**APPROVED PROFESSIONAL INFORMATION**

**SCHEDULING STATUS**

S4

## 1 NAME OF THE MEDICINE

**Tecentriq® 840 mg** (Concentrate for solution for infusion)

**Tecentriq® 1 200 mg** (Concentrate for solution for infusion)

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

*Active ingredient:* atezolizumab

Tecentriq is supplied as single-use vials containing preservative-free, colourless to slightly yellow solution, at an active ingredient concentration of 60 mg/mL, as follows:

- 14 mL vial containing a total of 840 mg atezolizumab
- 20 mL vial containing a total of 1 200 mg atezolizumab

Contains sugar (sucrose).

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Clear, colourless to slightly yellowish liquid.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

***Metastatic urothelial carcinoma***

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC):

- after platinum-containing chemotherapy, or
- who are considered cisplatin ineligible, and whose tumours have a PD-L1 expression ≥ 5 % (see section 5.1)

***Early-stage non-small cell lung cancer (early-stage NSCLC)***

Tecentriq as monotherapy is indicated as adjuvant treatment following resection and platinum-based chemotherapy for patients with stage II to IIIA (7th edition of the Union International Centre le Cancer/American Joint Committee on Cancer (UICC/AJCC)-staging system) NSCLC whose tumours have PD-L1 expression on ≥ 1 % tumour cells (TC).

***Non-small cell lung cancer (NSCLC)***

Tecentriq, combined with bevacizumab, paclitaxel and carboplatin is indicated as first-line treatment of patients with metastatic non-squamous non-small cell lung cancer (NSCLC). Patients with EGFR or ALK genomic tumour aberrations should have received targeted therapy, if clinically indicated, before receiving Tecentriq.

Tecentriq, combined with nab-paclitaxel and carboplatin as first-line treatment of patients with metastatic non-squamous non-small cell lung cancer who do not have EGFR or ALK genomic tumour aberrations.

Tecentriq as monotherapy is indicated for the first-line treatment of patients with metastatic NSCLC whose tumours have a PD-L1 expression ≥ 50 % tumour cells (TC) or ≥ 10 % tumour-infiltrating immune cells (IC) and who do not have EGFR or ALK genomic tumour aberrations.

Tecentriq as monotherapy is indicated for the treatment of patients with locally advanced or metastatic NSCLC after prior chemotherapy.

***Small cell lung cancer***

Tecentriq, combined with carboplatin and etoposide for first-line treatment of patients with extensive-stage small cell lung cancer (ES-SCLC).

***Triple-negative breast cancer (TNBC)***

***Metastatic breast cancer (mBC)***

Tecentriq, combined with nab-paclitaxel is indicated for the treatment of patients with unresectable locally advanced or metastatic TNBC whose tumours express PD-L1 ≥ 1 %, and who have not been given chemotherapy for metastatic disease.

***Early breast cancer (eBC)***

Tecentriq in combination with nab-paclitaxel and anthracycline-based chemotherapy, is indicated for the neoadjuvant treatment of patients with locally advanced or early TNBC.

***Hepatocellular carcinoma (HCC)***

Tecentriq, in combination with bevacizumab, is indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

## 4.2 Posology and method of administration

**General**

Tecentriq must be administered as an intravenous infusion under the supervision of a qualified healthcare professional. Do not administer as an IV push or bolus. Full resuscitative facilities must be present.

Do not co-administer other medicinal products through the same infusion line.

Substitution by any other biological medicinal product requires the consent of the prescribing doctor.

The initial dose of Tecentriq must be administered over 60 minutes. If the first infusion is tolerated all subsequent infusions may be administered over 30 minutes.

***Tecentriq monotherapy***

*1L cisplatin-ineligble mUC, early-stage-NSCLC, 1L NSCLC*

Patients should be selected for treatment based on the tumour expression of PD-L1 confirmed by a validated test.

***Tecentriq combination therapy***

For the use of Tecentriq in combination therapy, please also refer to the full professional information for the combination product. Tecentriq should be administered prior to IV combination therapy if given the same day.

**Table 1 Recommended dose for Tecentriq monotherapy by intravenous (IV) infusion**

| Indication | Recommended dose and schedule | Duration of treatment |
|---|---|---|
| **1L cisplatin-ineligible mUC** | • 840 mg every 2 weeks or<br>• 1 200 mg every 3 weeks or<br>• 1 680 mg every 4 weeks | Until loss of clinical benefit or unmanageable toxicity |
| **1L Metastatic NSCLC** | | Until loss of clinical benefit or unacceptable toxicity |
| **Early-stage NSCLC** | | For 1 year unless disease recurrence or unacceptable toxicity. |

**Table 2 Recommended dose for Tecentriq combination therapy by intravenous (IV) infusion**

| Indication | Recommended dose and schedule | | Duration of treatment |
|---|---|---|---|
| | **Tecentriq** | **Combination medicines** | |
| **1L non-squamous metastatic NSCLC:** Tecentriq with bevacizumab, paclitaxel, and carboplatin | *Induction Phase*:<br>• 840 mg every 2 weeks or<br>• 1 200 mg every 3 weeks or<br>• 1 680 mg every 4 weeks | *Induction phase*:<br>• Bevacizumab, paclitaxel, and then carboplatin are administered every 3 weeks.<br>*Maintenance phase*<br>• Bevacizumab is administered every 3 weeks. | |
| **1L non-squamous metastatic NSCLC:** Tecentriq with nab-paclitaxel and carboplatin | Tecentriq should be administered first when given on the same day.<br><br>*Maintenance phase (without chemotherapy):* Tecentriq is administered according to its dosing schedules by IV infusion. | *Induction Phase*:<br>• Nab-paclitaxel and carboplatin are administered every 3 weeks.<br>• For each 21-day cycle, nab-paclitaxel and carboplatin are administered on day 1.<br>• In addition, nab-paclitaxel is administered on days 8 and 15. | *Induction phase*:<br>• Four or six cycles<br><br>*Maintenance phase*:<br>• Until disease progression or unmanageable toxicity. |

| Indication | Recommended dose and schedule | | Duration of treatment |
|---|---|---|---|
| | **Tecentriq** | **Combination medicines** | |
| **1L ES-SCLC:**<br>Tecentriq with carboplatin and etoposide | | *Induction Phase*:<br>• Carboplatin and etoposide are administered by IV infusion every three weeks.<br>• Carboplatin and etoposide are administered on day 1 of each cycle, and etoposide is also administered on days 2 and 3. | |
| **Locally advanced or early TNBC with chemotherapy** | • 840 mg every 2 weeks or<br>• 1 200 mg every 3 weeks or<br>• 1 680 mg every 4 weeks<br><br>Tecentriq should be administered prior to chemotherapy when given on the same day. | The chemotherapy regimen consists of sequential nab-paclitaxel (125 mg/m$^2$ by IV infusion administered once every week for 12 doses), and an anthracycline + cyclophosphamide combination (by IV infusion administered once every 2 weeks for 4 doses). | Until disease progression or unmanageable toxicity.<br>For neoadjuvant treatment of locally advanced or early TNBC, Tecentriq should be administered with chemotherapy, as part of a complete |

| Indication | Recommended dose and schedule | | Duration of treatment |
|---|---|---|---|
| | **Tecentriq** | **Combination medicines** | |
| | | | treatment regimen |
| **1L unresectable locally advanced or metastatic TNBC**<br>Tecentriq with nab-paclitaxel | •840 mg every 2 weeks or<br>•1 200 mg every 3 weeks or<br>•1 680 mg every 4 weeks | Tecentriq should be administered prior to nab-paclitaxel when given on the same day.<br>100 mg/m$^2$ nab-paclitaxel is administered on days 1, 8 and 15 of each 28-day cycle. | Until disease progression or unmanageable toxicity.<br>Until disease progression or unmanageable toxicity |
| **HCC:**<br>Tecentriq with bevacizumab | • 840 mg every 2 weeks or<br>• 1 200 mg every 3 weeks or<br>• 1 680 mg every 4 weeks | Tecentriq should be administered prior to bevacizumab when given on the same day.<br>Bevacizumab is administered at 15 mg/kg body weight every 3 weeks. | Until loss of clinical benefit or unmanageable toxicity. |

**Delayed or Missed Doses**

If a planned dose of Tecentriq is missed, it should be administered as soon as possible. The schedule of administration should be adjusted to maintain the appropriate interval between doses.

**Dose Modifications**

No dose reductions of Tecentriq are recommended.

***Dose modifications for immune-mediated adverse reactions***

Recommendations for specific adverse drug reactions (see section 4.4, General and section 4.8) are presented in Table 3.

**Table 3: Recommended dose modifications for specific adverse drug reactions**

| **Adverse Reaction** | **Severity** | **Treatment modification** |
|---|---|---|
| **Immune-mediated Pneumonitis** | Grade 2 | Withhold[1] |
| | Grade 3 or 4 | Permanently discontinue |
| **Immune-mediated hepatitis in patients without Unresectable Hepatocellular Carcinoma (HCC)** | Grade 2 (ALT or AST > 3x ULN or blood bilirubin > 1,5x ULN for more than 5-7 days) | Withhold[1] |
| | Grade 3 or 4 (ALT or AST > 5,0x ULN or blood bilirubin > 3x ULN) | Permanently discontinue |
| **Immune-mediated hepatitis in patients with HCC** | If AST/ALT is within normal limits at baseline and increases to > 3x to ≤ 10x ULN<br>If AST/ALT is > 1 to ≤ 3x ULN at baseline and increases to > 5x to ≤ 10x ULN<br>If AST/ALT is > 3x to ≤ 5x ULN at baseline and increases to > 8x to ≤ 10x ULN | Withhold[1] |
| | If AST/ALT increases to > 10x ULN or total bilirubin increases to > 3x ULN | Permanently discontinue |
| **Immune-mediated colitis** | Grade 2 diarrhoea or colitis | Withhold[1] |
| | Grade 3 diarrhoea or colitis | Withhold[1] |

| Adverse Reaction | Severity | Treatment modification |
|---|---|---|
| | | Initiate IV corticosteroids and convert to oral corticosteroids after improvement |
| | Grade 4 diarrhoea or colitis | Permanently discontinue |
| **Immune-mediated hypothyroidism** | Symptomatic | Withhold[2]<br>Initiate thyroid hormone replacement therapy |
| **Immune-mediated hyperthyroidism** | Symptomatic | Withhold[2]<br>Initiate anti-thyroid therapy as needed |
| **Immune-mediated adrenal insufficiency** | Symptomatic | Withhold[1] |
| **Immune-mediated hypophysitis** | Grade 2 or 3 | Withhold[1] |
| | Grade 4 | Permanently discontinue |
| **Immune-mediated type 1 diabetes** | For ≥ Grade 3 hyperglycemia (fasting glucose > 250 mg/dL) | Withhold[2]<br>Initiate insulin |
| **Immune-mediated Meningitis, encephalitis, myasthenic syndrome/ myasthenia gravis, Guillain-Barré syndrome** | All grades | Permanently discontinue |
| **Immune-mediated pancreatitis** | Grade 2 or 3 | Withhold[1] |

| Adverse Reaction | Severity | Treatment modification |
|---|---|---|
| | ≥ Grade 3 increased serum amylase or lipase levels (> 2,0 ULN) | |
| | Grade 4 or any grade recurrent pancreatitis | Permanently discontinue |
| **Immune-mediated myocarditis** | Grade 2 or above | Permanently discontinue |
| **Immune-mediated myositis** | Grade 2 or 3 | Withhold |
| | Grade 4 or grade 3 recurrent myositis | Permanently discontinue |
| **Immune-mediated nephritis** | Grade 2 (creatinine level > 1,5 – 3,0x baseline or > 1,5 – 3,0x ULN) | Withhold[1] |
| | Grade 3 (creatinine level > 3,0x baseline or > 3,0 – 6,0 x ULN) or 4 (creatinine level > 6,0 x ULN) | Permanently discontinue |
| **Immune-mediated pericardial disorders** | Grade 1 pericarditis | Withhold[3] |
| | Grade 2 or above | Permanently discontinue |
| **Infusion related reactions** | Grade 1 or 2 | Reduce rate of infusion or withhold treatment<br>Premedication with antipyretic and antihistamines may be considered for subsequent doses |
| | Grade 3 or 4 | Permanently discontinue |
| | Grade 3 | Withhold[1] |

| Adverse Reaction | Severity | Treatment modification |
|---|---|---|
| **Rash/Severe cutaneous adverse reactions** | or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)[4] | |
| | Grade 4<br>or confirmed Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)[4] | Permanently discontinue[1] |

[1] Treatment with corticosteroid therapy (1-2 mg/kg/day prednisone or equivalent) should be initiated. Treatment with Tecentriq may be resumed in patients with complete or partial resolution (Grade 0 to 1) within 12 weeks, and after corticosteroids have been reduced to ≤ 10 mg/day oral prednisone or equivalent.

