Atezolizumab, CARBOplatin AUC 5 and Etoposide 100mg/m^2 - 21 Day Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
First-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).	C34	00689a	Atezolizumab: ODMS 01/03/2022 (IV) 01/06/2024 (SC) CARBOplatin: N/A Etoposide: N/A

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Induction phase: Atezolizumab (IV or SC) and CARBOplatin are administered on day 1 and etoposide is administered on days 1, 2 and 3 of a 21 day cycle, for 4 cycles or until disease progression or unacceptable toxicity occurs.

Maintenance phase: The induction phase is followed by a maintenance phase without chemotherapy during which atezolizumab (IV or SC) is administered every three weeks. An alternative maintenance administration schedule of atezolizumab 1680mg intravenously every 28 days may be considered as described in Regimen 00593 Atezolizumab 1680mg Monotherapy–28 Day.

Treatment with atezolizumab should continue until disease progression or unacceptable toxicity occurs.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

There are different formulations available for atezolizumab and etoposide. Please refer to Tables 2-4 below that outline the alternative treatment schedules.

Table 1: Treatment Schedule for Atezolizumab (IV), CARBOplatin (IV) and Etoposide (IV)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Atezolizumab	1200mg	IV infusion*	250mL 0.9% NaCl over 60 minutes[a]	Every 21 days[b]
2	1	CARBOplatin	AUC 5	IV infusion	500mL glucose 5% over 30 minutes	Every 21 days for 4 cycles
3	1,2,3	Etoposide	100mg/m^2	IV infusion**	1000mL 0.9% NaCl over 60 minutes	Every 21 days for 4 cycles
[a] Initial dose must be given over 60 minutes; subsequent doses may be given over 30 minutes if tolerated.						
[b] If a planned dose of atezolizumab is missed, it should be administered as soon as possible; it is recommended not to wait until the next planned dose. The schedule of administration must be adjusted to maintain a 3-week interval between doses.						
*See alternative treatment schedule for Atezolizumab SC below (Table 2). ** See alternative treatment schedule for Etoposide PO below (Table 3).						

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ALTERNATIVE TREATMENT SCHEDULES:

Table 2: Treatment Schedule for Atezolizumab (SC), CARBOplatin (IV) and Etoposide (IV)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Atezolizumab	1875mg	Subcutaneous*	Over 7 minutes[a]	Every 21 days[b]
2	1	CARBOplatin	AUC 5	IV infusion	500mL glucose 5% over 30 minutes	Every 21 days for 4 cycles
3	1,2,3	Etoposide	100mg/m^2	IV infusion**	1000mL 0.9% NaCl over 60 minutes	Every 21 days for 4 cycles
[a] Use of a subcutaneous infusion set (e.g. winged/butterfly) is recommended. The remaining residual hold-up volume in the tubing should not be administered to the patient. The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard.						
[b] If a planned dose of atezolizumab is missed, it should be administered as soon as possible; it is recommended not to wait until the next planned dose. The schedule of administration must be adjusted to maintain a 3-week interval between doses.						
*See alternative treatment schedule for Atezolizumab IV above (Table 1). **See alternative treatment schedule for Etoposide PO below (Table 3).						

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

Atezolizumab (IV or SC), CARBOplatin and Etoposide (Day 1 IV, Day 2 & 3 oral)

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Induction phase: Atezolizumab (IV or SC) and CARBOplatin are administered on day 1 and etoposide is administered as an IV infusion on Day 1 and then administered as PO doses on Days 2 and 3 for 4 cycles or until disease progression or unacceptable toxicity occurs.

Maintenance phase: The induction phase is followed by a maintenance phase without chemotherapy during which atezolizumab (IV or SC) is administered every three weeks. An alternative maintenance administration schedule of atezolizumab 1680mg intravenously every 28 days may be considered as described in Regimen 00593 Atezolizumab 1680mg Monotherapy–28 Day.

