פברואר 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 והעלון לצרכן של התכשיר Keytruda 100mg/4ml להכללת התוויות חדשות והעדכונים עפ"י המפורט מטה.

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

עדכונים שבוצעו בעלון לרופא:

1 THERAPEUTIC INDICATIONS
[…]
1.2 Non-Small Cell Lung Cancer
[…]
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 ~~nonsmall cell lung carcinoma~~ NSCLC at high risk of recurrence in adults (for selection criteria, see section 14 CLINICAL STUDIES).
[…]
1.6 Urothelial Cancer
KEYTRUDA, in combination with enfortumab vedotin, is indicated for the first-line treatment of adult patients with unresectable or metastatic urothelial cancer.
[…]
1.9 Gastric Cancer
[…]
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 ~~10 or MSI High,~~ as determined by a validated test.
[…]
1.11 Cervical Cancer
KEYTRUDA, in combination with chemoradiotherapy (CRT), is indicated for the treatment of patients with FIGO 2014 Stage III-IVA cervical cancer.
[…]
1.15 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~~ 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.
[…]

2 DOSAGE AND ADMINISTRATION
[…]
2.7 Recommended Dosage for Urothelial Cancer
The recommended dose of KEYTRUDA in patients with locally advanced or metastatic urothelial ~~carcinoma~~ cancer is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity, or up to 24 months.

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

[…]

2.12 Recommended Dosage for Cervical Cancer

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

The recommended dose of KEYTRUDA in adults in combination with chemoradiotherapy is 200 mg every 3 weeks for 5 or 6 cycles followed by 400 mg every 6 weeks, administered as an intravenous infusion over 30 minutes until disease progression, unacceptable toxicity, or for KEYTRUDA up to 24 months.

For combination therapy, administer KEYTRUDA prior to chemoradiotherapy or prior to chemotherapy with or without bevacizumab when given on the same day. Refer to the Prescribing Information for the agents administered in combination with KEYTRUDA for recommended dosing information, as appropriate.

2.16 Recommended Dosage for Endometrial Carcinoma

The recommended dose of KEYTRUDA in adults in combination with chemotherapy is 200 mg every 3 weeks administered as an intravenous infusion over 30 minutes until disease progression, unacceptable toxicity, or for up to 6 cycles.
When KEYTRUDA is administrated alone for maintenance therapy, the recommended dose is 400 mg every 6 weeks administered as an intravenous infusion over 30 minutes until disease progression, unacceptable toxicity, or for up to 24 months.
Administer KEYTRUDA prior to chemotherapy when given on the same day. Refer to the Prescribing Information for the agents administered in combination with KEYTRUDA for recommended dosing information, as appropriate.
[…]

6 ADVERSE REACTIONS

[…]

6.1 Clinical Trials Experience

[…]

עודכן מידע לגבי ההתוויות:

Urothelial Cancer - Keytruda in combination with enfortumab vedotin
Cervical Cancer - Keytruda in combination with chemoradiotherapy (CRT)
Endometrial carcinoma - Primary Advanced or Recurrent Endometrial Carcinoma
[…]

8.5 Geriatric Use

[…]
Of the 564 patients with locally advanced or metastatic urothelial cancer treated with KEYTRUDA in combination with enfortumab vedotin, 44% (n=247) were 65-74 years and 26% (n=144) were 75 years or older. No overall differences in safety or effectiveness were observed between patients 65 years of age or older and younger patients. Patients 75 years of age or older treated with KEYTRUDA in combination with enfortumab vedotin experienced a higher incidence of fatal adverse reactions than younger patients. The incidence of fatal adverse reactions was 4% in patients younger than 75 and 7% in patients 75 years or older.
[…]
Of 292 adult patients with FIGO 2014 Stage III-IVA cervical cancer who were treated with KEYTRUDA in combination with CRT in KEYNOTE-A18, 42 (14%) were 65 years and over. No overall differences in safety or efficacy were observed between elderly and younger patients.

[…]

14 CLINICAL STUDIES

עודכן מידע לגבי ההתוויות בסעיפים המפורטים מטה:

14.6 Urothelial Cancer
14.9 Gastric Cancer
14.11 Cervical Cancer
14.15 Endometrial Carcinoma
14.17 Cutaneous Squamous Cell Carcinoma

עדכונים שבוצעו בעלון לצרכן:

1. למה מיועדת קיטרודה?

[...]

- סרטן שלפוחית השתן ודרכי השתן (urothelial cancer).
  - ניתן להשתמש ב**קיטרודה** בשילוב עם התרופה אנפורטומאב ודוטין במבוגרים כאשר סרטן השלפוחית השתן או דרכי השתן שלך התפשט או לא ניתן להסירו על ידי ניתוח (סרטן מתקדם של דרכי השתן).

[...]