[2] Treatment with Tecentriq may be resumed when symptoms are controlled and the patient is clinically stable.

[3] Conduct a detailed cardiac evaluation to determine the etiology and manage appropriately

[4] Regardless of severity

For other immune-related reactions, based on the type and severity of the reaction, treatment with Tecentriq should be withheld for Grades 2 or 3 immune-mediated adverse reactions and corticosteroid therapy (1-2 mg/kg/day prednisone or equivalent) should be initiated. If symptoms improve to ≤ Grade 1, taper corticosteroids as clinically indicated. Treatment with Tecentriq may be resumed if the event improves to ≤ Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤ 10 mg oral prednisone or equivalent per day.

Treatment with Tecentriq should be permanently discontinued for Grade 4 immune-related adverse reactions, or when unable to reduce corticosteroid dose to the equivalent of ≤ 10 mg prednisone per day within 12 weeks after onset.

***Special Dosage Instructions***

***Paediatric use***

Tecentriq is not approved for use in patients under the age of 18 years. The safety and efficacy of Tecentriq in this population has not been established. Tecentriq did not demonstrate clinical benefit in paediatric patients in a clinical trial (see section 5.2, Pharmacokinetics in Special Populations).

***Geriatric use***

Based on a population pharmacokinetic analysis, no dose adjustment of Tecentriq is required in patients ≥ 65 years of age (see section 5.2, Pharmacokinetics in Special Populations).

***Renal Impairment***

Based on a population pharmacokinetic analysis, no dose adjustment is required in patients with renal impairment (see section 5.2, Pharmacokinetics in Special Populations).

***Hepatic Impairment***

Based on a population pharmacokinetic analysis, no dose adjustment is required for patients with mild hepatic impairment. There are no data in patients with moderate or severe hepatic impairment (see section 5.2, Pharmacokinetics in Special Populations).

*Instructions for dilution: see Special Instructions for use, Handling and Disposal*, section 6.6.

*Incompatibilities:* see section 6.2

## 4.3 Contraindications

Tecentriq is contraindicated in patients with a known hypersensitivity to atezolizumab or any of the excipients.

Live vaccines should not be used while receiving Tecentriq. See section 4.4.

Pregnancy and lactation, see section 4.6.

## 4.4 Special warnings and precautions for use

*Contains sucrose*. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption should not take Tecentriq.

Tecentriq contains sucrose which may have an effect on the control of your blood sugar if you have diabetes mellitus.

**Patients who had received or were to receive live vaccines were excluded from the clinical trials due to danger of systemic proliferation of the virus. The use of live virus vaccines is thus contraindicated with Tecentriq. The time that should pass before a live vaccine can be used since the last dose should be 5,5 x the typical elimination half-life ($t_{1/2}$) of 27 days, i.e.: 148,5 days.**

***General***

In order to improve the traceability of biological medicinal products, the trade name and the batch number of the administered product should be clearly recorded (or stated) in the patient file.

***Immune-mediated pneumonitis***

Cases of pneumonitis, including fatal cases, have been observed in clinical trials with Tecentriq (see section 4.8). Patients should be monitored for signs and symptoms of pneumonitis. See section 4.2 for recommended dose modifications.

***Immune-mediated hepatitis***

Cases of hepatitis, some leading to fatal outcomes, have been observed in clinical trials with Tecentriq (see section 4.8). Patients should be monitored for signs and symptoms of hepatitis. Monitor aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin prior to and periodically during treatment with Tecentriq. Consider appropriate management of patients with abnormal liver function tests (LFTs) at baseline. See section 4.2 for recommended dose modifications.

***Immune-mediated colitis***

Cases of diarrhoea or colitis have been observed in clinical trials with Tecentriq (see section 4.8). Patients should be monitored for signs and symptoms of colitis. See section 4.2 for recommended dose modifications.

***Immune-mediated endocrinopathies***

Hypothyroidism, hyperthyroidism, adrenal insufficiency, hypophysitis, and type 1 diabetes mellitus, including diabetic ketoacidosis, have been observed in clinical trials with Tecentriq (see section 4.8). Patients should be monitored for clinical signs and symptoms of endocrinopathies. Monitor thyroid function prior to and periodically during treatment with Tecentriq. Consider appropriate management of patients with abnormal thyroid function tests at baseline. Patients with abnormal thyroid function tests who are asymptomatic may receive Tecentriq. See section 4.2 for recommended dose modifications.

***Immune-mediated meningoencephalitis***

Meningoencephalitis has been observed in clinical trials with Tecentriq (see section 4.8). Patients should be monitored for clinical signs and symptoms of meningitis or encephalitis. See section 4.2 for recommended dose modifications

**Immune-mediated neuropathies**

Myasthenic syndrome/myasthenia gravis or Guillain-Barré syndrome, which may be life threatening, were observed in patients receiving Tecentriq (see section 4.8). Patients should be monitored for symptoms of motor and sensory neuropathy. See section 4.2 for recommended dose modifications.

**Immune-mediated pancreatitis**

Pancreatitis, including increases in serum amylase and lipase levels, has been observed in clinical trials with Tecentriq (see section 4.8). Patients should be closely monitored for signs and symptoms that are suggestive of acute pancreatitis. See section 4.2 for recommended dose modifications.

**Immune-mediated myocarditis**

Myocarditis, including fatal cases, has been observed in clinical trials with Tecentriq (see section 4.8). Patients should be monitored for signs and symptoms of myocarditis. Myocarditis may also be a clinical manifestation of myositis and should be managed accordingly. See section 4.2 for recommended dose modifications.

**Immune-mediated myositis**

Cases of myositis, including fatal cases, have been observed in clinical trials with Tecentriq (see section 4.8). Patients should be monitored for signs and symptoms of myositis. Patients with possible myositis should be monitored for signs of myocarditis. See section 4.2 for recommended dose modifications.

**Immune-mediated nephritis**

Nephritis has been observed in clinical trials with Tecentriq (see section 4.8). Patients should be monitored for changes in renal function. See section 4.2 for recommended dose modifications

**Infusion related reactions**

Infusion related reactions (IRRs) have been observed in clinical trials with Tecentriq (see section 4.8). See section 4.2 for recommended dose modifications.

**Immune-mediated severe cutaneous adverse reactions**

Immune-mediated severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients receiving Tecentriq. Patients should be monitored for suspected severe skin reactions and other causes should be excluded. Based on the severity of the adverse reaction, Tecentriq should be withheld for Grade 3 skin reactions until recovery to Grade ≤ 1 or permanently discontinued for Grade 4 skin reactions, and corticosteroids should be administered (see section 4.2).

For suspected SCARs patients should be referred to a dermatologist for further diagnosis and management. Tecentriq should be withheld with patients with suspected SJS or TEN. For confirmed SJS or TEN, Tecentriq should be permanently discontinued.

Caution should be used when considering the use of Tecentriq in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer medicines.

***Immune-mediated pericardial disorders***

Pericardial disorders, including pericarditis, pericardial effusion and cardiac tamponade, some leading to fatal outcomes, have been observed in clinical trials with Tecentriq (see section 4.8).

Patients should be monitored for clinical signs and symptoms of pericardial disorders. Refer to section 4.2 for recommended dose modifications.

**Special populations**

Patients with autoimmune disease were excluded from clinical trials with Tecentriq. In the absence of data, Tecentriq is not recommended for use in patients who have autoimmune diseases.

**Embryo-foetal toxicity**

Based on the mechanism of action, the use of Tecentriq may cause foetal harm. Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway can lead to increased risk of immune-mediated rejection of the developing foetus resulting in foetal death.

Pregnant women should be advised of the potential risk to the foetus. Women of childbearing potential should be advised to use highly effective contraception during treatment with Tecentriq and for 5 months after the last dose (see section 4.6, Females and Males of Reproductive Potential).

## 4.5 Interaction with other medicines and other forms of interaction

No formal pharmacokinetic interaction studies have been conducted with Tecentriq. Since Tecentriq is cleared from the circulation through catabolism, no metabolic drug-drug interactions are expected.

The use of systemic corticosteroids or immunosuppressants before starting Tecentriq should be avoided because of their potential interference with the pharmacodynamics activity and efficacy of Tecentriq. However, systemic corticosteroids or immunosuppressants can be used to treat immune-related adverse reactions after starting Tecentriq (See section 4.4).

## 4.6 Fertility, pregnancy and lactation

***Females and Males of Reproductive Potential***

***Fertility***

Based on animal studies, Tecentriq may impair fertility in females of reproductive potential while receiving treatment.

***Contraception***

Female patients of childbearing potential should use highly effective contraception and take active measures to avoid pregnancy while undergoing Tecentriq treatment and for at least 5 months after the last dose (see section 4.4, General, and Embryo-foetal Toxicity).

***Pregnancy***

Tecentriq is contraindicated for use during pregnancy (see section 4.4, Embryo-foetal Toxicity). Based on the mechanism of action, the use of Tecentriq may cause foetal harm. Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway can lead to increased immune-related rejection of the developing foetus resulting in foetal death.

***Lactation***

Women receiving Tecentriq must not breast feed their infants, or for 5 months after the last dose. Monoclonal antibodies, such as Tecentriq, are secreted in milk and may harm the infant. (See section 4.3).

## 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and to use machines have been performed. Infusion reactions may impair a patient's ability to drive or to handle machines.

## 4.8 Undesirable effects

**a. Summary of the safety profile**:

***Clinical Trials***

The corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000).

***Tecentriq monotherapy***

The safety of Tecentriq monotherapy is based on pooled data in 3 178 patients with multiple tumour types, with supporting data from the estimated cumulative exposure in > 13 000 patients across all clinical trials. Table 4 summarises the adverse drug reactions (ADRs) that have been reported in association with the use of Tecentriq.

