דצמבר 2023

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,

הנדון : <u>Kymriah, dispersion for infusion [162-91-35711]</u>

חברת נוברטיס ישראל בע"מ מבקשת להודיע על עדכון בעלון לרופא ובעלון לצרכן של התכשיר קימריה.

התוויות התכשיר:

Kymriah is indicated for the treatment of:
Paediatric and young adult patients up to and including 25 years of age with CD19+ B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse.
Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy.
Limitation of Use: KYMRIAH is not indicated for treatment of patients with primary or secondary central nervous system lymphoma.
Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy

חומר פעיל:

Tisagenlecleucel (1.2×10^6 to 6×10^8 CAR- positive viable T cells)

בעמודים העוקבים מצויינים סעיפים בהם נעשה שינוי משמעותי. למידע נוסף, יש לעיין בעלונים לצרכן ולרופא כפי שאושרו על ידי משרד הבריאות.
העלונים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על-ידי פניה לבעל הרישום: נוברטיס ישראל בע"מ. תוצרת הארץ 6, ת"ד 7126, תל אביב.

בברכה,

שירן חן גולדשטיין
רוקחת ממונה
נוברטיס ישראל בע"מ

להלן פירוט השינויים העיקריים (טקסט באדום עם קו תחתי מציין טקסט שהוסף לעלון ואילו טקסט שהושמט מסומן באדום עם קו חוצה)

בעלון לרופא:

4.2 Posology and method of administration

Kymriah must be administered in a qualified treatment centre. Therapy should be initiated under the direction of and supervised by a healthcare professional experienced in the treatment of haematological malignancies and trained for administration and management of patients treated with ~~Kymriah~~the medical product.

~~Tocilizumab for use i~~In the event of cytokine release syndrome (CRS), at least one dose of tocilizumab and emergency equipment must be available per patient prior to infusion. The treatment centre must have access to additional doses of tocilizumab within 8 hours. In the exceptional case where tocilizumab is not available due to a shortage that is listed in the Ministry of Health website, suitable alternative measures to treat CRS instead of tocilizumab must be available prior to infusion.

~~Kymriah is intended for autologous use only (see section 4.4).~~ Manufacture and release of Kymriah usually takes about 3-4 weeks.

Posology

Kymriah is intended for autologous use only (see section 4.4).

Treatment consists of a single dose for infusion containing a dispersion for infusion of CAR-positive viable T cells in one or more infusion bags.

Dos~~ag~~e in paediatric and young adult CD19+ B-cell ALL patients
The concentration of CAR-positive viable T cells is dependent on indication and patient body weight.

- For patients 50 kg and below: The dose is within a range of 0.2 to 5 ×~~x~~ 10^6 CAR-positive viable T cells/kg body weight.
- For patients above 50 kg: The dose is within a range of 0.1 to 2.5 ×~~x~~ 10^8 CAR-positive viable T cells (non-weight based).

Dos~~ag~~e in adult DLBCL and FL patients
- The dose is within a range of 0.6 to 6.0 ×~~x~~ 10^8 CAR-positive viable T cells (non-weight based).

See the accompanying batch specific documentation for additional information pertaining to dose.

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Method of administration

Kymriah is for intravenous use only.

~~*Precautions to be taken before handling or administering the medicinal product*~~
~~This medicinal product contains genetically modified human blood cells. Healthcare professionals handling Kymriah should take appropriate precautions (wearing gloves and glasses) to avoid potential transmission of infectious diseases as for any human-derived material.~~

Preparation for infusion
Kymriah is intended for autologous use only. Before administration,~~Prior to Kymriah infusion~~, it must be confirmed that the patient's identity matches the ~~essential~~ unique patient information on the Kymriah infusion bag~~(s)~~ and accompanying documentation. The total number of infusion bags to be administered should also be confirmed with the patient specific information on the batch specific

documentation (see section 4.4).

The timing of thaw of Kymriah and infusion should be coordinated. (Please refer to section 6.6). for details on inspection and thawing of the infusion bag. The infusion start time should be confirmed in advance and adjusted for thaw so that Kymriah is available for infusion when the recipient is ready. Once Kymriah has been thawed and is at room temperature (20°C -25°C), it should be infused within 30 minutes to maintain maximum product viability, including any interruption during the infusion.

Administration
Kymriah should be administered as an intravenous infusion through latex-free intravenous tubing without a leukocyte depleting filter, at approximately 10 to 20 mL per minute by gravity flow. All contents of the infusion bag(s) should be infused. Sodium chloride 9 mg/mL (0.9%) solution for injection should be used to prime the tubing prior to infusion and to rinse it after infusion. When the full volume of Kymriah has been infused, the infusion bag should be rinsed with 10 to 30 mL sodium chloride 9 mg/mL (0.9%) solution for injection by back priming to ensure as many cells as possible are infused into the patient.

If the volume of Kymriah to be administered is ≤20 mL, intravenous push may be used as an alternative method of administration.

For detailed instructions on preparation, administration, measures to take in case of accidental exposure and disposal of Kymriah, see section 6.6.
For special precautions for disposal see section 6.6.

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6.6 Special precautions for disposal and other handling

Precautions to be taken before handling or administering the medicinal product

Kymriah should be transported within the facility in closed, break-proof, leak-proof containers.

This medicinal product contains human blood cells. Healthcare professionals handling Kymriah must take appropriate precautions (wearing gloves and eye protection) to avoid potential transmission of infectious diseases.

Preparation prior to administration

Before administration, it must be confirmed that the patient's identity matches the unique patient information on the Kymriah infusion bags and accompanying documentation. The total number of infusion bags to be administered should also be confirmed with the patient specific information on the batch specific documentation accompanying the medicinal product.

The timing of thaw of Kymriah and infusion should be coordinated. The infusion start time should be confirmed in advance and adjusted for thaw so that Kymriah is available for infusion when the recipient is ready. Once Kymriah has been thawed and is at room temperature (20°C – 25°C), it should be infused within 30 minutes to maintain maximum product viability, including any interruption during the infusion.

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Administration

Kymriah intravenous infusion should be administered by a healthcare professional experienced with immunosuppressed patients and prepared to manage anaphylaxis. In the event of cytokine release syndrome (CRS), ensure that at least one dose of tocilizumab per patient and emergency equipment

are available prior to infusion. Hospitals must have access to additional doses of tocilizumab within 8 hours. In the exceptional case where tocilizumab is not available due to a shortage that is listed in the Ministry of Health website, ensure that suitable alternative measures to treat cytokine release syndrome are available on site.

The patient's identity should be matched with the patient identifiers on the infusion bag. Kymriah is intended solely for autologous use and must not, under any circumstances, be administered to other patients.

Kymriah should be administered as an intravenous infusion through latex-free intravenous tubing without a leukocyte depleting filter, at approximately 10 to 20 mL per minute by gravity flow. All contents of the infusion bag(s) should be infused. Sterile sodium chloride 9 mg/mL (0.9%) solution for injection should be used to prime the tubing prior to infusion and to rinse it after infusion. When the full volume of Kymriah has been infused, the infusion bag should be rinsed with 10 to 30 mL sodium chloride 9 mg/mL (0.9%) solution for injection by back priming to ensure as many cells as possible are infused into the patient.