- סרטן צוואר הרחם ~~שהינו חיובי ל-"PD-L1"~~.
  - ניתן להשתמש ב**קיטרודה** בשילוב עם כימותרפיה וטיפול קרינתי כאשר סרטן צוואר הרחם שלך התפשט לרקמות או איברים קרובים או השפיע על הכליות שלך (סרטן צוואר רחם בשלב III-IVA לפי סיווג FIGO 2014).
  - ניתן להשתמש ב**קיטרודה** בשילוב עם תרופות כימותרפיות, בשילוב או ללא התרופה בוואציזומאב, כאשר:
    - סרטן צוואר הרחם שלך לא נעלם (עיקש), חזר, או התפשט (סרטן מתקדם של צוואר הרחם)**, ו**
    - הגידול שלך הינו חיובי ל-"PD-L1".
  - ניתן להשתמש ב**קיטרודה** לבדה כאשר סרטן צוואר הרחם שלך:
    - חזר או התפשט (סרטן מתקדם של צוואר הרחם)**, ו**
    - קיבלת כימותרפיה שלא עבדה או שאינה עובדת יותר**, ו**
    - הגידול שלך הינו חיובי ל-"PD-L1".

[...]

- סרטן רחם מסוג קרצינומה מתקדמת או חוזרת של רירית הרחם.
  - ניתן להשתמש ב**קיטרודה** בשילוב עם התרופות הכימותרפיות קרבופלטין ופקליטקסל, ולאחר מכן להמשיך טיפול ב**קיטרודה** לבדה, במבוגרות כאשר:
    - הסרטן שלך התפשט (מתקדם)**, או** הסרטן שלך חזר**, ו**
      - הודגם על ידי בדיקת מעבדה כ-(pMMR) mismatch repair proficient וחלפו לפחות 12 חודשים לאחר שקיבלת תרופות כימותרפיות לאחר ניתוח**, או**
      - הודגם על ידי בדיקת מעבדה כ-(dMMR) mismatch repair deficient
  - ניתן להשתמש ב**קיטרודה** בשילוב עם התרופה לנווטיניב במבוגרות:
    - כאשר קיבלת כימותרפיה המכילה פלטינום, והיא אינה פועלת יותר**, ו**
    - הסרטן שלך לא ניתן לריפוי על ידי ניתוח או קרינה.

[...]

3. כיצד תשתמש בקיטרודה?

תמיד יש להשתמש ב**קיטרודה** לפי הוראות הרופא. עליך לבדוק עם הרופא שלך או הרוקח אם אינך בטוח בנוגע למינון ואופן הטיפול בתכשיר.

המינון ומשך הטיפול יקבעו על ידי הרופא בלבד.

- **קיטרודה** תינתן לך תוך-ורידית על ידי הרופא שלך, באמצעות צינורית תוך-ורידית במשך 30 דקות.
- למבוגרים, **קיטרודה** ניתנת בדרך כלל כל 3 שבועות או 6 שבועות בהתאם למינון של **קיטרודה** שאתה מקבל.
- לילדים, **קיטרודה** ניתנת בדרך כלל כל 3 שבועות.
- הרופא שלך יחליט כמה טיפולים אתה צריך.

[...]

4. תופעות לוואי

[...]

תופעות הלוואי הבאות דווחו עם קיטרודה כאשר ניתנת בשילוב עם תרופות כימותרפיות או עם תרופות כימותרפיות וטיפול קרינתי:

[...]

תופעות לוואי שכיחות מאוד (דווחו ביותר מ- 10% ופחות מ- 20% מהמטופלים)

רמות נמוכות של הורמון בלוטת התריס, רמות גבוהות של הורמון בלוטת התריס, קשיים בבליעה, זיהום בריאות, גרד ודימום, שלפוחיות או פריחה בכפות הידיים שלך ובכפות הרגליים שלך, כאב או צריבה בזמן הטלת שתן, כאב באזור האגן.

[...]

תופעות הלוואי הבאות דווחו עם קיטרודה כאשר ניתנת בשילוב עם אנפורטומאב ודוטין:

תופעות לוואי שכיחות מאד (דווחו ביותר מ- או שווה ל- 20% מהמטופלים)

פריחה, גרד, נשירת שיער, הרגשת עייפות, ירידה במשקל, עקצוץ, או חוסר תחושה של הזרועות או הרגליים, שינויים בחוש הטעם, ירידה בתיאבון, שלשול, בחילה, עצירות, יובש בעיניים, זיהום בדרכי השתן, ותוצאות לא תקינות של בדיקות מעבדה.

תופעות לוואי שכיחות מאוד (דווחו ביותר מ- 10% ופחות מ- 20% מהמטופלים)

חום, יובש בעור, הקאות, דלקת ריאות, רמות נמוכות של הורמון בלוטת התריס.

תופעות לוואי שכיחות (דווחו ב- 1% עד 10% מהמטופלים)

ראייה מטושטשת, דליפת תרופה ממקום עירוי.

<u>תופעות לוואי שאינן שכיחות (דווחו בפחות מ- 1% מהמטופלים)</u>
<u>כאב בשרירים, כאבים או רגישות.</u>
[...]

בעלונים לרופא ולצרכן 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.

בברכה,
דורית מאורי
רוקחת ממונה
MSD ישראל

Reference:
Keytruda_100mg_4ml-SPC-02_2025_clean
Keytruda_100mg_4ml-PIL-HEB-02_2025_clean

ההתוויות המאושרות לתכשיר:

<u>Melanoma</u>

- 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.

<u>Non-Small Cell Lung Cancer</u>

- 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.
- 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).

<u>Head and Neck Cancer</u>

- 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.

<u>Classical Hodgkin Lymphoma</u>

- 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.