**b. Tabulated list of adverse reactions**

**Table 4 Summary of adverse reactions occurring in patients treated with Tecentriq monotherapy in clinical trials**

| **ADR (MedDRA)** | **Tecentriq (n=3 178)** | | | |
|---|---|---|---|---|
| **System Organ Class** | All Grades (%) | Grade 3 - 4 (%) | Grade 5 (%) | Frequency (All Grades) |
| **Blood and Lymphatic System Disorders** | | | | |
| Thrombocytopenia [n] | 116 (3,7 %) | 27 (0,8 %) | 0 (0 %) | Common |
| **Cardiac Disorders** | | | | |
| Myocarditis [a] | - | - | - | Rare |
| Pericardial disorders [ee,ff] | 45 (1,4 %) | 22 (0,7 %) | 2 (<0,1 %) | Common |
| **Endocrine Disorders** | | | | |
| Hypothyroidism [b] | 164 (5,2 %) | 6 (0,2 %) | 0 (0 %) | Common |
| Hyperthyroidism [c] | 30 (0,9 %) | 1 (< 0,1 %) | 0 (0 %) | Uncommon |
| Adrenal insufficiency [d] | 11 (0,3 %) | 2 (< 0,1 %) | 0 (0 %) | Uncommon |
| Hypophysitis | 2 (<0,1%) | 0 (0 %) | 0 (0 %) | Rare |
| Diabetes mellitus [e] | 10 (0,3 %) | 6 (0,2 %) | 0 (0 %) | Uncommon |
| **Gastrointestinal Disorders** | | | | |
| Diarrhoea [o] | 626 (19,7 %) | 36 (1,1 %) | 0 (0 %) | Very Common |
| Dysphagia | 82 (2,6 %) | 16 (0,5 %) | 0 (0 %) | Common |
| Colitis [f] | 34 (1,1 %) | 18 (0,6 %) | 0 (0 %) | Common |
| Nausea | 747 (23,5 %) | 35 (1,1 %) | 0 (0 %) | Very Common |
| Vomiting | 477 (15,0 %) | 26 (0,8 %) | 0 (0 %) | Very Common |
| Abdominal pain | 268 (8,4 %) | 34 (1,1 %) | 0 (0 %) | Common |
| Pancreatitis [g] | 18 (0,6 %) | 13 (0,4 %) | 0 (0 %) | Uncommon |
| Oropharyngeal pain [q] | 131 (4,1 %) | 0 (0 %) | 0 (0 %) | Common |
| **General Disorders and Administration** | | | | |
| Chills | 207 (6,5 %) | 2 (< 0,1 %) | 0 (0 %) | Common |
| Fatigue | 1 142 (35,9 %) | 109 (3,4 %) | 0 (0%) | Very Common |

| **ADR (MedDRA)** | **Tecentriq (n=3 178)** | | | |
|---|---|---|---|---|
| **System Organ Class** | All Grades (%) | Grade 3 - 4 (%) | Grade 5 (%) | Frequency (All Grades) |
| Asthenia | 461 (14,5 %) | 63 (2,0 %) | 0 (0 %) | Very Common |
| Influenza like illness | 186 (5,9 %) | 1 (< 0,1 %) | 0 (0 %) | Common |
| Pyrexia | 638 (20,1 %) | 17 (0,5 %) | 0 (0 %) | Very Common |
| Infusion related reaction [h] | 34 (1,1 %) | 5 (0,2 %) | 0 (0 %) | Common |
| **Hepatobiliary Disorders** | | | | |
| Increased ALT | 167 (5,3%) | 46 (1,4 %) | 0 (0 %) | Common |
| Increased AST | 180 (5,7 %) | 46 (1,4 %) | 0 (0 %) | Common |
| Hepatitis [i] | 62 (2,0 %) | 25 (0,8 %) | 1 (< 0,1 %) | Common |
| **Immune System Disorders** | | | | |
| Hypersensitivity | 36 (1,1 %) | 3 (< 0,1 %) | 0 (0 %) | Common |
| **Infections and infestations** | | | | |
| Urinary tract infection [p] | 368 (11,6 %) | 86 (2,7 %) | 0 (0 %) | Very Common |
| **Metabolism and Nutrition Disorders** | | | | |
| Decreased appetite | 810 (25,5 %) | 35 (1,1 %) | 0 (0 %) | Very Common |
| Hypokalaemia [v] | 142 (4,5 %) | 33 (1,0 %) | 0 (0%) | Common |
| Hyponatraemia [w] | 171 (5,4 %) | 98 (3,1 %) | 0 (0 %) | Common |
| Hyperglycaemia | 103 (3,2 %) | 32 (1,0 %) | 0 (0 %) | Common |
| **Musculoskeletal and Connective Tissue Disorders** | | | | |
| Arthralgia | 441 (13,9 %) | 23 (0,7 %) | 0 (0 %) | Very Common |
| Back pain | 487 (15,3 %) | 52 (1,6 %) | 0 (0 %) | Very Common |
| Musculoskeletal pain [r] | 489 (15,4 %) | 36 (1,1 %) | 0 (0 %) | Very Common |
| Myositis [t,u] | 13 (0,4 %) | 5 (0,2 %) | 0 (0 %) | Uncommon |
| **Nervous System Disorders** | | | | |
| Headache | 352 (11,1 %) | 10 (0,3 %) | 0 (0 %) | Very common |

| ADR (MedDRA) | Tecentriq (n=3 178) | | | |
|---|---|---|---|---|
| **System Organ Class** | All Grades (%) | Grade 3 - 4 (%) | Grade 5 (%) | Frequency (All Grades) |
| Guillain-Barré syndrome [j] | 5 (0,2 %) | 4 (0,1 %) | 0 (0 %) | Uncommon |
| Meningoencephalitis [k] | 14 (0,4 %) | 6 (0,2 %) | 0 (0 %) | Uncommon |
| Myasthenic syndrome | 1 (< 0,1 %) | 0 (0 %) | 0 (0 %) | Rare |
| **Renal and urinary disorders** | | | | |
| Increased blood creatinine [aa] | 171 (5,4 %) | 14,0 (0,4 %) | 0 (0 %) | Common |
| Nephritis [s] | 3 (< 0,1 %) | 1 (< 0,1 %) | 0 (0 %) | Rare |
| **Respiratory, Thoracic, and Mediastinal Disorders** | | | | |
| Cough | 660 (20,8 %) | 9 (0,3 %) | 0 (0 %) | Very Common |
| Dyspnoea | 651 (20,5 %) | 117 (3,7 %) | 1 (< 0,1 %) | Very Common |
| Hypoxia | 75 (2,4 %) | 36 (1,1 %) | 0 (0 %) | Common |
| Pneumonitis [l] | 87 (2,7 %) | 27 (0,8 %) | 1 (< 0,1 %) | Common |
| Nasopharyngitis [bb] | 280 (8,8 %) | 0 (0 %) | 0 (0 %) | Common |
| **Skin and Subcutaneous Tissue Disorders** | | | | |
| Rash [m] | 619 (19,5 %) | 34 (1,1 %) | 1 (< 0,1 %) | Very Common |
| Pruritus | 400 (12,6 %) | 7 (0,2 %) | 0 (0 %) | Very Common |
| Dry skin | 187 (5,9 %) | 1 (< 0,1 %) | 0 (0 %) | Common |
| Psoriatic conditions [cc] | 19 (0,6 %) | 2 (< 0,1 %) | 0 (0 %) | Uncommon |
| Severe cutaneous adverse reactions [dd] | 22 (0,7 %) | 3 (< 0,1 %) | 1 (< 0,1 %) | Uncommon |
| **Vascular Disorders** | | | | |
| Hypotension | 102 (3,2 %) | 20 (0,6 %) | 0 (0 %) | Common |

[a.] Reported in studies outside the pooled dataset. The frequency is based on the program-wide exposure.

b. Includes reports of hypothyroidism, increased blood thyroid stimulating hormone, decreased blood thyroid stimulating hormone, thyroiditis, autoimmune hypothyroidism, euthyroid sick syndrome, myxoedema, abnormal thyroid function test, acute thyroiditis, decreased thyroxine

c. Includes reports of hyperthyroidism, Basedow's disease, endocrine ophthalmopathy, exophthalmos

d. Includes reports of adrenal insufficiency, primary adrenal insufficiency

e. Includes reports of diabetes mellitus, type 1 diabetes mellitus, diabetic ketoacidosis and ketoacidosis

f. Includes reports of colitis, autoimmune colitis, colitis ischaemic, colitis microscopic, ulcerative colitis

g. Includes reports of pancreatitis, autoimmune pancreatitis, acute pancreatitis, increased lipase and increased amylase

h. includes infusion related reaction and cytokine release syndrome

i. Includes reports of ascites, autoimmune hepatitis, hepatocellular injury, hepatitis, acute hepatitis, hepatotoxicity, liver disorder, drug-induced liver injury, hepatic failure, hepatic steatosis, hepatic lesion, esophageal varices haemorrhage, esophageal varices

j. Includes reports of Guillain-Barré syndrome and demyelinating polyneuropathy

k. Includes reports of encephalitis, meningitis, photophobia

l. Includes reports of pneumonitis, lung infiltration, bronchiolitis, interstitial lung disease, radiation pneumonitis.

m. Includes reports of rash, maculo-papular rash, erythema, pruritic rash, acneiform dermatitis, eczema, dermatitis, erythematous rash, skin ulcer, papular rash, folliculitis, macular rash, skin exfoliation, erythema multiforme, pustular rash, bullous dermatitis, furuncle, acne, drug eruption, palmar-plantar erythrodysaesthesia syndrome, seborrhoeic dermatitis, allergic dermatitis, generalised rash, erythema of eyelid, skin toxicity, toxic epidermal necrolysis, toxic skin eruption, exfoliative generalised dermatitis, exfoliative rash, eyelid rash, fixed eruption, generalised erythema, papulosquamous rash, vesicular rash

n. Includes reports of thrombocytopenia and decreased platelet count

o. Includes reports of diarrhoea, frequent bowel movements, and gastrointestinal hypermotility

p. Includes reports of urinary tract infection, cystitis, pyelonephritis, Escherichia urinary tract infection, acute pyelonephritis, bacterial urinary tract infection, kidney infection, fungal urinary tract infection, pseudomonal urinary tract infection

q. Includes reports of oropharyngeal pain, throat irritation, oropharyngeal discomfort

r. Includes reports of musculoskeletal pain, myalgia, bone pain

s. Includes reports of nephritis and Henoch-Schonlein Purpura nephritis

t. Includes reports of myositis, rhabdomyolysis, polymyalgia rheumatica, dermatomyositis, muscle abscess, present myoglobin urine

u. Fatal cases have been reported in studies outside the pooled dataset

v. Includes reports of hypokalaemia and decreased blood potassium

[w.] Includes reports of hyponatraemia and blood sodium decreased

[x.] Includes reports of hypoxia, oxygen saturation decreased, $PO_2$ decreased

[y.] Includes reports of hypophysitis and temperature regulation disorder

[z.] Includes report of myasthenia gravis

[aa.] Includes reports of blood creatinine increased and hypercreatininaemia

[bb.] Includes reports of nasopharyngitis, nasal congestion and rhinorrhoea

[cc.] Includes reports of dermatitis psoriasiform and psoriasis.

