



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 July 2024¹
EMA/PRAC/260034/2024
Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 10-13 June 2024 PRAC

The product information wording in this document is extracted from the document entitled 'PRAC recommendations on signals' which contains the whole text of the PRAC recommendations for product information update, as well as some general guidance on the handling of signals. It can be found on the webpage for [PRAC recommendations on safety signals](#) (in English only).

New text to be added to the product information is underlined. Current text to be deleted is ~~struck through~~.

1. Axicabtagene ciloleucel; brexucabtagene autoleucel; ciltacabtagene autoleucel; idecabtagene vicleucel; lisocabtagene maraleucel; tisagenlecleucel – Secondary malignancy of T-cell origin (EPITT no 20040)

Abecma

Summary of product characteristics

4.4 Special warnings and precautions for use

Secondary malignancies including of T-cell origin

Patients treated with Abecma may develop secondary malignancies. T-cell malignancies have been reported following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T-cell therapy, including Abecma. T-cell malignancies, including CAR-positive malignancies, have been reported within weeks and up to several years following administration of a CD19- or BCMA-, directed CAR T-cell therapy. There have been fatal outcomes. [...]

¹ Expected publication date. The actual publication date can be checked on the webpage dedicated to [PRAC recommendations on safety signals](#).



4.8 Undesirable effects

Table 3. Adverse reactions observed in patients treated with Abecma

Secondary malignancy of T-cell origin should be added into the Table of adverse reactions under the SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps).

Frequency: rare

Package leaflet

2. What you need to know before you are given Abecma

Warnings and precautions

Patients treated with Abecma may develop new types of cancers. There have been reports of patients developing cancer, beginning in a type of white blood cells called T-cells, after treatment with Abecma and similar medicines. Talk to your doctor if you experience any new swelling of your glands (lymph nodes) or changes in your skin such as new rashes or lumps.

4. Possible side effects

Other side effects

Rare: may affect up to 1 in 1,000 people

- A new type of cancer beginning in a type of white blood cells called T-cells (secondary malignancy of T-cell origin)

ANNEX II D CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Educational programme

HCP Educational programme

All HCPs who are expected to prescribe, dispense and administer Abecma shall be provided with a healthcare professional guide, which will contain information about:

risk of secondary malignancy of T-cell origin

Breyanzi

Summary of product characteristics

4.4 Special warnings and precautions for use

Secondary malignancies including of T-cell origin

Patients treated with Breyanzi may develop secondary malignancies. T-cell malignancies have been reported following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T-cell therapy, including Breyanzi. T-cell malignancies, including CAR-positive malignancies, have been reported within weeks and up to several years following administration of a CD19- or BCMA-, directed CAR T-cell therapy. There have been fatal outcomes. [...]

4.8 Undesirable effects

Table 3: Adverse drug reactions identified with Breyanzi

Secondary malignancy of T-cell origin should be added under the SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps). Frequency: Uncommon

Package leaflet

2. What you need to know before you are given Breyanzi

Warnings and precautions

Patients treated with Breyanzi may develop new types of cancers. There have been reports of patients developing cancer, beginning in a type of white blood cells called T-cells, after treatment with Breyanzi and similar medicines. Talk to your doctor if you experience any new swelling of your glands (lymph nodes) or changes in your skin such as new rashes or lumps.

4. Possible side effects

Other possible side effects

Uncommon: may affect up to 1 in 100 people

- A new type of cancer beginning in a type of white blood cells called T-cells (secondary malignancy of T-cell origin)

ANNEX II D CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Educational programme

HCP Educational programme

All HCPs who are expected to prescribe, dispense and administer Breyanzi shall be provided with a healthcare professional guide, which will contain information about:

- risk of secondary malignancy of T-cell origin

Carvykti

Summary of product characteristics

4.4 Special warnings and precautions for use

Secondary malignancies including of T-cell origin

Patients treated with CARVYKTI may develop secondary malignancies. T-cell malignancies have been reported following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T-cell therapy, including CARVYKTI. T-cell malignancies, including CAR-positive malignancies, have been reported within weeks and up to several years following administration of a CD19- or BCMA-, directed CAR T-cell therapy. There have been fatal outcomes. A case of CAR-positive T-cell lymphoma has been reported in an ongoing study. [...]