Table 3: Treatment Schedule for Atezolizumab (IV), CARBOplatin (IV) and Etoposide (IV and PO)

Admin Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Atezolizumab	1200mg	IV infusion*	250mL 0.9% NaCl over 60 minutes[a]	Every 21 days[b]
2	1	CARBOplatin	AUC 5	IV Infusion	500mL glucose 5% over 30 minutes	Every 21 days for 4 cycles
3	1	Etoposide	100mg/m^2	IV Infusion	1000mL 0.9% NaCl over 60 minutes	Every 21 days for 4 cycles
1	2, 3	Etoposide[c]	100mg/m^2 twice daily	PO**		Every 21 days for 4 cycles
[a] Initial dose must be given over 60 minutes; subsequent doses may be given over 30 minutes if tolerated.						
[b] If a planned dose of atezolizumab is missed, it should be administered as soon as possible; it is recommended not to wait until the next planned dose. The schedule of administration must be adjusted to maintain a 3-week interval between doses.						
[c] Etoposide is available in 50mg and 100mg capsules. The capsules should be taken on an empty stomach.						
*See alternative treatment schedule for Atezolizumab SC below (Table 4). **See alternative treatment schedule for Etoposide IV above (Table 1).						

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

Table 4: Treatment Schedule for Atezolizumab (SC), CARBOplatin (IV) and Etoposide (IV and PO)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Atezolizumab	1875mg	Subcutaneous*	Over 7 minutes[a]	Every 21 days[b]
2	1	CARBOplatin	AUC 5	IV infusion	500mL glucose 5% over 30 minutes	Every 21 days for 4 cycles
3	1	Etoposide	100mg/m^2	IV infusion	1000mL 0.9% NaCl over 60 minutes	Every 21 days for 4 cycles
1	2, 3	Etoposide[c]	100mg/m^2 twice daily	PO**		Every 21 days for 4 cycles
[a] Use of a subcutaneous infusion set (e.g. winged/butterfly) is recommended. The remaining residual hold-up volume in the tubing should not be administered to the patient. The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard.						
[b] If a planned dose of atezolizumab is missed, it should be administered as soon as possible; it is recommended not to wait until the next planned dose. The schedule of administration must be adjusted to maintain a 3-week interval between doses.						
[c] Etoposide is available in 50mg and 100mg capsules. The capsules should be taken on an empty stomach.						
*See alternative treatment schedule for Atezolizumab IV above (Table 3). **See alternative treatment schedule for Etoposide IV above (Table 2).						

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

CARBOplatin dose:

The dose in mg of CARBOplatin to be administered is calculated as follows:

Dose (mg) = target AUC (mg/mL x minute) x (GFR mL/minute +25)

- **Measured GFR** (e.g. nuclear renogram) is preferred whenever feasible.
- **Estimation of GFR (eGFR)** can be done by using the Wright formula or using the Cockcroft and Gault formula to measure creatinine clearance.
- The GFR used to calculate the AUC dosing should not exceed 125mL/minute.
- For obese patients and those with a low serum creatinine, for example due to low body weight or post-operative asthenia, the formulae may not give accurate results and measured GFR is recommended.
  - Where obesity (body mass index [BMI] ≥ 30 kg/m^2) or overweight (BMI 25-29.9) is likely to lead to an overestimate of GFR and isotope GFR is not available, the use of the adjusted ideal body weight for Cockcroft and Gault may be considered.
  - Where serum creatinine is less than 63 micromol/L, the use of a creatinine value of 62 micromol/L or a steady pre-operative creatinine value may be considered.
- These comments do not substitute for the clinical judgement of a physician experienced in prescription of CARBOplatin.

WRIGHT FORMULA

There are two versions of the formula depending on how serum creatinine values are obtained, by the kinetic Jaffe method or the enzymatic method. The formula can be further adapted if covariant creatine kinase (CK) values are available (not shown).

1. *SCr measured using enzymatic assay*.

$$\text{GFR (mL/minute)} = \frac{(6230 - 32.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.23 \times \text{Sex})}{\text{SCr (micromol/minute)}}$$

2. *SCr measured using Jaffe assay*

$$\text{GFR (mL/minute)} = \frac{(6580 - 38.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.168 \times \textit{Sex})}{\text{SCr (micromol/minute)}}$$

Key: Sex = 1 if female, 0 if male; Age in years; BSA= DuBois BSA

COCKCROFT-GAULT FORMULA

$$\text{GFR (mL/minute)} = \frac{\text{S} \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

S= 1.04 for females and 1.23 for males

ELIGIBILITY:

- Indications as above
- ≥18 years
- ECOG status 0-1
- No prior systemic treatment for ES-SCLC
- Adequate haematological and organ function

USE WITH CAUTION:

Use with caution in:

- Patients with clinically significant autoimmune disease

EXCLUSIONS:

- Hypersensitivity to atezolizumab, CARBOplatin, etoposide or any of the excipients.
- Symptomatic central nervous system (CNS) metastases
- Any active clinically significant infection requiring therapy
- Pregnancy or lactation
- Symptomatic interstitial lung disease
- Information regarding prior therapy with an anti PD-1 or anti PD-L1 antibody is available here
- Any medical condition that requires immunosuppressive doses of systemic corticosteroids or other immunosuppressive medication(s) (defined as >10mg prednisolone/daily (or steroid equivalent, excluding inhaled or topical steroids

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, liver and renal profile
- Glucose
- TFTs
- Virology Screen: Hepatitis B (HBsAg, HBcoreAb) and Hepatitis C
- Isotope GFR measurement (preferred) or GFR / creatinine clearance estimation

Regular tests:

- FBC, liver, renal and glucose profile prior to each cycle
- TFTs every 3 to 6 weeks

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- Atezolizumab:
  - Dose reduction not recommended.
  - Atezolizumab treatment may be interrupted or discontinued due to toxicity. Please refer to Table 7 below for treatment modification.
- CARBOplatin and etoposide:
  - Dose modifications are permitted for CARBOplatin and etoposide to manage haematological toxicities and renal and hepatic impairment. Please refer to Tables 5 and 6 below.

Haematological:

Table 5: Dose modification for CARBOplatin and etoposide for haematological toxicity on Day 1

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
≥ 1.0	and	≥ 100	100%
0.5 to <1.0	and/or	75 to <100	Delay one week until recovery
<0.5 or neutropenic fever	and/or	<50	Delay and consider dose reduction for etoposide and carboplatin by 25%

Renal and Hepatic Impairment:

Table 6: Dose modification in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment	
Atezolizumab[a]	**CrCl (mL/minute)**	**Dose**	**Mild**	No dose adjustment is needed
	≥30	No dose adjustment is needed	**Moderate/Severe**	No need for dose adjustment is expected
	<30	No need for dose for dose adjustment is expected		
	Haemodialysis	No need for dose for dose adjustment is expected		
CARBOplatin [b]	See note below*		Probably no dose modification required	
Etoposide [c]	**CrCl (mL/minute)**	**Dose**	**Hepatic Impairment**	
	>50	No dose adjustment is needed	Bilirubin < 50 µmol/L and Normal albumin and Normal renal function	No need for dose adjustment is expected
	10-50	75% of the original dose, increase if tolerated	Bilirubin ≥ 50 µmol/L or Decreased albumin levels	Consider 50% of the dose, increase if tolerated
	Haemodialysis	Not dialysed, consider 75% of the original dose		

[a] Atezolizumab (renal and hepatic – Giraud et al. (2023)
[b] CARBOplatin (renal and hepatic – NCCP Standardisation)
[c] Etoposide (renal and hepatic – Giraud et al. (2023)

*Renal Dysfunction and CARBOplatin

- Patients with creatinine clearance values of <60mL/minute are at greater risk of developing myelosuppression.
- If GFR between 20 to ≤ 30mL/minute, CARBOplatin should be administered with extreme caution
- In case of GFR ≤ 20mL/minute CARBOplatin should not be administered at all.
- If Cockcroft & Gault or Wright formula are used, the dose should be calculated as required on each cycle based on a serum creatinine obtained within 48 hrs of drug administration.
- If isotope GFR is used, the dose can remain the same provided the serum creatinine is ≤110% of its value at the time of the isotope measurement. If the serum creatinine increases, consideration should be given to re-measuring the GFR or to estimating it using Cockcroft & Gault or Wright formulae.

Management of adverse events:

Table 7: Guidelines for withholding or discontinuation of atezolizumab

Immune-mediated adverse reaction	Treatment modification
Pneumonitis Grade 2 Grade 3 or 4	Withhold atezolizumab. Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤ 10 mg prednisolone or equivalent per day. Permanently discontinue atezolizumab
Hepatitis Grade 2: (ALT or AST > 3 to 5 x upper limit of normal [ULN] or blood bilirubin > 1.5 to 3 x ULN) Grade 3 or 4: (ALT or AST > 5 x ULN or blood bilirubin > 3 x ULN)	Withhold atezolizumab. Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisolone or equivalent per day. Permanently discontinue atezolizumab
Colitis Grade 2 or 3 Diarrhoea (increase of ≥ 4 stools/day over baseline) or Symptomatic Colitis Grade 4 Diarrhoea or Colitis (life threatening; urgent intervention indicated)	Withhold atezolizumab. Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisolone equivalent per day. Permanently discontinue atezolizumab
Hypothyroidism or hyperthyroidism Symptomatic	Withhold atezolizumab. **Hypothyroidism:** Treatment may be resumed when symptoms are controlled by thyroid replacement therapy and TSH levels are decreasing. **Hyperthyroidism:** Treatment may be resumed when symptoms are controlled by anti-thyroid medicinal product and thyroid function is improving.
Adrenal insufficiency Symptomatic	Withhold atezolizumab. Treatment may be resumed when the symptoms improve to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisolone or equivalent per day and patient is stable on replacement therapy.
Hypophysitis Grade 2 or 3 Grade 4	Withhold atezolizumab. Treatment may be resumed when the symptoms improve to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisolone or equivalent per day and patient is stable on replacement therapy. Permanently discontinue atezolizumab
Type 1 diabetes mellitus Grade 3 or 4 hyperglycaemia (fasting glucose >250 mg/dL or 13.9 mmol/L)	Withhold atezolizumab. Treatment may be resumed when metabolic control is achieved on insulin replacement therapy.
Rash/Severe cutaneous adverse reaction	

Immune-mediated adverse reaction	Treatment modification
Grade 3 or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)[1] Grade 4 or confirmed Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)[1]	Withhold atezolizumab. Treatment may be resumed when the symptoms improve to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisolone or equivalent per day. Permanently discontinue atezolizumab
Myasthenic syndrome/ myasthenia gravis, Guillain-Barré syndrome, Meningoencephalitis and Facial paresis Facial paresis Grade 1 or 2 All grades or Facial paresis Grade 3 or 4	 Withhold atezolizumab. Treatment may be resumed if the event fully resolves. If the event does not fully resolve while withholding atezolizumab, permanently discontinue atezolizumab. Permanently discontinue atezolizumab
Myelitis Grade 2,3 or 4	 Permanently discontinue atezolizumab
Pancreatitis Grade 3 or 4 serum amylase or lipase levels increased (> 2 x ULN) or Grade 2 or 3 pancreatitis Grade 4 or any grade of recurrent pancreatitis	 Withhold Atezolizumab. Treatment may be resumed when serum amylase and lipase levels improve to Grade 0 or Grade 1 within 12 weeks, or symptoms of pancreatitis have resolved, and corticosteroids have been reduced to ≤ 10 mg prednisolone or equivalent per day. Permanently discontinue atezolizumab
Myocarditis Grade 2 or above	 Permanently discontinue atezolizumab
Nephritis Grade 2: (creatinine level > 1.5 to 3.0 x baseline or > 1.5 to 3.0 x ULN) Grade 3 or 4: (creatinine level > 3.0 x baseline or > 3.0 x ULN)	 Withhold atezolizumab. Treatment may be resumed when the event improves to Grade 0 or Grade 1 within 12 weeks and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day. Permanently discontinue atezolizumab
Myositis Grade 2 or 3 Grade 4 or recurrent Grade 3	 Withhold atezolizumab Permanently discontinue atezolizumab
Pericardial disorders Grade 1 Grade 2 or above	 Withhold atezolizumab[2] Permanently discontinue atezolizumab
Haemophagocytic lymphohistiocytosis	

Immune-mediated adverse reaction	Treatment modification
Suspected haemophagocytic lymphohistiocytosis[1]	Permanently discontinue atezolizumab
Other immune-mediated adverse reactions Grade 2 or Grade 3 Grade 4 or recurrent Grade 3	 Withhold until adverse reactions recovers to Grade 0-1 within 12 weeks, and corticosteroids have been reduced to ≤ 10mg prednisolone or equivalent per day. Permanently discontinue atezolizumab (except endocrinopathies controlled with replacement hormones).
Other adverse reactions **Infusion-related or Subcutaneous-related Reactions** Grade 1 or 2 Grade 3 or 4	 Reduce infusion rate or interrupt. Treatment may be resumed when the event is resolved Permanently discontinue atezolizumab
Note: Toxicity should be graded with the current version of National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE).	
[1] Regardless of severity [2] Conduct a detailed cardiac evaluation to determine the etiology and manage appropriately	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting linked here:

Atezolizumab: Minimal **(Refer to local policy)**
CARBOplatin: High **(Refer to local policy)**
Etoposide: Low **(Refer to local policy)**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - link here
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - link here

PREMEDICATIONS:

- None usually required unless patient has experienced a previous hypersensitivity reaction.
- Patients with Grade 1 or 2 atezolizumab infusion-related or subcutaneous-related reaction may continue to receive atezolizumab with close monitoring; premedication with antipyretic and antihistamine may be considered.