[dd.] Includes reports of bullous dermatitis, exfoliative rash, erythema multiforme, generalised exfoliative dermatitis, toxic skin eruption, toxic epidermal necrolysis

[ee.] Includes reports of pericarditis, pericardial effusion, cardiac tamponade and constrictive pericarditis

[ff.] Reported from post marketing experience outside the pooled dataset. The frequency is based on the program-wide exposure.

***Tecentriq combination therapy***

Additional ADRs identified in clinical trials (not reported in monotherapy trials) associated with the use of Tecentriq in combination therapy across multiple indications are summarised in Table 5. ADRs with a clinically relevant difference when compared to monotherapy (refer to Table 4) are also presented.

**Table 5: Summary of adverse reactions occurring in patients treated with Tecentriq combination therapy in clinical trials**

| **ADR (MedDRA)** | **Tecentriq + Combination Treatments (n = 4 371)** | | | |
|---|---|---|---|---|
| **System Organ Class** | **All Grades (%)** | **Grade 3-4 (%)** | **Grade 5 (%)** | **Frequency (All Grades)** |
| **Blood and Lymphatic System Disorders** | | | | |
| Anaemia[*] | 1 608 (36,8 %) | 631 (14,4 %) | 0 (0 %) | Very Common |
| Lymphopenia[*, k] | 145 (3,3 %) | 63 (1,4 %) | 0 (0 %) | Common |
| Neutropenia[*,+,a] | 1 565 (35,8 %) | 1 070 (24,5 %) | 6 (0, 1 %) | Very Common |

| ADR (MedDRA) | Tecentriq + Combination Treatments (n = 4 371) | | | |
|---|---|---|---|---|
| **System Organ Class** | **All Grades (%)** | **Grade 3-4 (%)** | **Grade 5 (%)** | **Frequency (All Grades)** |
| Thrombocytopenia[*,‡,b] | 1 211 (27,7 %) | 479 (11,0 %) | 1 (< 0, 1 %) | Very Common |
| Leukopenia[*,l] | 571 (13,1 %) | 245 (5,6 %) | 0 (0 %) | Very common |
| **Endocrine Disorders** | | | | |
| Hypothyroidism[*,‡,c] | 586 (13,4 %) | 9 (0,2 %) | 0 (0 %) | Very Common |
| Hyperthyroidism[‡] | 193 (4,4 %) | 7 (0,2 %) | 0 (0 %) | Common |
| Adrenal insufficiency[+,‡,d] | 40 (0,9 %) | 8 (0,2 %) | 1 (< 0,1 %) | Uncommon |
| Hypophysitis[‡,e] | 13 (0,3 %) | 5 (0,1 %) | 0 (0 %) | Uncommon |
| **Gastrointestinal Disorders** | | | | |
| Constipation[*] | 1 123 (25,7 %) | 24 (0,5 %) | 0 (0 %) | Very Common |
| Stomatitis[*] | 351 (8,0 %) | 23 (0,5 %) | 0 (0 %) | Common |
| **General Disorders and Administration Site Conditions** | | | | |
| Peripheral oedema[*] | 451 (10,3 %) | 11 (0,3 % | 0 (0 %) | Very Common |
| **Infections & Infestations** | | | | |
| Lung infection[+,*,h] | 564 (12,9 %) | 226 (5,2 %) | 26 (0,6 %) | Very Common |
| **Investigations** | | | | |
| Increased blood alkaline phosphatase | 200 (4,6 %) | 26 (0,6 %) | 0 (0 %) | Common |
| **Metabolism and Nutrition Disorders** | | | | |
| Hypomagnesaemia[*] | 403 (9,2 %) | 22 (0,5 %) | 0 (0 %) | Common |
| **Nervous System Disorders** | | | | |

| ADR (MedDRA) | Tecentriq + Combination Treatments (n = 4 371) | | | |
|---|---|---|---|---|
| **System Organ Class** | **All Grades (%)** | **Grade 3-4 (%)** | **Grade 5 (%)** | **Frequency (All Grades)** |
| Dizziness[*] | 408 (9,3 %) | 9 (0,2 %) | 0 (0 %) | Common |
| Dysgeusia[*] | 269 (6,2 %) | 0 (0,0 %) | 0 (0 %) | Common |
| Peripheral neuropathy[*,f] | 1 007 (23,0 %) | 107 (2,4 %) | 0 (0 %) | Very Common |
| Syncope[*] | 68 (1,6 %) | 36 (0,8 %) | 0 (0 %) | Common |
| **Renal and Urinary Disorders** | | | | |
| Nephritis [‡,l] | 23 (0,5 %) | 15 (0,3 %) | 0 (0 %) | Uncommon |
| Proteinuria[*,g] | 359 (8,2 %) | 61 (1,4 %) | 0 (0 %) | Common |
| **Respiratory, Thoracic and Mediastinal Disorders** | | | | |
| Dysphonia[*] | 236 (5,4 %) | 4 (0,1 %) | 0 (0 %) | Common |
| Nasopharyngitis [o] | 442 (10,1 %) | 1 (< 0,1 %) | 0 (0 %) | Very common |
| **Skin and Subcutaneous Tissue disorders** | | | | |
| Alopecia [n] | 1 152 (26,4 %) | 3 (< 0,1 % | 0 (0 %) | Very common |
| Severe cutaneous adverse reactions [p] | 27 (0,6 %) | 8 (0,2 %) | 0 (0 %) | Uncommon |
| **Vascular Disorders** | | | | |
| Hypertension[*,m] | 611 (14,0 %) | 258 (5,9 %) | 0 (0 %) | Very common |

∗ ADR occurring at a frequency ≥ 5 % (All grades) or ≥ 2 % (Grades 3-4) compared to the control arm.

+ Fatal cases of neutropenia, adrenal insufficiency and lung infection have been observed when Tecentriq is given in combination treatment

‡ Observed rate in the combination represents a clinically relevant difference in comparison to Tecentriq monotherapy

a. Includes reports of neutropenia, neutrophil count decreased, febrile neutropenia, neutropenic sepsis, granulocytopenia

b. Includes reports of thrombocytopenia and decreased platelet count

c. Includes reports of hypothyroidism, increased blood thyroid stimulating hormone, decreased blood thyroid stimulating hormone, autoimmune thyroiditis, goitre, thyroiditis, decreased free thyroxine, decreased free tri−iodothyronine, thyroid disorder, increased free thyroxine, increased thyroxine, decreased tri−iodothyronine, increased free tri−iodothyronine, abnormal blood thyroid stimulating hormone, euthyroid sick syndrome, myxedema coma, abnormal thyroid function test, decreased thyroxine, abnormal tri−iodothyronine

d. Includes reports of adrenal insufficiency, acute adrenocortical insufficiency, secondary adrenocortical insufficiency, adrenocorticotropic abnormal hormone stimulation test, addison's disease, adrenalitis, adrenocorticotropic hormone deficiency

e. Includes reports of hypophysitis and temperature regulation disorder

f. Includes reports of peripheral neuropathy, peripheral sensory neuropathy, polyneuropathy, herpes zoster, peripheral motor neuropathy, autoimmune neuropathy, neuralgic amyotrophy, peripheral sensorimotor neuropathy, axonal neuropathy, lumbosacral plexopathy, neuropathic arthropathy and toxic neuropathy, peripheral nerve infection

g. Includes reports of proteinuria, protein urine present, haemoglobinuria, and nephrotic syndrome

h. Includes reports of pneumonia, bronchitis, lower respiratory tract infection, infective exacerbation of chronic obstructive airway disease, infectious pleural effusion, atypical pneumonia, lung abscess, pleural infection, pyopneumothorax

i. Includes reports of decreased white blood cell count and leukopenia

j. Includes reports of hypomagnesaemia and decreased blood magnesium

k. Includes reports of lymphopenia and decreased lymphocyte count

l. Includes reports of nephritis, tubulointerstitial nephritis, autoimmune nephritis, allergic nephritis, glomerulonephritis, nephrotic syndrome and mesangioproliferative glomerulonephritis

m. Includes reports of hypertension, increased blood pressure, hypertensive crisis, increased blood pressure systolic, diastolic hypertension, blood pressure inadequately controlled and hypertensive retinopathy

n. Includes reports of alopecia, madarosis, alopecia areata, alopecia totalis and hypotrichosis

o. Includes reports of nasopharyngitis, nasal congestion and rhinorrhoea

[p.] Includes reports of bullous dermatitis, exfoliative rash, erythema multiforme, generalised dermatitis exfoliative, toxic skin eruption, Stevens-Johnson syndrome, drug reaction with eosinophilia and systemic symptoms, toxic epidermal necrolysis, cutaneous vasculitis

**c. Additional information for selected adverse reactions**

The data below reflect information for significant adverse reactions for Tecentriq monotherapy. Details for the significant adverse reactions for Tecentriq when given in combination are presented if clinically relevant differences were noted in comparison to Tecentriq monotherapy. See section 4.4, General, for management of the following:

***Immune-mediated pneumonitis***

Pneumonitis occurred in 2,7 % (87/3 178) of patients who received Tecentriq monotherapy. Of the 87 patients, one event was fatal. The median time to onset was 3,4 months (range: 0,1 to 24,8 months). The median duration was 1,4 months (range 0 to 21,2+ months; + denotes a censored value). Pneumonitis led to discontinuation of Tecentriq in 12 (0,4 %) patients. Pneumonitis requiring the use of corticosteroids occurred in 1,6 % (51/3 178) of patients receiving Tecentriq.

***Immune-mediated hepatitis***

Hepatitis occurred in 2,0 % (62/3 178) of patients who received Tecentriq monotherapy. Of the 62 patients, two events were fatal. The median time to onset was 1,5 months (range 0,2 to 18,8 months). The median duration was 2,1 months (range 0 to 22,0+ months; + denotes a censored value). Hepatitis led to discontinuation of Tecentriq in 6 (0,2 %) patients. Hepatitis requiring the use of corticosteroids occurred in 0,6 % (18/3 178) of patients receiving Tecentriq.

***Immune-mediated colitis***

Colitis occurred in 1,1 % (34/3 178) of patients who received Tecentriq. The median time to onset was 4,7 months (range 0,5 to 17,2 months). The median duration was 1,2 months (range: 0,1 to 17,8+ months; + denotes a censored value). Colitis led to discontinuation of Tecentriq in 8 (0,3 %) patients. Colitis requiring the use of corticosteroids occurred in 0,6 % (19/3 178) of patients receiving Tecentriq.

***Immune-mediated endocrinopathies***

*Thyroid Disorders*

Hypothyroidism occurred in 5,2 % (164/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 4,9 months (range 0 to 31,3 months).

Hyperthyroidism occurred in 0,9 % (30/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 2,1 months (range 0,7 to 15,7 months). The median duration was 2,6 months (range: 0+ to 17,1+ months; + denotes a censored value).

Hyperthyroidism occurred in 4,9 % (23/473) of patients who received Tecentriq in combination with carboplatin and nab-paclitaxel. Hyperthyroidism led to discontinuation in 1 (0,2 %) patient.

*Adrenal Insufficiency*

Adrenal insufficiency occurred in 0,4 % (12/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 5,5 months (range: 0,1 to 19,0 months). The median duration was 16,8 months (range: 0 to 16,8 months). Adrenal insufficiency led to discontinuation of Tecentriq in 1 (< 0,1 %) patient. Adrenal insufficiency requiring the use of corticosteroids occurred in 0,3 % (9/3 178) of patients receiving Tecentriq.

