ATEZOLIZUMAB (Tecentriq) CARBOPLATIN ETOPOSIDE

INDICATION (ICD10) C34

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (ATE7)

1. For the first-line treatment of adult patients with extensive-stage small cell lung cancer (Not received previous systemic therapy for his/her extensive stage disease. Previous treatment with concurrent chemoradiotherapy for limited stage SCLC is allowed as long as therapy was completed at least 6 months prior to the diagnosis of recurrent and extensive stage disease) No symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1. (TA638)

REGIMEN SC

Cycles 1 to 4

Day 1	ATEZOLIZUMAB	1875mg SC
	CARBOPLATIN	AUC 5 in #ml glucose 5% IV infusion over 30 minutes Dose calculated by EDTA GFR or calculated CrCl + 25 x AUC. (Maximum dose when using CrCl 125+25 x AUC)
	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes
Day 2	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes
Day 3	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes

Cycles 5 onwards

Day 1	ATEZOLIZUMAB	1875mg SC

Atezolizumab 1875mg SC – Administer in the thigh over 7 minutes. Alternate thighs, administer at least 2.5cm from the old site.

REGIMEN IV

Cycles 1 to 4

Day 1	ATEZOLIZUMAB	1200mg in #ml sodium chloride 0.9% IV infusion
	CARBOPLATIN	AUC 5 in #ml glucose 5% IV infusion over 30 minutes Dose calculated by EDTA GFR or calculated CrCl + 25 x AUC. (Maximum dose when using CrCl 125+25 x AUC)
	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes
Day 2	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes
Day 3	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes

Cycles 5 onwards

Day 1	ATEZOLIZUMAB	1200mg in #ml sodium chloride 0.9% IV infusion

diluent volume for dose prescribed as per national standardised product specification

Atezolizumab 1200mg IV – The initial dose should be delivered over 60 minutes.
If the first infusion is tolerated without infusion-associated adverse events, the second infusion may be delivered over 30 minutes.
If the 30-minute infusion is well tolerated, all subsequent infusions may be delivered over 30 minutes.

NB Etoposide - days 2 and 3 can be given orally ETOPOSIDE 200mg/m^2/day but is not recommended as oral absorption is variable (it may cause reduced efficacy or severe toxicity in patients), the intravenous route is preferred. However for logistical reasons the oral route may be necessary.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for 4 cycles
Atezolizumab monotherapy from cycle 5 may continue until disease progression.

ANTI-EMETICS

Moderate emetic risk day 1 cycles 1 to 4
Low emetic risk days 2 and 3 cycles 1 to 4
Low risk day 1 cycle 5 onwards

CONCURRENT MEDICATION REQUIRED

Carboplatin	Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously. Dexamethasone 20mg IV bolus Chlorphenamine 10mg IV bolus Carboplatin should be given at a slower rate e.g. 2-4 hours.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Atezolizumab IV – neutral
Carboplatin – irritant
Etoposide - irritant

Atezolizumab IV use of 0.2-5micron filter is optional
Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Mg^{++} baseline and then as clinically indicated
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Ideally EDTA GFR should be used
Creatinine clearance (GFR) calculated, at the Consultants discretion
Serum creatinine - each cycle
Thyroid function baseline and every 1 to 2 cycles
Random cortisol baseline and every 1 to 2 cycles
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Atezolizumab	Immune mediated pneumonitis Immune mediated hepatitis Immune mediated colitis Immune mediated endocrinopathies
Carboplatin	Ototoxicity - monitor Neurotoxicity – monitor.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Carboplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Carboplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

DOSE MODIFICATIONS

Non-haematological

Atezolizumab

Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline.

If the drug-related toxicity does not resolve to grade 0-1 within 12 weeks after onset of toxicity, discontinuation is recommended.

Hepatic impairment

Etoposide

Bilirubin 26-51micromol/L or AST 60-180u/L	give 50% dose
Bilirubin >51micromol/L or AST >180u/L	Clinical decision

Renal impairment

Carboplatin

GFR / calculated CrCl ≤20ml/min or ≤30ml/min with pre-existing severe renal impairment	contraindicated

Etoposide

CrCl >50ml/min	give 100% dose
CrCl 15-50ml/min	give 75% dose
CrCl <15ml/min	further dose reduction required

REFERENCES

1. Horn, L et al; NEJM 2018; 379: 2220 - 2229