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Summary of Investigation Results

Axicabtagene ciloleucel
Idecabtagene vicleucel
Tisagenlecleucel
Lisocabtagene maraleucel

March 28, 2024

Non-proprietary name

a. Axicabtagene ciloleucel

b. Idecabtagene vicleucel

c. Tisagenlecleucel

d. Lisocabtagene maraleucel

Brand name (marketing authorization holder)

See attachment.

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

It should be added in the Other Precautions section that occurrence of lymphoid neoplasm of CAR-positive T-cell origin has been reported in patients treated with another regenerative medical product containing CAR-expressing T-cells.

Investigation results and background of the revision

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A case involving lymphoid neoplasm of CAR-positive T-cell origin was evaluated. As a result of consultation with expert advisors regarding the causality assessment of the case and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary for the following reason:

- No cases in which it was definitely determined that occurrence of lymphoid neoplasm of CAR-positive T-cell origin was observed have been reported for the 4 products investigated this time. However, since an event judged to be lymphoid neoplasm of CAR-positive T-cell origin has been reported in a patient treated with another regenerative medical product containing CAR-expressing T-cells, it is highly possible that events judged to be lymphoid neoplasm of CAR-positive T-cell origin may occur hereafter for the 4 investigated products, which also contain CAR-expressing T-cells.

Reference: Number of cases* and patient mortalities involving lymphoid neoplasm of CAR-positive T-cell origin reported in Japan and overseas

a.–d.

No cases have been reported in Japan to date.

c.

One case has been reported overseas to date. (A causal relationship between the product and event could not be established for this case.)

One instance of patient mortality has been reported overseas to date. (A causal relationship between the product and death subsequent to the event could not be established for this case.)

a., b., d.

No cases have been reported overseas to date.

*Cases collected in the PMDA's database for defects or adverse events, etc. reports

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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Attachment

No.	Non-proprietary name	Brand name (marketing authorization holder)	Japanese market launch	Indications or Performance
a.	Axicabtagene ciloleucel	Yescarta Intravenous Drip Infusion (Gilead Sciences K.K.)	May 2022	The following relapsed or refractory large B-cell lymphoma: ・ Diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, transformed follicular lymphoma, and high-grade B-cell lymphoma Yescarta should be used only in patients who have not received prior infusion of chimeric antigen receptor-expressing T-cells targeted at CD19 antigen.
b.	Idecabtagene vicleucel	Abecma Intravenous Infusion (Bristol-Myers Squibb K.K.)	April 2022	Relapsed or refractory multiple myeloma Abecma should be used only in patients meeting all of the following criteria: ・ Patients with no history of BCMA-targeted chimeric antigen receptor-expressing T cell infusion therapy ・ Patients who have received at least 2 prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD 38 monoclonal antibody, and showed disease progression or relapse after the last prior therapy
c.	Tisagenlecleucel	Kymriah Suspension for Intravenous Infusion (Novartis Pharma K.K.)	May 2019	1. Relapsed or refractory CD19-positive B-cell acute lymphoblastic leukemia Kymriah should be used only in patients meeting any of the following criteria who are naïve to CD19-targeted chimeric antigen receptor T-cell infusion therapy: ・ Newly diagnosed patients who failed to achieve remission with ≥2 lines of standard chemotherapy ・ Patients with relapsed disease who failed to achieve remission with ≥1 line of chemotherapy ・ Patients who are ineligible for, or relapsed after, allogeneic haematopoietic stem cell transplantation

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				2. Relapsed or refractory diffuse large B-cell lymphoma Kymriah should be used only in patients meeting any of the following criteria who are naïve to CD19-targeted chimeric antigen receptor T cell infusion therapy and are ineligible for, or relapsed after, autologous haematopoietic stem cell transplantation: ・ Newly diagnosed patients who failed to achieve a complete response to ≥2 lines of chemotherapy; newly diagnosed patients who achieved a complete response to ≥2 lines of chemotherapy but subsequently relapsed; patients who received ≥1 line of chemotherapy after relapse but failed to achieve a complete response; or patients who received ≥1 line of chemotherapy after relapse and achieved a complete response but subsequently relapsed again ・ Patients with diffuse large B-cell lymphoma transformed from follicular lymphoma who failed to achieve a complete response to ≥2 lines of chemotherapy including ≥1 line after the transformation, or who achieved a complete response to ≥2 lines of chemotherapy including ≥1 line after the transformation but subsequently relapsed 3. Relapsed or refractory follicular lymphoma Kymriah should be used only in patients meeting any of the following criteria who are naïve to CD19-targeted chimeric antigen receptor T-cell infusion therapy: ・ Newly diagnosed patients who failed to achieve a response to ≥2 lines of systemic therapy; newly diagnosed patients who achieved a response to ≥2 lines of systemic therapy but subsequently relapsed; patients who received ≥1 line of systemic therapy after relapse but failed to achieve a response; or patients who received ≥1 line of systemic therapy after relapse and achieved a response but subsequently relapsed again

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d.	Lisocabtagene maraleucel	Breyanzi Suspension for Intravenous Infusion (Bristol-Myers Squibb K.K.)	May 2021	The following relapsed or refractory large B-cell lymphoma: ・ Diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, transformed low-grade non-Hodgkin's lymphoma, high-grade B-cell lymphoma Relapsed or refractory follicular lymphoma Breyanzi should be used only in patients who have not received prior infusion of chimeric antigen receptor-expressing T-cells targeted at CD19 antigen.

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