Adrenal insufficiency occurred in 1,5 % (7/473) of patients who received Tecentriq in combination with carboplatin and nab-paclitaxel. Adrenal insufficiency requiring the use of corticosteroids occurred in 0,8 % (4/473) of patients receiving Tecentriq in combination with carboplatin and nab-paclitaxel.

*Hypophysitis*

Hypophysitis occurred in < 0,1 % (2/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 7,2 months (range: 0,8 to 13,7 months). One patient required the use of corticosteroids and treatment with Tecentriq was discontinued.

Hypophysitis occurred in 0,8 % (3/393) of patients who received Tecentriq with bevacizumab, paclitaxel, and carboplatin. The median time to onset was 7,7 months (range: 5,0 to 8,8 months). Two patients required the use of corticosteroids. Hypophysitis led to the discontinuation of treatment in one patient.

*Diabetes Mellitus*

Diabetes mellitus occurred in 0,3 % (11/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 4,2 months (range 0,1 to 9,9 months). The median duration was 1,6 months (range: 0,1 to 15,2+ months; + denotes a censored value). Diabetes mellitus led to the discontinuation of Tecentriq in 3 (< 0,1 %) patients.

***Immune-mediated meningoencephalitis***

Meningoencephalitis occurred in 0,4 % (13/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 0,5 months (range 0 to 12,5 months). The median duration was 0,7 months (range 0,2 to 14,5+ months; + denotes a censored value). Meningoencephalitis requiring the use of corticosteroids occurred in 0,2 % (6/3 178) of patients receiving Tecentriq and led to discontinuation of Tecentriq in 4 (0,1 %) patients.

***Immune-mediated neuropathies***

Neuropathies, including Guillain-Barré syndrome and demyelinating polyneuropathy, occurred in 0,2 % (5/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 7,0 months (range: 0,6 to 8,1 months). The median duration was 8,0 months (0,6 to 8,3+ months; + denotes a censored value). Guillain-Barré syndrome led to the discontinuation of Tecentriq in 1 (< 0,1 %) patient. Guillain-Barré syndrome requiring the use of corticosteroids occurred in < 0,1 % (2/3 178) of patients receiving Tecentriq.

***Immune-mediated pancreatitis***

Pancreatitis, including increased amylase and increased lipase, occurred in 0,6 % (18/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 5,0 months (range: 0,3 to 16,9 months). The median duration was 0,8 months (range 0,1 to 12,0+ months; + denotes a censored value). Pancreatitis led to discontinuation of Tecentriq in 3 (< 0,1 %) patients. Pancreatitis requiring the use of corticosteroids occurred in 0,1 % (4/3 178) of patients receiving Tecentriq.

***Immune-mediated myositis***

Myositis occurred in 0,4 % (13/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 5,1 months (range: 0,7 to 11,0 months). The median duration was 5,0 months (range 0,7 to 22,6+ months, + denotes a censored value). Myositis led to discontinuation

of Tecentriq in 1 (< 0,1 %) patient. Myositis requiring the use of corticosteroids occurred in 0,2 % (7/3 178) of patients receiving Tecentriq.

***Immune-mediated nephritis***

Nephritis, occurred in < 0,1 % (3/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 13,1 months (range: 9,0 to 17,5 months). The median duration was 2,8 days (range 0,5 to 9,5+ months; + denotes a censored value). Nephritis led to discontinuation of Tecentriq in 2 (< 0,1 %) patients. One patient required the use of corticosteroids.

***Immune-mediated severe cutaneous adverse reactions***

Severe cutaneous adverse reactions (SCARs) occurred in 0,7 % (22/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 5,9 months (range 0,1 to 15,5 months). The median duration was 1,6 months (range 0 to 22,1+ months; + denotes a censored value). SCARs led to discontinuation of Tecentriq in 3 (< 0,1 %) patients. SCARs requiring the use of systemic corticosteroids occurred in 0,2 % (6/3 178) of patients receiving Tecentriq monotherapy.

***Immune-mediated pericardial disorders***

Pericardial disorders occurred in 1,4 % (45/3 178) of patients who received Tecentriq monotherapy. The median time to onset was 1,4 months (range 0,2 to 17,5 months). The median duration was 1,4 months (range 0 to 19,3 months). Pericardial disorders led to discontinuation of Tecentriq in 3 (<0,1 %) patients. Pericardial disorders requiring the use of corticosteroids occurred in 0,2 % (7/3178) patients.

***Post Marketing Experience***

Cases of pericardial disorders have been reported during post-marketing use of Tecentriq (see section 4.4).

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reaction

Report Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

### 4.9 Overdose

There is no information on overdose with Tecentriq.

In case of overdose, patients should be closely monitored for signs or symptoms of adverse reactions, and appropriate symptomatic treatment instituted.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agent, humanised immunoglobulin G1 (IgG1) monoclonal antibody. ATC Code – L01FF05

***Mechanism of action***

Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells suppresses cytotoxic T-cell activity through the inhibition of T-cell proliferation and cytokine production. PD-L1 may be expressed on tumour cells and tumour-infiltrating immune cells, and can contribute to the inhibition of the antitumour immune response in the microenvironment.

Atezolizumab is an Fc-engineered humanised immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to PD-L1 and blocks interactions with the PD-1 and B7.1 receptors, releasing PD-L1 / PD-1 pathway-mediated inhibition of the immune response, including reactivating the antitumor immune response. Atezolizumab leaves the PD-L2/PD-1 interaction intact. In syngeneic mouse tumour models, blocking PD-L1 activity resulted in decreased tumour growth.

### 5.2 Pharmacokinetic properties

The pharmacokinetics of atezolizumab have been characterised in patients in multiple clinical trials at doses 0,01 mg/kg to 20 mg/kg every 3 weeks including the fixed dose of 1 200 mg. Exposure to atezolizumab increased dose proportionally over the dose range of 1 mg/kg to 20 mg/kg. A population analysis that included 472 patients described atezolizumab

pharmacokinetics for the dose range: 1 - 20 mg/kg with a linear two-compartment disposition model with first-order elimination. The pharmacokinetic properties of atezolizumab 840 mg administered every 2 weeks and 1 200 mg administered every 3 weeks, are comparable. A population pharmacokinetic analysis suggests that steady-state is obtained after 6 to 9 weeks after multiple doses. The maximum systemic accumulation ratio across dosing regimens is 3,3.

Based on an analysis of exposure, safety and efficacy data, the following factors have no clinically relevant effect: age (21-89 years), body weight, gender, positive ADA status, albumin levels, tumour burden, region or ethnicity, renal impairment, mild hepatic impairment, level of PD-L1 expression, or ECOG status.

*Absorption*

Tecentriq is administered as an IV infusion. There have been no studies performed with other routes of administration.

*Distribution*

A population pharmacokinetic analysis indicates that central compartment volume of distribution (V1) is 3,28 L and volume at steady-state (Vss) is 6,91 L in the typical patient.

*Metabolism*

The metabolism of Tecentriq has not been directly studied. Antibodies are cleared principally by catabolism.

*Elimination*

A population pharmacokinetic analysis indicates that the clearance of atezolizumab is 0,200 L/day and the typical terminal elimination half-life ($t_{1/2}$) is 27 days.

***Pharmacokinetics in Special Populations***

***Paediatric population***

The pharmacokinetic results from one early-phase, multi-centre open-label study that was conducted in paediatric (<18 years, n=69) and young adult patients (18-30 years, n=18), show that the clearance and volume of distribution of atezolizumab were comparable between paediatric patients receiving 15 mg/kg and young adult patients receiving 1 200 mg of

atezolizumab every 3 weeks when normalised by body weight, with exposure trending lower in paediatric patients as body weight decreased. These differences were not associated with a decrease in atezolizumab concentrations below the therapeutic target exposure. Data for children <2 years is limited thus no definitive conclusions can be made.

***Geriatric population***

No dedicated studies of Tecentriq have been conducted in geriatric patients. The effect of age on the pharmacokinetics of atezolizumab was assessed in a population pharmacokinetic analysis. Age was not identified as a significant covariate influencing atezolizumab pharmacokinetics based on patients of age range of 21-89 years (n=472), and median of 62 years of age. No clinically important difference was observed in the pharmacokinetics of atezolizumab among patients < 65 years (n=274), patients between 65–75 years (n=152) and patients > 75 years (n=46) (see section 4.2; Special Dosage Instructions).

***Renal impairment***

No dedicated studies of Tecentriq have been conducted in patients with renal impairment. In the population pharmacokinetic analysis, no clinically important differences in the clearance of atezolizumab were found in patients with mild (eGFR 60 to 89 mL/min/1,73 $m^2$; n=208) or moderate (eGFR 30 to 59 mL/min/1,73 $m^2$. n=116) renal impairment compared to patients with normal (eGFR greater than or equal to 90 mL/min/1,73 $m^2$; n=140) renal function. Only a few patients had severe renal impairment (eGFR 15 to 29 mL/min/1,73 $m^2$; n=8) (see section 4.2; Special Dosage Instructions).

***Hepatic impairment***

No dedicated studies of Tecentriq have been conducted in patients with hepatic impairment. In the population pharmacokinetic analysis, there were no clinically important differences in the clearance of atezolizumab between patients with mild hepatic impairment (bilirubin ≤ ULN and AST > ULN or bilirubin > 1,0 to 1,5· ULN and any AST, or moderate hepatic impairment (bilirubin > 1,5 to 3x ULN and any AST). No data are available in patients with severe (bilirubin > 3,0· ULN

and any AST) hepatic impairment. Hepatic impairment was defined by the National Cancer Institute (NCI) criteria of hepatic dysfunction (see section 4.2; Special Dosage Instructions).

***Immunogenicity***

There is the potential for immune response to atezolizumab. Across multiple phase III studies, 13,1 % to 36,4 % of patients developed treatment-emergent anti-drug antibodies (ADAs) and 4,3 % to 19,7 % of patients developed neutralising antibodies (NAbs). ADA and NAb status appeared to have no clinically relevant impact on pharmacokinetics. Although some variability was observed across the studies, overall, ADA positivity appeared to have no clinically relevant impact on efficacy.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

*Excipients*:

Glacial acetic acid,

L-histadine,

polysorbate 20,

sucrose,

water for injections.

### 6.2 Incompatibilities

No incompatibilities have been observed between Tecentriq and IV bags with product-contacting surfaces of polyvinyl chloride (PVC), polyethylene (PE) or polyolefin bags. In addition, no incompatibilities have been observed with in-line filter membranes composed of polyethersulfone or polysulfone, and infusion sets and other infusion aids composed of PVC, PE, polybutadiene, or polyetherurethane.

## 6.3 Shelf life

36 months

## 6.4 Special precautions for storage

Store between 2 - 8 °C. Do not freeze. Do not shake.

Keep the vial in the outer carton, in order to protect from light, until required for use.

Keep out of reach of children.

Do not use after the expiry date (EXP) shown on the pack.

The diluted solution for infusion should be used immediately. If the solution is not used immediately, it can be stored for up to 30 days at 2°C - 8°C, or 8 hours at ambient temperature (≤ 25°C), if prepared under aseptic conditions.

*Disposal of unused/expired medicines*

The release of pharmaceuticals in the environment should be minimised. Medicines should not be disposed of via wastewater and disposal through household waste should be avoided. Use established “collection systems”, if available in your location.

