts, and market dynamics.
3. **Market Share:** Assumes 20-30% share, but actual share could vary based on competition, clinical data, and payer policies.
4. **Treatment Duration:** Assumes 9 months of therapy; actual duration may differ based on real-world evidence.

For more precise figures, access to proprietary market research (e.g., IQVIA, EvaluatePharma) or real-world data on TMB-H testing and treatment patterns would be required.