

יולי 2025

רופא/ה יקר/ה
רוקח/ת יקר/ה,

הנדון: **KEYTRUDA® 100 mg/4 mL**
קיטרודה 100 מ"ג/4 מ"ל

Dosage form and Composition:
Pembrolizumab 100 mg/4 ml; Concentrate for Solution for Intravenous Infusion

חברת מרק שארפ ודוהם (ישראל-1996) בע"מ, (MSD ישראל), מבקשת ליידע על עדכון העלון לרופא של התכשיר
Keytruda 100mg/4ml עפ"י המפורט מטה.

(טקסט שהוסף לעלון לרופא מודגש בקו תחתון, טקסט שנמחק מהעלון לרופא מסומן בקו חוצה)

עדכונים שבוצעו בעלון לרופא:

6 ADVERSE REACTIONS

[...]

6.1 Clinical Trials Experience

[...]

Gastric Cancer

First-line Treatment of Locally Advanced Unresectable or Metastatic HER2-Positive Gastric or Gastroesophageal Junction Adenocarcinoma

The safety of KEYTRUDA was evaluated in 696433 patients with HER2-positive gastric or GEJ cancer enrolled in KEYNOTE-811, which included 247 350 patients treated with KEYTRUDA 200 mg, trastuzumab, and CAPOX (n=489297) or FP (n=2853) every 3 weeks, compared to 216 346 patients-treated with placebo, trastuzumab, and CAPOX (n=487298) or FP (n=2948) every 3 weeks [see *Clinical Studies (14.9)*].

The median duration of exposure to KEYTRUDA was 5.89.2 months (range: 1 day to 47.733.6 months).

The study population characteristics were: median age of 63 years (range: 19 to 84), 43% age 65 or older; 81% male; 58% White, 35% Asian, and 0.9% Black; 44% ECOG PS of 0 and 56% ECOG PS of 1. **Fatal adverse reactions occurred in 3 patients who received KEYTRUDA in combination with trastuzumab and CAPOX or FP and included pneumonitis in 2 patients and hepatitis in 1 patient.**

KEYTRUDA and placebo were/was discontinued due to adverse reactions in 6.13% of patients in each arm. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA in ≥1% of patients were was pneumonitis (4.42.0%) and **pneumonia (1.1%)**.

Adverse reactions leading to interruption of KEYTRUDA occurred in 58.71% of patients; the most common adverse reactions or laboratory abnormalities leading to interruption of KEYTRUDA (≥2%) were neutropenia (48.21%), thrombocytopenia (42.13%), diarrhea (6.7%), pneumonia (5%), anemia (3.74.9%), **COVID-19 (3.1%)**, hypokalemia (3.71%), fatigue/asthenia (3.24.9%), decreased appetite (3.24%), increased AST (2.83.7%), increased blood bilirubin (2.84.6%), pneumonia (2.8%), increased ALT (2.39%), and vomiting (2.36%), **pneumonitis (2.3%), pyrexia (2.3%), increased blood creatinine (2%), and colitis (2%)**.

In the KEYTRUDA arm versus placebo, there was a difference of ≥5% incidence between patients treated with KEYTRUDA versus standard of care for diarrhea (53% vs 44-47%), **rash (35% vs. 28%), hypothyroidism (11% vs. 5%), and pneumonia (11% vs. 5%)** and nausea (49% vs 44%). There were no clinically meaningful differences in incidence of Grade 3-4 toxicity between arms.

There was a difference of ≥5% incidence between patients treated with KEYTRUDA versus standard of care for **decreased leukocytes (60% vs. 54%), decreased calcium (56% vs. 46%), decreased lymphocytes (59% vs. 51%), decreased potassium (41% vs. 36%), increased bilirubin (33% vs. 25%), increased creatinine (28% vs 18%), and decreased glucose (17% vs. 11%)**; increased creatinine (20% vs 10%). There were no clinically meaningful differences in incidence of Grade 3-4 toxicity between arms.

[...]

14 CLINICAL STUDIES

14.2 Non-Small Cell Lung Cancer

בוצעו עדכונים ונוסף מידע בסעיפים המפורטים מטה:

- 14.3 Head and Neck Squamous Cell Cancer
- 14.9 Gastric Cancer
- 14.10 Esophageal Cancer
- 14.11 Cervical Cancer
- 14.15 Endometrial Carcinoma
- 14.18 Triple Negative Breast Cancer

בעלון לרופא בוצעו עידכונים נוספים שאינם נכללים בהודעה זו.
למידע מלא ולהוראות מתן מפורטות, יש לעיין בעלון לרופא המאושר על ידי משרד הבריאות.
העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום, חברת MSD, בטלפון 09-9533333.

Keytruda 100mg/4ml מופצת ע"י חברת נובולוג בע"מ.

דיווח על תופעות לוואי לתכשירים רשומים הינו חשוב ומאפשר המשך מעקב אחר מאזן התועלת/סיכון של התכשיר. ניתן לדווח על תופעות לוואי למשרד הבריאות באמצעות לחיצה על הקישור "דיווח על תופעות לוואי עקב טיפול תרופתי" שנמצא בדף הבית של אתר משרד הבריאות (www.health.gov.il) המפנה לטופס המקוון לדיווח על תופעות לוואי, או ע"י כניסה לקישור: <https://sideeffects.health.gov.il>. כמו כן ניתן לדווח על תופעות לוואי לחברת MSD ישראל באמצעות פנייה טלפונית ל-09-9533333.