## 6.5 Nature and contents of container

Type I glass-vial with a butyl rubber stopper containing 20 mL of solution.

Pack of one vial.

## 6.6 Special Instructions for Use, Handling and Disposal

*Instructions for dilution*

Tecentriq should be prepared by a healthcare professional using aseptic technique. Use a sterile needle to prepare Tecentriq. Withdraw the required volume of Tecentriq liquid concentrate from the vial and dilute to the required administration volume with 0,9 % sodium chloride solution. Dilute with 0,9 % Sodium Chloride Injection only. After dilution, the final concentration of the diluted solution should be between 3,2 and 16,8 mg/mL.

This medicine must not be mixed with other medicines.

No preservative is used in Tecentriq therefore each vial is for single use only. Discard any unused portion.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

Roche Products (Pty) Ltd

90 Bekker Road, Hertford Office Park,

Building E, Vorna Valley, Midrand,

Johannesburg, 1686

South Africa

Roche Ethical Assistance Line (REAL) toll-free: 0800 21 21 25

## 8. REGISTRATION NUMBERS

**Tecentriq® 840 mg** 54/30.1/0060

**Tecentriq® 1 200 mg** 54/30.1/0061

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 29 September 2020

## 10. DATE OF REVISION OF THE TEXT: 14 March 2023

| | | |
|---|---|---|
| Tecentriq® 1 200 mg/20 mL: | Namibia: NS2 22/30.1/0025 | Botswana: S2 BOT2103779 |
| Tecentriq® 840 mg/14 mL: | Namibia: NS2 22/30.1/0024 | Botswana: S2 BOT2103778 |

**Approved Manufacturers:**

Roche Diagnostics GmbH

Sandhofer Straße 116, 68305 Mannheim

Germany

F. Hoffmann-La Roche Ltd

Wurmisweg, CH-4303 Kaiseraugst

Switzerland

# PATIENT INFORMATION LEAFLET

## SCHEDULING STATUS

S4

**Tecentriq® 840 mg** (Concentrate for solution for infusion)

**Tecentriq® 1 200 mg** (Concentrate for solution for infusion)

The active substance is atezolizumab

Contains sugar (sucrose 21 mg/mL)

**Read all of this leaflet carefully before you start taking Tecentriq**

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.

**What is in this leaflet**



## 1. What Tecentriq is and what it is used for

**What Tecentriq is**

Tecentriq is an anti-cancer medicine that contains the active substance atezolizumab. It belongs to a group of medicines called monoclonal antibodies. A monoclonal antibody is a type of protein designed to recognise and attach to a specific target in the body.

**What Tecentriq is used for**

Tecentriq is used to treat adults with:

- a cancer that affects the bladder and the urinary system, called urothelial carcinoma. It is used when this cancer has:

- spread to other parts of the body
- come back after previous treatment
- or, if you cannot receive cisplatin treatment, and your doctor has tested your cancer and found high levels of a specific protein in your body called programmed death-ligand 1 (PD-L1).

- a cancer that affects the lungs, called non-small cell lung cancer. It is used when this cancer has:
  - spread to other parts of the body
  - come back after previous treatment.
- A cancer that affects the breast, called triple negative breast cancer.
- A cancer of the liver which cannot be removed surgically, called hepatocellular carcinoma. You will receive Tecentriq with another medicine called bevacizumab.

**How Tecentriq works**

Tecentriq works by attaching to a specific protein in your body called programmed death-ligand 1 (PD-L1). This protein suppresses the body's immune (defence) system, thereby protecting cancer cells from being attacked by the immune cells. By attaching to the protein, Tecentriq helps your immune system to fight your cancer.

## 2. Tecentriq should not be administered to you

**Do not receive Tecentriq**

- If you are allergic to atezolizumab or to any of the other ingredients of this medicine, listed in "What Tecentriq contains". If you are not sure, talk to your doctor or nurse before taking Tecentriq.
- If you need to be vaccinated or have been given a live, attenuated vaccine. You can only be administered Tecentriq two months after you were last vaccinated.
- If you are pregnant or breastfeeding your baby.

**Warnings and precautions**

Talk to your doctor or healthcare professional before you receive Tecentriq if you:

- have an auto-immune disease (a condition where the body attacks its own cells)
- have been told that your cancer has spread to your brain
- have any history of inflammation of your lungs (called pneumonitis)
- have or have had chronic viral infection of the liver, including hepatitis B (HBV) or hepatitis C (HCV)
- have human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS)
- have an abnormally functioning thyroid gland
- have had serious side effects because of other antibody therapies that help your immune system to fight cancer
- have been given medicines to stimulate your immune system
- have been given medicines to suppress your immune system

If any of the above applies to you (or you are not sure), talk to your doctor or nurse before you are given Tecentriq.

Tecentriq may cause some side effects that you must tell your doctor about straight away. They may happen weeks or months after your last dose. Tell your doctor straight away if you notice any of the symptoms below:

- inflammation of the lung (pneumonitis): symptoms may include new or worsening cough, shortness of breath, and chest pain
- inflammation of the liver (hepatitis): symptoms may include yellowing of skin or eyes, nausea, vomiting, bleeding or bruising, dark urine, and stomach pain
- inflammation of the intestines (colitis): symptoms may include diarrhoea (watery, loose or soft stools), blood in stools, and stomach pain.
- inflammation of the thyroid, adrenal glands and the pituitary gland (hypothyroidism, hyperthyroidism, adrenal insufficiency or hypophysitis): symptoms may include tiredness,

weight loss, weight gain, change in mood, hair loss, constipation, dizziness, headaches, increased thirst, increased urination and changes in vision.

- type 1 diabetes, including acid in the blood produced from diabetes (diabetic ketoacidosis): symptoms may include feeling more hungry or thirsty than usual, need to urinate more often, weight loss, and feeling tired
- inflammation of the brain (encephalitis) or inflammation of the membrane around the spinal cord and brain (meningitis): symptoms may include neck stiffness, headache, fever, chills, vomiting, eye sensitivity to light, confusion and sleepiness
- inflammation or problems of the nerves (neuropathy): symptoms may include muscle weakness and numbness, tingling in hands and feet
- inflammation of the pancreas (pancreatitis): symptoms may include abdominal pain, nausea and vomiting
- inflammation of the heart muscle (myocarditis): symptoms may include shortness of breath, decreased exercise tolerance, feeling tired, chest pain, swelling of the ankles or legs, irregular heart beat, and fainting
- inflammation of the thin, sac-like membrane surrounding the heart (pericardium). The most common symptom is a sharp, stabbing chest pain that may travel to the left shoulder and neck.
- inflammation of the muscles (myositis); symptoms may include muscle weakness, fatigue after walking or standing, tripping or falling, and trouble swallowing or breathing
- severe reactions associated with infusion (events occurring during the infusion or within one day of the infusion): may include fever, chills, shortness of breath and flushing
- you experience or have previously experienced a combination of any of the following symptoms: rash, red skin, blistering of the lips eyes and mouth, skin peeling, high fever, flu-like symptoms, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes (signs of severe skin reactions), see section 4, Possible side effects. If you experience any of these effects your doctor may stop your treatment with Tecentriq and ask you to see a dermatologist.

If you notice any of the symptoms above, tell your doctor straight away.

Do not try to treat yourself with other medicines. Your doctor may:

- Give you other medicines to prevent complications and reduce symptoms.
- Delay giving your next dose of Tecentriq
- Stop your treatment with Tecentriq.

**Tests and checks**

Before your treatment, your doctor will check your general health. You will also have blood tests during your treatment.

**Children and adolescents**

This medicine should not be given to children or adolescents below 18 years of age. This is because the effects of Tecentriq in this age group are not known.

**Other medicines and Tecentriq**

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, including herbal medicines.

**Pregnancy and Breastfeeding**

If you are pregnant or breastfeeding, think you might be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

**Contraception**

- You will not be given Tecentriq if you are pregnant. This is because the effect of Tecentriq could harm your unborn baby.
- If you could become pregnant, you must use effective contraception;
  - while you are being treated with Tecentriq and
  - for 5 months after the last dose.

**Pregnancy**

- Women who are pregnant or plan to be come pregnant must not use Tecentriq (see" Do not receive Tecentriq"). This is because Tecentriq could harm your unborn baby.
- If you become pregnant while you are being treated with Tecentriq tell your doctor.

**Breastfeeding**

Women receiving Tecentriq should not breastfeed their babies, nor for 5 months after the last infusion. This type of medicine is likely to be excreted in breast milk and may harm your baby.

**Driving and using machines**

Tecentriq has an influence on your ability to drive and use machines. If you feel tired, do not drive or use machines until you feel better. This is more likely to occur shortly after your infusion has been given.

Tecentriq contains sugar (sucrose) which may have an effect on the control of your blood sugar if you have diabetes mellitus.

## 3. How you are given Tecentriq

Do not share medicines prescribed for you with any other person.

Always follow your doctor's instruction exactly. You should check with your doctor or pharmacist if you are unsure.

**How much Tecentriq is given**

The recommended dose is:

- 840 milligrams (mg) every 2 weeks
- 1 200 milligrams (mg) every 3 weeks or
- 1 680 milligrams (mg) every 4 weeks.

You will not be expected to give yourself Tecentriq. It will be given to you by a person who is qualified to do so.

**How Tecentriq is given**

Tecentriq is given as a drip into a vein (an intravenous infusion).

Your first infusion will be given over 60 minutes.

- Your doctor will monitor you carefully during the first infusion.
- If you do not have an infusion reaction during the first infusion, the next infusions will be given to you over a period of 30 minutes.

Your doctor will tell you how long your treatment with Tecentriq will last. Do not stop treatment early after receiving Tecentriq.

If you have the impression that the effect of Tecentriq is too strong or too weak, tell your doctor or pharmacist.

**If you receive more Tecentriq than you should**

If you receive more Tecentriq than you should, talk to a doctor straight away. Take the medicine package and this leaflet with you.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

**If you miss a dose of Tecentriq**

If you miss an appointment, make another one straight away. For the treatment to be fully effective, it is very important to keep having the infusions.

**Effects when treatment with Tecentriq is stopped**

Do not stop treatment with Tecentriq unless you have discussed this with your doctor. This is because stopping treatment may stop the effect of the medicine.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

## 4. Possible side effects

Tecentriq can have side effects.

Not all side effects reported for Tecentriq are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other healthcare professional for advice.

**Severe skin reactions**

If you get a severe skin reaction, tell your doctor immediately.

The signs may include:

- A severe rash that develops quickly, with blisters or peeling of the skin and possibly blisters in the mouth (Stevens-Johnson syndrome and toxic epidermal necrolysis which are also known as SJS and TEN).
- A combination of any of the following symptoms: widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome).

**Frequent**

- fever
- nausea
- vomiting
- feeling very tired with no energy (fatigue)
- lack of energy
- itching of the skin
- diarrhoea
- joint pain
- rash
- loss of appetite
- shortness of breath
- urinary tract infection
- back pain
- cough
- headache
- leukopenia

- peripheral oedema
- alopecia
- hypertension
- inflammation of the lungs
- low oxygen levels which may cause shortness of breath as a consequence of inflamed lungs (pneumonitis)
- stomach pain
- inflammation of the liver
- elevated liver enzymes (shown in tests) - may be a sign of an inflamed liver
- difficulty swallowing
- blood tests showing low levels of potassium (hypokalaemia) or sodium (hyponatraemia)
- low blood pressure (hypotension)
- underactive thyroid gland (hypothyroidism)
- allergic reaction (infusion-related reaction or hypersensitivity)
- flu-like illness
- pain in the muscles and bones
- chills
- overactive thyroid gland (hyperthyroidism)
- inflammation of the intestines
- low platelet count, which may make you more likely to bruise or bleed
- blocked nose (nasal congestion)
- abnormal kidney test (possible kidney damage)
- dry skin
- swelling and irritation of the thin, sac-like membrane surrounding the heart (pericarditis).