4.8 Undesirable effects

Table 4: Adverse reaction in patients with multiple myeloma treated with CARVYKTI (N=396)

Secondary malignancy of T-cell origin should be added under the SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps). Frequency uncommon

Package leaflet

2. What you need to know before you are given CARVYKTI

Warnings and precautions

Patients treated with CARVYKTI may develop new types of cancers. There have been reports of patients developing cancer, beginning in a type of white blood cells called T-cells, after treatment with CARVYKTI and similar medicines. Talk to your doctor if you experience any new swelling of your glands (lymph nodes) or changes in your skin such as new rashes or lumps.

Tell your doctor before you are given CARVYKTI if you have: [...]

4. Possible side effects

Other side effects

Uncommon (may affect up to 1 in 100 people):

- A new type of cancer beginning in a type of white blood cells called T-cells (secondary malignancy of T-cell origin)

ANNEX II D CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Educational programme: Prior to the launch of CARVYKTI in each Member State the MAH must agree the content and format of the educational materials with the National Competent Authority.

HCP Educational programme

The MAH shall ensure that in each Member State where CARVYKTI is marketed, all HCPs who are expected to prescribe, dispense, and administer CARVYKTI shall be provided with guidance:

- risk of secondary malignancy of T-cell origin

Kymriah

Summary of product characteristics

4.4 Special warnings and precautions for use

Secondary malignancies including of T-cell origin

Patients treated with Kymriah may develop secondary malignancies or recurrence of their cancer. T-cell malignancies have been reported following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T-cell therapy, including Kymriah. T-cell malignancies, including CAR-positive malignancies, have been reported within weeks and up to several years following administration of a CD19- or BCMA-, directed CAR T-cell therapy. There have been fatal outcomes. They Patients should be monitored life-long for secondary malignancies. [...]

4.8 Undesirable effects

Tabulated list of adverse reactions

The adverse reactions described in this section were identified in 79, 115 and 97 patients in the ongoing multicentre pivotal clinical studies (CCTL019B2202, CCTL019C2201 and CCTL019E2202), as well as 64 and 69 patients in the supportive studies (CCTL019B2205J and CCTL019B2001X), and from post marketing reporting. Adverse drug reactions ~~from these clinical studies~~ (Table 2) are listed by MedDRA system organ class.

Table 2 Adverse drug reactions ~~observed in clinical studies~~

The following should be added to the Table of adverse drug reactions:

Secondary malignancy of T-cell origin; SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps); Frequency: rare
Anaphylactic reaction; SOC Immune system disorders; Frequency: unknown
Neurotoxicity; SOC Nervous system disorders; Frequency: unknown

~~Post-marketing experience~~

~~The following adverse drug reactions have been derived from post-marketing experience with Kymriah via spontaneous case reports, literature cases, expanded access programs, and clinical studies other than the global registration studies. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to tisagenlecleucel exposure.~~

~~Frequency unknown: Anaphylactic reaction/infusion related reaction, neurotoxicity.~~

Package leaflet

2. What you need to know before you are given Kymriah

Warnings and precautions

Kymriah is made from your own white blood cells and should only be given to you.

Patients treated with Kymriah may develop new types of cancers. There have been reports of patients developing cancer, beginning in a type of white blood cells called T-cells, after treatment with Kymriah and similar medicines. Talk to your doctor if you experience any new swelling of your glands (lymph nodes) or changes in your skin such as new rashes or lumps.