בברכה,
דורית מאורי
רוקחת ממונה
MSD ישראל

Reference:
Keytruda_100mg_4ml-SPC-07_2025_clean

ההתוויות המאושרות לתכשיר:

Melanoma

- KEYTRUDA is indicated for the treatment of adult and pediatric (12 years and older) patients with unresectable or metastatic melanoma.
- KEYTRUDA is indicated for the adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma following complete resection.

Non-Small Cell Lung Cancer

- KEYTRUDA, in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC) negative for EGFR or ALK genomic tumor aberrations.
- KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
- KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 [Tumor Proportion Score (TPS) $\geq 50\%$] as determined by a validated test. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on or after platinum-containing chemotherapy and an approved therapy for these aberrations prior to receiving KEYTRUDA.
- KEYTRUDA, as a single agent, is indicated for the treatment of patients with advanced NSCLC whose tumors express PD-L1 as determined by a validated test, with disease progression on or after platinum containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on approved therapy for these aberrations prior to receiving KEYTRUDA.
- KEYTRUDA, as a single agent, is indicated as adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC.
- KEYTRUDA, in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment, is indicated for the treatment of resectable NSCLC at high risk of recurrence in adults (for selection criteria, see section 14 CLINICAL STUDIES).

Head and Neck Cancer

- KEYTRUDA, in combination with platinum and fluorouracil (FU), is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC).
- KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by a validated test.

- KEYTRUDA, as a single agent, is indicated for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

Classical Hodgkin Lymphoma

- KEYTRUDA is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL).
- KEYTRUDA is indicated for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

Primary Mediastinal large B-Cell Lymphoma

KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL), or who have relapsed after 2 or more prior lines of therapy.

Limitation of Use: KEYTRUDA is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

Urothelial Cancer

- KEYTRUDA, as a single agent, is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy and whose tumors express PDL1 (CPS ≥ 10) as determined by a validated test, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.
- KEYTRUDA, as a single agent, is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- KEYTRUDA, as a single agent, is indicated for the treatment of patients with Bacillus Calmette-Guerin (BCG) unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.
- KEYTRUDA, in combination with enfortumab vedotin, is indicated for the first-line treatment of adult patients with unresectable or metastatic urothelial cancer.

Microsatellite Instability-High Cancer

KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI H) or mismatch repair deficient (dMMR).

- solid tumors that have progressed following prior systemic treatment and who have no satisfactory alternative treatment options,

or

- colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Limitation of Use: The safety and effectiveness of KEYTRUDA in pediatric patients with MSI H central nervous system cancers have not been established.

Gastric Cancer

- KEYTRUDA, in combination with trastuzumab, fluoropyrimidine and platinum-containing chemotherapy, is indicated for the first-line treatment of locally advanced unresectable or metastatic HER2-positive gastric or gastro-oesophageal junction (GEJ) adenocarcinoma in adults whose tumors express PD-L1 with a CPS ≥ 1 as determined by a validated test.
- KEYTRUDA, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 with a CPS ≥ 1 as determined by a validated test.

Cervical Cancer

- KEYTRUDA, in combination with chemoradiotherapy (CRT), is indicated for the treatment of patients with FIGO 2014 Stage III-IVA cervical cancer.
- KEYTRUDA, in combination with chemotherapy, with or without bevacizumab, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥ 1) as determined by a validated test.
- KEYTRUDA, as a single agent, is indicated for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥ 1) as determined by a validated test.

Biliary Tract Cancer

KEYTRUDA, in combination with gemcitabine and cisplatin, is indicated for the treatment of patients with locally advanced unresectable or metastatic biliary tract cancer (BTC).

Merkel Cell Carcinoma

KEYTRUDA is indicated for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).

Renal Cell Carcinoma

- KEYTRUDA, in combination with axitinib, is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma (RCC).
- KEYTRUDA, in combination with lenvatinib, is indicated for the first-line treatment of adult patients with advanced RCC.
- KEYTRUDA is indicated for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

Esophageal Cancer

- KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (Siewert type I) carcinoma that is not amenable to surgical resection or definitive chemoradiation in combination with platinum- and fluoropyrimidine-based chemotherapy.
- KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic squamous cell carcinoma of the esophagus whose tumors express PD-L1 (CPS ≥ 10) as determined by a validated test, with disease progression after one or more prior lines of systemic therapy.

Cutaneous Squamous Cell Carcinoma

KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC that is not curable by surgery or radiation.

Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (CRC)

KEYTRUDA is indicated for the first-line treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC).

Tumor Mutational Burden-High Cancer

KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] solid tumors, as determined by a validated test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

Limitations of Use: The safety and effectiveness of KEYTRUDA in pediatric patients with TMB-H central nervous system cancers have not been established.

Triple Negative Breast Cancer

- KEYTRUDA, in combination with chemotherapy, is indicated for the treatment of patients with locally recurrent unresectable or metastatic triple negative breast cancer (TNBC) whose tumors express PD-L1 (CPS ≥ 10) as determined by a validated test.
- KEYTRUDA is indicated for the treatment of patients with high risk early stage triple negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.

Endometrial carcinoma

- KEYTRUDA, in combination with carboplatin and paclitaxel, followed by KEYTRUDA as a single agent, for the treatment of adult patients with primary advanced or recurrent pMMR endometrial carcinoma at least 12 months from prior adjuvant chemotherapy, and dMMR endometrial carcinoma regardless of prior adjuvant treatment.
- KEYTRUDA, in combination with lenvatinib, is indicated for the treatment of advanced or recurrent endometrial carcinoma in adults who have disease progression on or following prior treatment with a platinum containing therapy and who are not candidates for curative surgery or radiation.