**Less frequent**

- inflammation of the pancreas
- high levels of amylase - may be a sign of an inflamed pancreas (shown in blood tests)
- numbness or paralysis - these may be signs of Guillain-Barré syndrome
- inflammation of the membrane around the spinal cord and brain
- low levels of adrenal hormones
- type 1 diabetes
- high levels of lipase - may be a sign of an inflamed pancreas (shown in blood tests)
- inflammation of the heart muscle
- inflammation of the brain
- myasthenia gravis - an illness that can cause muscle weakness
- inflammation of the pituitary gland situated at the base of the brain
- inflammation of muscles (myositis)
- red, dry, scaly patches of thickened skin (psoriasis)
- a severe rash that develops quickly, with blisters or peeling of the skin and possibly blisters in the mouth. Widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (severe cutaneous adverse reactions)
- inflammation of the kidneys

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

**Reporting of side effects**

If you get side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of Tecentriq.

## 5. How to store Tecentriq

Store all medicines out of reach of children.

Store between 2 - 8 °C. Do not freeze. Do not shake.

The diluted solution for infusion should be used immediately. If the solution is not used immediately, it can be stored for up to 30 days at 2°C - 8°C, or 8 hours at ambient temperature (≤ 25°C), if prepared under aseptic conditions.

Store in the original package.

Keep the container in the outer carton to protect from light.

Do not use after the expiry date on the carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

## 6. Contents of the pack and other information

### What Tecentriq contains

Tecentriq is supplied as single-use vials containing preservative-free, colourless to slightly yellow solution, at an active ingredient concentration of 60 mg/mL, as follows:

- 14 mL vial containing a total of 840 mg atezolizumab
- 20 mL vial containing a total of 1 200 mg atezolizumab

Contains sugar (sucrose 21 mg/mL).

*Excipients:* Glacial acetic acid, L-histadine, polysorbate 20, sucrose, water for injections.

### What Tecentriq looks like and contents of the pack

A clear, colourless to slightly yellowish liquid, packed in a type I glass vial with a butyl rubber stopper containing 20 mL of solution.

Pack of one vial.

### Holder of Certificate of Registration

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**This leaflet was last revised on**

Registration date: 29 September 2020

Last Revision: 14 March 2023

**Registration numbers**

**Tecentriq® 840 mg:** 54/30.1/0060

**Tecentriq® 1 200 mg:** 54/30.1/0061

# VOORGESTELDE PASIËNTINLIGTINGSBLAADJIE

## SKEDULERINGSTATUS

S4

**Tecentriq® 840 mg** (konsentraat vir oplossing vir infusie)

**Tecentriq® 1 200 mg** (konsentraat vir oplossing vir infusie)

Die aktiewe middel is atezolizumab.

Bevat suiker (sukrose 21 mg/ml).

**Lees hierdie hele blaadjie noukeurig deur voor jy begin om Tecentriq te gebruik.**

- Hou hierdie blaadjie. Jy sal dit dalk later weer moet lees.
- As jy verdere vrae het, vra asseblief vir jou dokter of jou apteker.

**Wat is in hierdie blaadjie**



## 1. Wat Tecentriq is en waarvoor dit gebruik word

**Wat Tecentriq is**

Tecentriq is ’n medisyne teen kanker wat die aktiewe middel atezolizumab bevat. Dit behoort aan ’n groep medisyne genaamd monoklonale teenliggaampies. ’n Monoklonale teenliggaampie is ’n tipe proteïen wat ontwerp is om ’n spesifieke teiken in die liggaam te herken en daaraan te heg.

**Waarvoor Tecentriq gebruik word**

Tecentriq word gebruik om volwassenes met die volgende toestande te behandel:

- kanker wat die blaas en die urienstelsel aantas, genaamd uroteelkarsinoom. Dit word gebruik wanneer hierdie kanker:
  - na ander dele van die liggaam versprei het
  - terugkeer ná vorige behandeling
  - of, as jy nie sisplatienbehandeling kan ontvang nie, en jou dokter jou kanker getoets het en hoë vlakke van ’n spesifieke proteïen, genaamd geprogrammeerdedoodligand-1 (PD-L1), in jou liggaam gevind het.
- kanker wat die longe aantas, genaamd niekleinsellongkanker. Dit word gebruik wanneer hierdie kanker:
  - na ander dele van die liggaam versprei het
  - terugkeer ná vorige behandeling.
- kanker wat die bors affekteer, wat drievoudige negatiewe borskanker genoem word.
- kanker van die lewer wat nie chirurgies verwyder kan word nie, wat hepatosellulêre karsinoom genoem word. Jy sal Tecentriq ontvang saam met ’n ander medisyne wat bevacizumab genoem word.

**Hoe Tecentriq werk**

Tecentriq werk deur te bind aan ’n spesifieke proteïen in jou liggaam, genaamd geprogrammeerdedoodligand-1 (PD-L1). Hierdie proteïen onderdruk die liggaam se immuunstelsel (verdedigingstelsel), en beskerm daardeur kankerselle teen aanvalle deur die immuunselle. Deur aan die proteïen te heg, help Tecentriq jou immuunstelsel om jou kanker te beveg.

## 2. Wanneer Tecentriq nie aan jou toegedien moet word nie

**Moenie Tecentriq ontvang nie**

- As jy allergies is vir atezolizumab of vir enige van die ander bestanddele van hierdie medisyne, soos gelys onder “Wat Tecentriq bevat”. As jy onseker is, gesels met jou dokter of verpleegkundige voordat jy Tecentriq neem.
- As jy ingeënt moet word of ’n lewende, geattenueerde entstof aan jou gegee is. Tecentriq kan slegs aan jou toegedien word twee maande nadat jy laas ingeënt is.
- As jy swanger is of jou baba borsvoed.

**Waarskuwings en voorsorgmaatreëls**

Praat met jou dokter of gesondheidsorgkundige voordat jy Tecentriq ontvang as:

- jy ’n outo-immuunsiekte het (’n toestand waar die liggaam sy eie selle aanval)
- jy ingelig is dat jou kanker na jou brein versprei het
- jy ’n geskiedenis van inflammasie van die longe het (wat longontsteking genoem word)
- jy chroniese virusinfeksie in die lewer het of gehad het, insluitende hepatitis B (HBV) of hepatitis C (HCV)
- jy menslike immunogebreksvirus- (MIV-)infeksie of verworwe immuniteitsgebreksindroom (vigs) het
- jou skildklier abnormaal funksioneer
- jy ernstige newe-effekte gehad het as gevolg van ander teenliggaampieterapieë wat jou immuunstelsel help om kanker te beveg
- jy medisyne gekry het om jou immuunstelsel te stimuleer
- jy medisyne gekry het om jou immuunstelsel te onderdruk

As enige van bogenoemde op jou van toepassing is (of as jy onseker is), praat met jou dokter voordat Tecentriq aan jou toegedien word.

Tecentriq kan sekere newe-effekte veroorsaak waarvan jy jou dokter dadelik moet vertel. Dit kan weke of maande ná jou laaste dosis plaasvind. Lig dadelik jou dokter in indien jy enige van die simptome hier onder ontwikkel:

- inflammasie van die longe (longontsteking); simptome kan nuwe of verergerde hoes, kortasemheid en borskaspyn insluit

- inflammasie van die lewer (hepatitis): simptome kan insluit vergeling van die vel of oë, naarheid, braking, bloeding of kneusplekke, donker urien en maagpyn
- inflammasie van die ingewande (kolitis): simptome kan insluit diarree (waterige, loperige of sagte stoelgange), bloed in stoelgange en maagpyn.
- inflammasie van die skildklier, byniere en die pituïtêre klier (hipotiroïdisme, hipertiroïdisme, bynierontoereikendheid of hipofisitis): simptome kan insluit moegheid, gewigverlies,
- gewigtoename, verandering in gemoedstoestand, haarverlies, hardlywigheid, duiseligheid, hoofpyne, toenemende dors, toenemende urinering en sigveranderings.
- tipe 1-diabetes, insluitende suur in die bloed veroorsaak deur diabetes (diabetiese keto-asidose): simptome kan insluit meer honger of dors as gewoonlik, behoefte om meer gereeld te urineer, gewigsverlies en moegheid
- inflammasie van die brein (enkefalitis) of inflammasie van die membraan rondom die rugmurg en brein (meningitis): simptome kan nekstyfheid, hoofpyn, koors, kouekoors, braking, oë wat sensitief is vir lig, verwarring en slaperigheid insluit
- inflammasie of senuweeprobleme (neuropatie): simptome kan insluit spierswakheid en dooie gevoel, tinteling in hande en voete
- inflammasie van die pankreas (pankreatitis); simptome kan buikpyn, naarheid en braking insluit
- inflammasie van die hartspier (miokarditis); simptome kan kortasemheid, verlaagde oefeningtoleransie, moegheid, borskaspyn, swelling van die enkels of bene, onreëlmatige hartklop en floutes insluit
- inflammasie van die dun, sakagtige membraan om die hart (perikardium). Die algemeenste simptoom is ’n skerp steekpyn in die borskas wat tot by die linkerskouer en -nek kan strek.
- inflammasie van die spiere (miositis); simptome kan insluit spierswakheid, uitputting ná stap of staan, struikeling of val, en probleme met sluk of asemhaling
- ernstige reaksies wat verband hou met infusies (gebeure wat gedurende die infusie of binne een dag ná die infusie plaasvind): kan insluit koors, kouekoors, kortasemheid en blosing

- ’n kombinasie van enige van die volgende simptome ervaar of voorheen ervaar het: uitslag, rooi vel, blaasvorming van die lippe, oë en mond, afskilferende vel, hoë koors, griepagtige simptome, toenemende vlakke lewerensieme wat in bloedtoetse gesien word en ’n toename in ’n tipe witbloedsel (eosinofilie) en vergrote limfkliere (tekens van erge velreaksies, sien afdeling 4 “Moontlike newe-effekte”). As jy enige van hierdie effekte ervaar, kan jou dokter jou behandeling met Tecentriq staak en vra dat jy ’n dermatoloog gaan sien.

Lig dadelik jou dokter in as jy enige van die simptome hier bo ontwikkel.

Moenie probeer om jouself met ander medisyne te behandel nie. Jou dokter kan:

- jou ander medisyne gee om komplikasies te voorkom en simptome te verminder.
- jou volgende dosis Tecentriq uitstel.
- jou behandeling met Tecentriq staak.

**Toetse en ondersoeke**

Voor jou behandeling sal jou dokter jou algemene gesondheid ondersoek. Jy sal ook gedurende jou behandeling bloedtoetse doen.

**Kinders en adolessente**

Hierdie medisyne moet nie aan kinders of adolessente jonger as 18 jaar gegee word nie. Dit is omdat die uitwerking van Tecentriq in hierdie ouderdomsgroep nie bekend is nie.