4. Possible side effects

Other possible side effects

Rare (may affect up to 1 in 1,000 people)

- A new type of cancer beginning in a type of white blood cells called T-cells (secondary malignancy of T-cell origin)

ANNEX II D CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Educational programme

HCP Educational programme

The MAH shall ensure that in each Member State where KYMRIAH is marketed, all HCPs who are expected to prescribe, dispense ~~and~~ and administer KYMRIAH shall be provided with a guidance document to:

- risk of secondary malignancy of T-cell origin

Tecartus

Summary of product characteristics

4.4 Special warnings and precautions for use

Secondary malignancies including of T cell origin

Patients treated with Tecartus may develop secondary malignancies. T-cell malignancies have been reported following treatment of haematological malignancies with a BCMA- or CD19-directed CART-cell therapy. T-cell malignancies, including CAR-positive malignancies, have been reported within weeks and up to several years following administration of a CD19- or BCMA-, directed CAR T-cell therapy. There have been fatal outcomes. [...]

4.8 Undesirable effects

Description of selected adverse reactions from ZUMA-2 and ZUMA-3 (n=182), and from post marketing reporting

[...]

Secondary malignancies

There have been cases of the following adverse effect(s) reported after treatment with other CAR T-cell products, which might also occur after treatment with Tecartus: secondary malignancy of T-cell origin.

Package leaflet

2. What you need to know before you are given Tecartus

Warnings and precautions

Tecartus is made from your own white blood cells and must only be given to you (autologous use).

Patients treated with Tecartus may develop new types of cancers. There have been reports of patients developing cancer, beginning in a type of white blood cells called T-cells, after treatment with other similar medicines. Talk to your doctor if you experience any new swelling of your glands (lymph nodes) or changes in your skin such as new rashes or lumps.

4. Possible side effects

[...]

A new type of cancer beginning in a type of white blood cells called T-cells (secondary malignancy of T-cell origin) has been reported for other similar medicines.

Reporting of side effects
[...]

ANNEX II D CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Educational program

HCP Educational program

The MAH shall ensure that in each Member State where Yescarta is marketed, all HCPs who are expected to prescribe, dispense, and administer Yescarta shall be provided with a guidance document to:

- [...] risk of secondary malignancy of T-cell origin

Yescarta

Summary of product characteristics

4.4 Special warnings and precautions for use

Secondary malignancies including of T-cell origin

Patients treated with Yescarta may develop secondary malignancies. T-cell malignancies have been reported following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T-cell therapy, including Yescarta. T-cell malignancies, including CAR-positive malignancies, have been reported within weeks and up to several years following administration of a CD19- or BCMA-, directed CAR T-cell therapy. There have been fatal outcomes. [...]

4.8 Undesirable effects

Table 3: Adverse drug reactions identified with Yescarta*

Secondary malignancy of T-cell origin should be added under the SOC *Neoplasms benign, malignant and unspecified (including cysts and polyps)*. Frequency: rare

~~* Adverse drug reactions were identified from a pooled analysis of 397 adult patients treated with Yescarta in ZUMA 1, ZUMA 5, and ZUMA 7 and from post-marketing experience~~

Package leaflet

2. What you need to know before you are given Yescarta

Warnings and precautions

Yescarta is made from your own white blood cells and must only be given to you (autologous use).

Patients treated with Yescarta may develop new types of cancers. There have been reports of patients developing cancer, beginning in a type of white blood cells called T-cells, after treatment with Yescarta

and similar medicines. Talk to your doctor if you experience any new swelling of your glands (lymph nodes) or changes in your skin such as new rashes or lumps.

4. Possible side effects

Rare (may affect up to 1 in 1,000 people)

- A new type of cancer beginning in a type of white blood cells called T-cells (secondary malignancy of T-cell origin)

ANNEX II D CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Educational program

HCP Educational program

The MAH shall ensure that in each Member State where Yescarta is marketed, all HCPs who are expected to prescribe, dispense, and administer Yescarta shall be provided with a guidance document to:

[...]

risk of secondary malignancy of T-cell origin