Unit: Technical Assessment Unit

Public assessment report for biological products

Tecentriq

Administrative information:

Trade name of the medicinal product:	**Tecentriq1875mg/15ml**
INN (or common name) of the active substance(s):	**Atezolizumab**
Manufacturer of the finished product	**Roche Diagnostics GmbH Sandhofer Strasse 116, 68305 Mannheim – GERMANY.**
Marketing Authorization holder	**Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 Grenzach-Wyhlen - Germany – GERMANY.**
Applied Indication(s):	**Urothelial carcinoma (UC)** **Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic UC: after prior platinum-containing chemotherapy, or who are considered cisplatin ineligible, and whose tumours have a PD-L1 expression ≥ 5%** **Early-stage non-small cell lung cancer (NSCLC)** **Tecentriq as monotherapy is indicated as adjuvant treatment following complete resection and platinum-based chemotherapy for adult patients with NSCLC with a high risk of recurrence whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR-mutant or ALK-positive NSCLC.** **Advanced NSCLC** **Tecentriq, in combination with bevacizumab, paclitaxel and carboplatin, is indicated for the first-line treatment of adult patients with**

	metastatic non-squamous NSCLC. In patients with EGFR-mutant or ALK-positive NSCLC, Tecentriq, in combination with bevacizumab, paclitaxel and carboplatin, is indicated only after failure of appropriate targeted therapies. **Tecentriq, in combination with nab-paclitaxel and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous NSCLC who do not have EGFR-mutant or ALK-positive NSCLC.** **Tecentriq as monotherapy is indicated for the first-line treatment of adult patients with metastatic NSCLC whose tumours have a PD-L1 expression ≥ 50% TC or ≥ 10% tumour-infiltrating immune cells (IC) and who do not have EGFR-mutant or ALK-positive NSCLC.** **Tecentriq as monotherapy is indicated for the first-line treatment of adult patients with advanced NSCLC who are ineligible for platinum-based therapy (see section 5.1 for selection criteria).** **Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic NSCLC after prior chemotherapy. Patients with EGFR-mutant or ALK-positive NSCLC should also have received targeted therapies before receiving Tecentriq.** **Small cell lung cancer (SCLC)** **Tecentriq, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).** **Triple-negative breast cancer (TNBC)** **Tecentriq in combination with nab-paclitaxel is indicated for the treatment**

	of adult patients with unresectable locally advanced or metastatic TNBC whose tumours have PD-L1 expression ≥ 1% and who have not received prior chemotherapy for metastatic disease. **Hepatocellular carcinoma (HCC)** **Tecentriq, in combination with bevacizumab, is indicated for the treatment of adult patients with advanced or unresectable HCC who have not received prior systemic therapy.**
Pharmaceutical form(s) and strength(s):	**- Solution for injection** **-1875mg/15ml. (125 mg/ml).**
Route of administration	**S.C**
Approved Pack	**A carton box of one vial containing 15 ml solution and insert leaflet** **-Vial: 20 mL type I glass, borosilicate, colorless** **-Rubber Stopper: Gray butyl rubber (isoprene-isobutylene copolymer (IRR)) laminated with a flurotec film (Fluoro resin laminated)** **-Seal: aluminum seal fitted with a plastic flip-off (Violet) cap, cap made of aluminum and disc made of suitable plastic.**
Registration track	**Reliance Level 1**
Type of registration (EMA/FDA – Local)	**EMA approved**

List of abbreviations:

ADA	anti-drug antibody
Atezo	Atezolizumab
B7.1	B7 homolog 1
CHO	Chinese hamster ovary
cGMP	Current Good Manufacturing Practice
DP	Drug product

DS	Drug substance
IC	immune cells
I.V	Intravenous
mg	Milligram
NSCLC	non-small-cell lung cancer
ORR	objective response rate
PD-L1	programmed-death ligand-1
PD-1	programmed-death -1
PFS	progression-free survival
TC	tumour cells

Table of contents

Dossier initial submission and evaluation process:

The file evaluated according to EDA Reliance Model & the company submitted data which are the followings:

1. Quality module-3 from the CTD file.
2. EMA Unredacted Assessment

1. Introduction

- Atezolizumab is a humanized monoclonal antibody based on a human IgG1 framework, expressed in Chinese Hamster Ovary (CHO) cells. It consists of two heavy chains (448 amino acids each) and two light chains (214 amino acids each). The structure of the atezolizumab-SC active substance (AS) is identical to that of the approved commercial atezolizumab for intravenous administration (atezolizumab-IV). The physicochemical,

biological, and immunological properties of the atezolizumab-SC AS are the same as those of the atezolizumab-IV AS. Additionally, the formulation of the atezolizumab-SC AS is similar to that of the commercial atezolizumab-IV AS, with the only differences being increased concentrations of protein and sucrose.