**Ander medisynes en Tecentriq**

Vertel altyd jou gesondheidsorgkundige as jy enige ander medisyne neem. (Dit sluit aanvullende of tradisionele medisyne in.)

Stel asseblief jou dokter of verpleegkundige in kennis as jy onlangs enige ander medisynes geneem het. Dit sluit in medisynes wat sonder voorskrif verkry word, insluitende kruiemedisyne.

**Swangerskap en borsvoeding**

As jy swanger is of borsvoed, dink dat jy swanger kan wees of beplan om ’n baba te hê, vra jou dokter of apteker se raad voordat jy hierdie medisyne neem.

**Voorbehoeding**

- Tecentriq sal nie aan jou gegee word as jy swanger is nie. Dit is omdat Tecentriq jou ongebore baba skade kan aandoen.
- As jy swanger kan raak, moet jy doeltreffende voorbehoedmiddels gebruik;
  - terwyl jy met Tecentriq behandel word en
  - 5 maande ná die laaste dosis.

**Swangerskap**

- Vroue wat swanger is of beplan om swanger te raak moet nie Tecentriq gebruik nie (sien “Moenie Tecentriq ontvang nie”). Dit is omdat Tecentriq jou ongebore baba skade kan aandoen.
- As jy swanger raak terwyl jy met Tecentriq behandel word, moet jy dit vir jou dokter vertel.

**Borsvoeding**

Vroue wat Tecentriq kry, moenie hulle babas borsvoed nie, ook nie 5 maande ná die laaste infusie nie. Hierdie tipe medisyne sal waarskynlik in borsmelk uitgeskei word en kan jou baba skade aandoen.

## 3. Motorbestuur en die gebruik van masjinerie

Tecentriq het ’n invloed op jou vermoë om te bestuur en masjiene te gebruik. As jy moeg voel, moet jy totdat jy beter voel nie bestuur of masjiene gebruik nie. Dit is meer waarskynlik dat dit sal gebeur kort nadat jou infusie gegee is.

Tecentriq bevat suiker (sukrose), wat ’n uitwerking kan hê op die beheer van jou bloedsuiker as jy diabetes mellitus het.

1. Hoe Tecentriq aan jou gegee word

Moenie medisyne wat vir jou voorgeskryf is, met enigiemand anders deel nie.

Volg altyd jou dokter se voorskrif presies. Jy moet jou dokter of apteker raadpleeg as jy nie seker is nie.

Hoeveel Tecentriq gegee word

Die aanbevole dosis is:

- 840 milligram (mg) elke 2 weke

- 1 200 milligram (mg) elke 3 weke of
- 1 680 milligram (mg) elke 4 weke.

Daar sal nie van jou verwag word om self Tecentriq toe te dien nie. Dit sal vir jou gegee word deur ’n persoon wat gekwalifiseer is om dit te doen.

**Hoe Tecentriq gegee word**

Tecentriq word as ’n drup in ’n aar gegee (’n binneaarse infusie).

Jou eerste infusie sal oor 60 minute gegee word.

- Jou dokter sal jou gedurende die eerste infusie noukeurig monitor.
- As jy gedurende die eerste infusie nie ’n infusiereaksie het nie, sal die volgende infusies oor ’n tydperk van 30 minute aan jou gegee word.

Jou dokter sal jou sê hoe lank jou behandeling met Tecentriq sal duur. Moenie behandeling vroeg staak nadat jy Tecentriq ontvang het nie.

As jy vermoed dat die effek van Tecentriq te sterk of te swak is, praat met jou dokter of apteker.

**As jy meer Tecentriq kry as wat jy moet**

As jy meer Tecentriq kry as wat jy moet, praat dadelik met ’n dokter. Neem die medisynepakket en hierdie blaadjie saam met jou.

In die geval van oordosering, raadpleeg jou dokter of apteker. As nie een van hulle beskikbaar is nie, kontak die naaste hospitaal of gifsentrum.

**As jy ’n dosis Tecentriq oorslaan**

As jy ’n afspraak misloop, maak dadelik ’n ander een. Dit is baie belangrik om met die infusies aan te hou om die behandeling ten volle doeltreffend te maak.

**Uitwerking wanneer behandeling met Tecentriq gestaak word**

Moenie die behandeling met Tecentriq staak nie, tensy jy dit met jou dokter bespreek het. Dit is omdat die staking van die behandeling die uitwerking van die medisyne kan stop.

As jy enige verdere vrae oor die gebruik van hierdie medisyne het, vra jou dokter, apteker of verpleegkundige.

## 4. Moontlike newe-effekte

Tecentriq kan newe-effekte hê.

Nie alle newe-effekte wat vir Tecentriq aangemeld is, is in hierdie blaadjie ingesluit nie. As jou algemene gesondheid vererger of as jy enige ongunstige effekte ondervind terwyl jy hierdie medisyne neem, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgkundige vir raad.

**Erge velreaksies**

As jy ’n erge velreaksie kry, vertel jou dokter onmiddellik.

Die tekens kan insluit:

- ’n Erge uitslag wat vinnig ontwikkel, met blase of afskilfering van die vel en moontlik blase in die mond (Stevens-Johnson-sindroom en toksiese epidermale nekrolise wat ook bekend is as SJS en TEN).
- ’n Kombinasie van enigeen van die volgende simptome: wydverspreide uitslag, hoë liggaamstemperatuur, lewerensiemverhoging, bloedabnormaliteite (eosinofilie), vergrote limfkliere en betrokkenheid van ander organe (medikasiereaksie met eosinofilie en sistemiese simptome, ook bekend as DRESS of medikasiehipersensitiwiteitsindroom).

**Gereeld**

- koors
- naarheid
- braking
- voel baie moeg met geen energie nie (uitputting)
- gebrek aan energie
- jeukerigheid van die vel
- diarree
- gewrigspyn

- uitslag
- verlies aan eetlus
- kortasemheid
- urienweginfeksie
- rugpyn
- hoes
- hoofpyn
- leukopenie
- perifere edeem
- alopesie
- hipertensie
- inflammasie van die longe
- lae suurstofvlakke wat kortasemheid kan veroorsaak as gevolg van inflammasie van die longe (longontsteking)
- maagpyn
- inflammasie van die lewer
- verhoogde lewerensieme (aangedui in toetse) – kan ’n teken wees van inflammasie in die lewer
- sukkel om te sluk
- bloedtoetse wat lae vlakke van kalium (hipokalemie) of natrium (hiponatriemie) toon
- lae bloeddruk (hipotensie)
- onderaktiewe skildklier (hipotiroïdisme)
- allergiese reaksie (infusieverwante reaksie of hipersensitiwiteit)
- griepagtige siekte
- pyn in die spiere en beendere
- kouekoors
- ooraktiewe skildklier (hipertiroïdisme)
- inflammasie van die ingewande

- lae plaatjietelling, wat dalk sal veroorsaak dat jy makliker kneus of bloei
- toeneus (neuskongestie)
- abndormale niertoetse (moontlike nierskade)
- droë vel
- swelling en irritasie van die dun, sakagtige membraan om die hart (perikarditis).

**Minder gereeld**

- inflammasie van die pankreas
- hoë vlakke van amilase – kan ’n teken wees van inflammasie van die pankreas (aangedui in bloedtoetse)
- dooie gevoel of verlamming – dit kan tekens wees van die Guillain-Barré-sindroom
- inflammasie van die membraan om die rugmurg en die brein
- lae vlakke van bynierhormone
- tipe 1-diabetes
- hoë vlakke van lipase – kan ’n teken wees van inflammasie van die pankreas (aangedui in bloedtoetse)
- inflammasie van die hartspier
- inflammasie van die brein
- myasthenia gravis – ’n siekte wat spierswakheid kan veroorsaak
- inflammasie van die pituïtêre klier by die basis van die brein
- inflammasie van die spiere (miositis)
- rooi, droë, skubagtige kolle verdikte vel (psoriase)
- ’n erge uitslag wat vinnig ontwikkel, met blase of afskilfering van die vel en moontlik blase in die mond. Wydverspreide uitslag, hoë liggaamstemperatuur, lewerensiemverhogings, bloedabnormaliteite (eosinofilie), vergrote limfnodusse en betrokkenheid van ander organe (erge ongunstige velreaksies)
- inflammasie van die niere

As jy enige newe-effekte opmerk wat nie in hierdie blaadjie genoem word nie, stel asseblief jou dokter of apteker in kennis.

**Hoe om newe-effekte te rapporteer**

As jy newe-effekte ondervind, praat met jou dokter of verpleegkundige. Dit sluit enige moontlike newe-effekte in wat nie in hierdie blaadjie genoem word nie. Jy kan ook newe-effekte by SAHPRA rapporteer via die rapporteringsvorm vir ongewenste reaksie op middels ("6.04 Adverse Drug Reaction Reporting Form"), wat aanlyn onder SAHPRA se publikasies gevind kan word: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte aan te meld, kan jy help om meer inligting oor die veiligheid van Tecentriq te verskaf.

## 5. Hoe om Tecentriq te bêre

Bêre alle medisyne buite die bereik van kinders.

Bêre tussen 2 en 8 °C. Moenie vries nie. Moenie skud nie.

Die verdunde oplossing vir infusie moet onmiddellik gebruik word. As die oplossing nie onmiddellik gebruik word nie, kan dit tot 30 dae teen 2 °C-8 °C, of 8 uur teen omgewingstemperatuur (≤ 25 °C) geberg word, as dit in 'n steriele omgewing voorberei is.

Bêre in die oorspronklike verpakking.

Bêre die houer in die buitenste karton om dit teen lig te beskerm.

Moenie gebruik na die vervaldatum wat op die karton aangedui word nie.

Neem alle ongebruikte medisyne na jou apteker terug.

Moenie ongebruikte medisyne in dreine of rioolstelsels (bv. toilette) weggooi nie.

## 6. Inhoud van die pakkie en ander inligting

**Wat Tecentriq bevat**

Tecentriq word voorsien as enkelgebruikflessies wat preserveermiddelvrye, kleurlose tot effens geel oplossing bevat, met 'n aktiewe bestanddeelkonsentrasie van 60 mg/ml, soos volg:

- 14 ml flessie bevat altesaam 840 mg atezolizumab
- 20 ml flessie bevat altesaam 1 200 mg atezolizumab

Bevat suiker (sukrose 21 mg/ml).

*Bindmiddels:* Ysasynsuur, L-histidien, polisorbaat 20, sukrose en water vir inspuitings.

**Hoe Tecentriq lyk en die inhoud van die pakkie**

'n Helder, kleurlose tot effens gelerige vloeistof, verpak in 'n tipe I-glasflessie met 'n butielrubberprop wat 20 ml oplossing bevat.

Pakkie met een flessie.

Houer van registrasie sertifikaat

Roche Products (Edms.) Bpk.

Bekkerweg 90, Hertford Office Park

Gebou E, Vorna Valley, Midrand,

Johannesburg,1686

Suid-Afrika

Roche etiek hulplyn (Ethical Assistance Line), tolvry: 0800 21 21 25

**Hierdie blaadjie is laas hersien op**

Registrasiedatum: 29 September 2020

Vorige hersiening: 14 Maart 2023

**Registrasienommers**

**Tecentriq® 840 mg:** 54/30.1/0060

**Tecentriq® 1 200 mg:** 54/30.1/0061