



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Pharmacovigilance Risk Assessment Committee (PRAC)

## New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 27-30 November 2023 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 [here](#) (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 – Progressive multifocal leukoencephalopathy (PML) (EPITT no 19940)

#### Summary of product characteristics

##### 4.4. Special warnings and precautions for use

~~HBV~~ Viral reactivation

[...]

Reactivation of JC virus, leading to progressive multifocal leukoencephalopathy (PML), has been reported in patients treated with Yescarta who have also received prior treatment with other immunosuppressive medications. Cases with fatal outcome have been reported. The possibility of PML should be considered in immunosuppressed patients with new onset or worsening neurological symptoms and appropriate diagnostic evaluations should be performed.

#### Package leaflet

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

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



## After you have been given Yescarta

**Tell your doctor or nurse immediately if you have any of the following:**

[...]

- Blurred vision, loss of vision or double vision, difficulty speaking, weakness or clumsiness of an arm or a leg, a change in the way you walk or problems with your balance, personality changes, changes in thinking, memory and orientation leading to confusion. These may all be symptoms of a serious and potentially fatal brain condition known as progressive multifocal leukoencephalopathy (PML). These symptoms may start several months after treatment has ended and they usually develop slowly and gradually over weeks or months. It is important that your relatives or caregivers are also aware of these symptoms, since they may notice symptoms that you are not aware of.

## 2. Dabrafenib; trametinib – Peripheral neuropathy (EPITT no 19947)

### Tafinlar (dabrafenib) - Summary of product characteristics

#### 4.8. Undesirable effects

Tabulated list of adverse reactions

Table 3 (Adverse reactions with dabrafenib monotherapy) and Table 4 (Adverse reactions with dabrafenib in combination with trametinib)

Nervous system disorders

Common: Peripheral neuropathy (including sensory and motor neuropathy)

### Tafinlar (dabrafenib) - Package leaflet

#### 4. Possible side effects

Possible side effects in patients taking Tafinlar alone and Possible side effects when Tafinlar and trametinib are taken together

Common side effects (may affect up to 1 in 10 people)

Problem with the nerves that can produce pain, loss of sensation or tingling in hands and feet and/or muscle weakness (peripheral neuropathy)

### Mekinist (trametinib) - Summary of product characteristics

#### 4.8. Undesirable effects

Tabulated list of adverse reactions

Table 4 (Adverse reactions with trametinib monotherapy) and Table 5 (Adverse reactions with trametinib in combination with dabrafenib)

Nervous system disorders (new SOC for table 4)

Common: Peripheral neuropathy (including sensory and motor neuropathy)

## **Mekinist (trametinib) - Package leaflet**

### 4. Possible side effects

Possible side effects in patients taking Mekinist alone and Side effects when Mekinist and dabrafenib are taken together

Common side effects (may affect up to 1 in 10 people)

Problem with the nerves that can produce pain, loss of sensation or tingling in hands and feet and/or muscle weakness (peripheral neuropathy)

## **3. Pirfenidone – Drug reaction with eosinophilia and systemic symptoms (DRESS) (EPITT no 19920)**

### **Summary of product characteristics**

#### 4.4. Special warnings and precautions for use

##### **Severe skin reactions**

Stevens-Johnson syndrome (SJS), ~~and~~ toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported post-marketing in association with *<product name>* treatment. If signs and symptoms suggestive of these reactions appear, *<product name>* should be withdrawn immediately. If the patient has developed SJS, ~~or~~TEN or DRESS with the use of *<product name>*, treatment with *<product name>* must not be restarted and should be permanently discontinued.

#### 4.8. Undesirable effects

##### **Skin and subcutaneous tissue disorders**

Frequency: Not known - Stevens-Johnson syndrome<sup>1</sup>; toxic epidermal necrolysis<sup>1</sup>; drug reaction with eosinophilia and systemic symptoms (DRESS)<sup>1</sup>

Footnote <sup>1</sup>: Identified through post-marketing surveillance (see section 4.4)

### **Package leaflet**

#### 2. Warning and precautions

- Stevens-Johnson syndrome, ~~and~~ toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS), have been reported in association with *<product name>* treatment. Stop using *<product name>* and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

#### 4. Possible side effects

Stop taking *<product name>* and ~~tell your doctor~~ seek medical attention immediately if you notice any of the following symptoms or signs

- ~~If you experience s~~Swelling of the face, lips and/or tongue, itching, hives, difficulty breathing or wheezing, or feeling faint, which are signs of angioedema, a serious allergic reaction or anaphylaxis.
- ~~If you experience y~~Yellowing of the eyes or skin, or dark urine, potentially accompanied by itching of the skin, pain on the upper right side of your stomach area (abdomen), loss of appetite, bleeding or bruising more easily than normal, or feeling tired. These may be signs of abnormal liver function and could indicate liver injury, which is an uncommon side effect of *<product name>*.
- ~~If you experience r~~Reddish non-elevated, or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals, and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms. ~~These signs and symptoms may indicate~~ (Stevens-Johnson syndrome, or toxic epidermal necrolysis).
- Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).