- **Quality aspects:**

  - **Manufacturer(s):**

- **Drug Substance**

  - The Active substance is manufactured at Roche Diagnostics GmbH, Nonnenwald 2, 82377 Penzberg, Germany – GERMANY.

- **Drug product**

  - The Finished product is manufactured at Roche Diagnostics GmbH Sandhofer Strasse 116, 68305 Mannheim – GERMANY.

-Manufacturing of both DS and DP are performed in accordance with cGMP regulations.

  - **Stability**

- **Drug substance:**

- Approved shelf life for the Active substance: 36 months.
- Approved Storage Conditions of the Active substance: -20 °C.

Drug product:

-Approved shelf life for the Finished product: 24 months.
-Approved Storage Conditions:
Finished product
-Store in a refrigerator (2 – 8 °C).
-Do not freeze.
-Do not shake
-Keep the vial in the outer carton in order to protect from light.
Prepared syringe:
-Once transferred from the vial into the syringe, Tecentriq solution for injection is physically and
chemically stable for up to 30 days at 2 °C to 8 °C and for up to 8 hours at ≤ 30 °C in diffuse daylight
and from the time of preparation.

- **Non –Clinical aspect & Clinical aspect:**

-Atezolizumab targets human programmed death-ligand 1 (PD-L1) on tumor-infiltrating immune cells (ICs) and tumor cells (TCs) and inhibits its interaction with its receptors programmed death1 (PD-1) and B7.1, both of which can provide inhibitory signals to T cells.

-**Pre-Clinical Studies** have been evaluated before as a part of the registration process of Tecentriq 1200mg/20ml and there is no new data submitted regarding this aspect. The choice of 1875 mg as the dose for SC route is based on a clinical trial.

Clinical Efficacy conclusion:

-The overall efficacy was comparable between the two arms (Atezo SC and the Atezo IV arms). The ORR and median duration of PFS were similar between the Atezo SC and the Atezo IV arms. No meaningful differences were observed between arms across the majority of clinically relevant subgroups. OS and DOR were not mature at the time of analyses. Global health status/quality of life, physical functioning, role functioning, and satisfaction with treatment were all comparable between the two arms.

Clinical Safety conclusion:

-Atezolizumab SC was generally well tolerated and had a safety profile comparable to atezolizumab IV.

-Amajority of patients preferred atezo SC regardless of treatment sequence and more satisfied with the atezo SC administration over the atezo IV administration.

-Switching between atezo SC and IV (and vice versa) was generally well-tolerated and well-managed. Analysis of the safety and tolerability of switching between atezo IV and atezo SC route of administration (and vice versa) did not reveal any new or clinically relevant safety concerns compared to results from the overall safety.

Clinical Immunogenicity conclusion:

- The atezolizumab treatment-emergent ADA incidence was generally comparable between arms (Atezo SC and the Atezo IV arms). There appeared to be no clinically relevant impact of ADAs on PK, efficacy, or safety.
- Most HCPs were satisfied or very satisfied with atezolizumab SC and that the treatment was easy to administer.

-In conclusion the overall benefit/risk of of Tecentriq; Solution for injection, 1875 mg/ 15 ml (125 mg/ ml) *is favorable in the treatment of Urothelial carcinoma, Early-stage non-small cell lung cancer, Advanced NSCLC, Small cell lung cancer, Triple-negative breast cancer and Hepatocellular carcinoma.*

General Conclusion and Recommendations if any:

Based on the review of CTD modules and other supplementary documents, the product is approved.

For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/assessment-report/tecentriq-epar-public-assessment-report_en.pdf