



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

6 April 2020<sup>1</sup>  
EMA/PRAC/111218/2020 Corr<sup>2,3</sup>  
Pharmacovigilance Risk Assessment Committee (PRAC)

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

Adopted at the 9-12 March 2020 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. Immune check point inhibitors: atezolizumab; cemiplimab; durvalumab – Tuberculosis (EPITT no 19464)**

#### **IMFINZI (durvalumab)**

##### **Summary of product characteristics**

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

Immune-mediated pneumonitis

[..]

~~Patients with s~~Suspected pneumonitis should be ~~evaluated~~ confirmed with radiographic imaging and other infectious and disease-related aetiologies excluded, and managed as recommended in section 4.2.

#### **LIBTAYO (cemiplimab)**

##### **Summary of product characteristics**

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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](#).

<sup>2</sup> A footnote was deleted on 8 April 2020 for the signal on thiazide and thiazide-like diuretics (see page 3).

<sup>3</sup> A minor edit was implemented in the product information of the signal on thiazide and thiazide-like diuretics on 5 June 2020 (see page 4).



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

##### Immune-related adverse reactions

[...]

For suspected immune-related adverse reactions, patients should be evaluated to confirm an immune-related adverse reaction and to exclude other possible causes, including infection. [...]

##### Immune-related pneumonitis

[...] Patients should be monitored for signs and symptoms of pneumonitis and causes other than immune-related pneumonitis should be ruled out.

## **TECENTRIQ (atezolizumab)**

### **Summary of product characteristics**

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

##### Immune-related pneumonitis

[...] Patients should be monitored for signs and symptoms of pneumonitis and causes other than immune-related pneumonitis should be ruled out.

## **2. Nivolumab – Haemophagocytic lymphohistiocytosis<sup>4</sup> (EPITT no 19467)**

### **Summary of product characteristics**

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

Haemophagocytic lymphohistiocytosis (HLH) has been observed with nivolumab as monotherapy and nivolumab in combination with ipilimumab. Caution should be taken when nivolumab is administered as monotherapy or in combination with ipilimumab. If HLH is confirmed, administration of nivolumab or nivolumab in combination with ipilimumab should be discontinued and treatment for HLH initiated.

#### 4.8. Undesirable effects

Table 5: Adverse reactions with nivolumab monotherapy

##### Blood and lymphatic system disorders

Haemophagocytic lymphohistiocytosis (Frequency 'Not known')

Table 6: Adverse reactions with nivolumab in combination with ipilimumab

##### Blood and lymphatic system disorders

Haemophagocytic lymphohistiocytosis (Frequency 'Not known')

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<sup>4</sup> This signal was discussed at the 10-13 February 2020 PRAC meeting.

## Package leaflet

### 2. What you need to know before you use OPDIVO

#### Warnings and precautions

Haemophagocytic lymphohistiocytosis. A rare disease in which our immune system makes too many of otherwise normal infection fighting cells called histiocytes and lymphocytes. Symptoms may include enlarged liver and/or spleen, skin rash, lymph node enlargement, breathing problems, easy bruising, kidney abnormalities, and heart problems.

### 4. Possible side effects

The following side effects have been reported with nivolumab alone:

A condition where the immune system makes too many infection-fighting cells called histiocytes and lymphocytes that may cause various symptoms (called haemophagocytic lymphohistiocytosis)

The following side effects have been reported with nivolumab in combination with ipilimumab:

A condition where the immune system makes too many infection-fighting cells called histiocytes and lymphocytes that may cause various symptoms (called haemophagocytic lymphohistiocytosis)

## 3. Paroxetine – Microscopic colitis (EPITT no 19474)

### Summary of product characteristics

#### 4.8. Undesirable effects

##### Gastrointestinal disorders

Frequency “not known”: Colitis microscopic

## Package leaflet

### 4. Possible side effects

Side effects of which the frequency is not known:

Inflammation of the colon (causing diarrhoea)

## 4. Thiazide, thiazide-like diuretics and combinations<sup>5</sup> – choroidal effusion (EPITT no 19468)

### Summary of product characteristics

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

Choroidal effusion, acute myopia and secondary angle-closure glaucoma:

Sulfonamide or sulfonamide derivative drugs can cause an idiosyncratic reaction resulting in choroidal effusion with visual field defect, transient myopia and acute angle-closure glaucoma. [...]

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<sup>5</sup> The footnote listing some of the active substances and combinations was deleted on 8 April 2020.

#### 4.8. Undesirable effects

For hydrochlorothiazide-, chlortalidone- and indapamide-containing products:

Eye disorders: choroidal effusion (frequency not known)

For bendroflumethiazide, cicletanine, clopamide, cyclopenthiazide, hydroflumethiazide, metipamide, metolazone, xipamide-containing products (choroidal effusion has not yet been reported but is considered a class effect):

*c. Description of selected adverse reactions:*

Cases of choroidal effusion with visual field defect have been reported after the use of thiazide and thiazide-like diuretics.

### **Package leaflet**

#### 2. What you need to know before you take [product name]

Warnings and precautions

Talk to your doctor, pharmacist, or nurse before taking [product name]

If you experience a decrease in vision or eye pain. These could be symptoms of fluid accumulation in the vascular layer of the eye (choroidal effusion) or an increase of pressure in your eye and can happen within hours to weeks<sup>6</sup> of taking [product name]. [...]

#### 4. Possible side effects

Decrease in vision or pain in your eyes due to high pressure (possible signs of fluid accumulation in the vascular layer of the eye (choroidal effusion) or acute angle-closure glaucoma)

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<sup>6</sup> 'a week' was replaced by 'weeks' on 5 June 2020.