פברואר 2024

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 ולצרכן של התכשיר Keytruda 100mg/4ml להכללת תוספת התוויה שאושרה.

עדכונים מהותיים שבוצעו בעלון לרופא (טקסט שהוסף לעלון לרופא מודגש בקו תחתון):

1 THERAPEUTIC INDICATIONS
[…]

1.12 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).

2 DOSAGE AND ADMINISTRATION
[…]

2.13 Recommended Dosage for Biliary Tract Cancer
The recommended dose of KEYTRUDA is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression, unacceptable toxicity, or up to 24 months.

When administering KEYTRUDA in combination with chemotherapy, administer KEYTRUDA prior to chemotherapy when given on the same day. Refer to the Prescribing Information for the chemotherapy agents administered in combination with KEYTRUDA for recommended dosing information, as appropriate.

6 ADVERSE REACTIONS
[…]

6.1 Clinical Trials Experience
[…]

BTC

The safety of KEYTRUDA in combination with gemcitabine and cisplatin, was investigated in KEYNOTE-966, a multicenter, double-blind, randomized, placebo-controlled trial in patients with locally advanced unresectable or metastatic BTC who had not received prior systemic therapy in the advanced disease setting *[see Clinical Studies (14.13)]*. A total of 1063 patients received either KEYTRUDA 200 mg plus gemcitabine and cisplatin chemotherapy (n=529) or placebo plus gemcitabine and cisplatin chemotherapy (n=534) every 3 weeks.
The median duration of exposure to KEYTRUDA was 6 months (range: 1 day to 28 months). KEYTRUDA was discontinued for adverse reactions in 15% of patients. The most common adverse reaction resulting in permanent discontinuation of KEYTRUDA (≥1%) was pneumonitis (1.3%).
Adverse reactions leading to the interruption of KEYTRUDA occurred in 55% of patients. The most common adverse reactions or laboratory abnormalities leading to interruption of KEYTRUDA (≥2%) were decreased neutrophil count (18%), decreased platelet count (10%), anemia (6%), decreased white blood count (4%), pyrexia (3.8%), fatigue (3.0%), cholangitis (2.8%), increased ALT (2.6%), increased AST (2.5%), and biliary obstruction (2.3%).

In the KEYTRUDA plus chemotherapy versus placebo plus chemotherapy arms, there was a difference of ≥5% incidence in adverse reactions between patients treated with KEYTRUDA versus placebo for pyrexia (26% vs 20%), rash (21% vs 13%), pruritus (15% vs 10%), and hypothyroidism (9% vs. 2.6%). There were no clinically meaningful differences in incidence of Grade 3-4 toxicity between arms.

There was a difference of ≥5% incidence in laboratory abnormalities between patients treated with KEYTRUDA plus chemotherapy versus placebo plus chemotherapy for decreased lymphocytes (69% vs 61%). There were no clinically meaningful differences in incidence of Grade 3-4 toxicity between arms.

14 CLINICAL STUDIES

עדכונים בפרק

נוסף מידע לגבי ההתוויה Biliary Tract Cancer (BTC).

עדכונים מהותיים שבוצעו בעלון לצרכן (טקסט שהוסף לעלון לצרכן מודגש בקו תחתון):

[…]

1. למה מיועדת קיטרודה?

- סרטן של צינור המרה או כיס המרה הנקרא סרטן של דרכי המרה. ניתן להשתמש בקיטרודה בשילוב עם התרופות הכימותרפיות ג'מציטבין וציספלטין כאשר סרטן דרכי המרה שלך התפשט או אינו ניתן להסרה על ידי ניתוח.

ההתוויות המאושרות לתכשיר:

Melanoma
•KEYTRUDA (pembrolizumab) 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) ≥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.

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 Carcinoma
•KEYTRUDA 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 PD-L1 [Combined Positive Score (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 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.

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.
•KEYTRUDA, as a single agent, is indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or GEJ whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by a validated test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu targeted therapy.

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.

Non-Muscle Invasive Bladder Cancer (NMIBC)
KEYTRUDA 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.

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 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.

למידע מלא ולהוראות מתן מפורטות, יש לעיין בעלון לרופא ולצרכן המאושרים על ידי משרד הבריאות.

העלונים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום, חברת MSD, בטלפון 09-9533333.
Keytruda 100mg/4ml מופצת ע"י חברת נובולוג בע"מ.

בברכה,
דורית מאורי
רוקחת ממונה
MSD ישראל

References:
Keytruda_100mg_4ml-SPC-02-2024a
Keytruda_100mg_4ml-PIL-HEB-02-2024a