OTHER SUPPORTIVE CARE:

- Women of childbearing potential have to use effective contraception during and for 5 months after treatment with atezolizumab.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP

Patient Alert Card (Atezolizumab)
https://www.hpra.ie/img/uploaded/swedocuments/53ca611d-f634-4438-83db-4da11cebd0c6.pdf

REFERENCES:

1. Horn L, Mansfield AS, Szczęsna A, et al (2018) First-line atezolizumab plus chemotherapy in extensive-stage small cell lung cancer. N Engl J Med 379:2220–2229. https://www.nejm.org/doi/pdf/10.1056/NEJMoa1809064
2. Liu SV et al. Updated Overall Survival and PD-L1 Subgroup Analysis of Patients With Extensive-Stage Small-Cell Lung Cancer Treated With Atezolizumab, Carboplatin, and Etoposide (IMpower133). Journal of Clinical Oncology 2021 Feb 20;39(6):619-630. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8078320/
3. Mansfield AS et al. Safety and patient-reported outcomes of atezolizumab, carboplatin, and etoposide in extensive-stage small-cell lung cancer (IMpower133): a randomized phase I/III trial. Annals of Oncology 2020; 31(2):310-7. https://pubmed.ncbi.nlm.nih.gov/31959349/
4. Micke P et al. Staging small-cell lung cancer: Veterans Administration Lung Study Group versus Association for the Study of Lung Cancer – what limits limited disease? Lung Cancer 2002; 37:271-6.
5. Riemsma R et al. Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer: a Single Technology Assessment. York 2019; Kelijnen Systematic Reviews Ltd.
6. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2012; 30 (13) 1553-1561.
7. Ekhart C, Rodenhuis S et al. Carboplatin dosing in overweight and obese patients with normal renal function, does weight matter? Cancer Chemother Pharmacol 2009; 64:115-122.
8. NCCN CARBOplatin dosing in adults https://www.nccn.org/docs/default-source/clinical/order-templates/appendix_b.pdf?sfvrsn=6286822e_6
9. Wright JG, Boddy AV, et al, Estimation of glomerular filtration rate in cancer patients. British Journal of

Cancer 2001; 84(4):452-459
10. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
11. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
12. NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Medical Oncology). V7 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/antiemetic-medicines-for-inclusion-in-ncis-medical-oncology-.pdf
13. HPRA. Direct Healthcare Professional Communication (DHPC). Important Safety Information from Roche Products (Ireland) Ltd on Risk of Severe Cutaneous Adverse Reactions (SCARs) of Tecentriq (atezolizumab) 25/03/2021. Available at: https://www.hpra.ie/docs/default-source/default-document-library/important-safety-information---tecentriq-(atezolizumab)414c0f2697826eee9b55ff00008c97d0.pdf?sfvrsn=0
14. Atezolizumab (Tecentriq®) Summary of product characteristics. Last updated 21/05/2024. Accessed 06/06/2024. Available at: https://www.ema.europa.eu/en/documents/product-information/tecentriq-epar-product-information_en.pdf
15. CARBOplatin Summary of product characteristics. Accessed Nov 2022. Available at:https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-032-001_15082022102053.pdf
16. Etoposide Summary of product characteristics. Accessed Nov 2022. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-036-001_17052021114619.pdf

Version	Date	Amendment	Approved By
1	20/01/2022		Prof Maccon Keane
2	08/07/2022	Addition of wording giving option to administer atezolizumab 1680mg every 28 days. Amended CARBOplatin infusion time. Updated wording for CARBOplatin dosing.	Prof Maccon Keane
3	24/03/2023	Reviewed. Updated management of adverse events section. Added alternate treatment schedule.	Prof Maccon Keane
4	14/06/2024	- Amended regimen title - Added atezolizumab subcutaneous formulation option (Table 2 and Table 4) - Updated PD-L1 information in Exclusion section - Updated Table 6 (dose modification in renal and hepatic impairment to align with Giraud et al (2023)) - Updated Table 7 to align with revised SmPC - Updated Supportive Care section to align with revised SmPC - Updated Adverse Effects and Drug Interactions section to align with NCCP Standardisation - NCCP Standardisation	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.