ATEZOLIZUMAB (Tecentriq)

INDICATION (ICD10) C34, C66, C67, C68
Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)
Atezolizumab for treating previously platinum-treated locally advanced / metastatic non-squamous or squamous non-small cell lung cancer which has been prospectively determined before this application to be PD-L1 positive or PD-L1 negative or PD-L1 unquantifiable at PD-L1 assay or one in which PD-L1 status cannot be determined on account of insufficient lung cancer tissue being available for PD-L1 assay (TA520):
2. The prescribing clinician is fully aware of the management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies and hepatitis.
3. Histologically- or cytologically-confirmed diagnosis of stage IIIB or IV non-small cell lung cancer and is either non-squamous or squamous in type.
4. Either progressed after previously receiving at least 2 cycles of platinum-containing chemotherapy for stage IIIB or IV non-small cell lung cancer and also a targeted treatment if the tumour is EGFR positive or ALK positive or progressed within 6 months of completing platinum-based chemotherapy given as adjuvant or neoadjuvant therapy or concurrent with radiotherapy
5. PD-L1 testing with an approved and validated test to determine the Tumour Proportion Score (TPS) has been attempted prior to this application.
6. Performance status (PS) of 0 or 1 and would otherwise be potentially fit for docetaxel-based 2nd line chemotherapy.
7. No symptomatically active brain metastases or leptomeningeal metastases.
8. Atezolizumab will be administered as monotherapy.
9. Not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody.
10. To be treated until disease progression and loss of clinical benefit or excessive toxicity or patient choice, whichever is the sooner.
11. A maximum treatment duration of 2 years of uninterrupted treatment or 35 administrations (where administered every 3 weeks) with atezolizumab, whichever is later*.*Where treatment is interrupted any restart and continuation of drug must be in line with the treatment break policy outlined in Specialised Services Circular (SSC) 1918.
12. A formal medical review as to whether treatment with atezolizumab should continue or not will be scheduled to occur at least by the end of the first 9 weeks of treatment
13. Atezolizumab will otherwise be used as set out in its Summary of Product Characteristics (SPC).

For untreated PD-L1 positive metastatic non-small-cell lung cancer (TA705);
2. The prescribing clinician is fully aware of the management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies, hepatitis and skin toxicity.
3. Histologically or cytologically confirmed diagnosis of non-small cell lung cancer (squamous or non-squamous).
4. Stage IIIB or stage IIIC or stage IV non-small cell lung cancer.
5. An approved and validated test has demonstrated that there is PD-L1 expression in ≥50% of tumour cells or in ≥10% of tumour-infiltrating immune cells.
6. Tumour does not have an EGFR activated mutation or an ALK gene rearrangement or a ROS1 gene rearrangement.
7. Has not received previous systemic therapy for advanced/metastatic disease.
-has not received any previous systemic therapy for NSCLC
-was previously treated with adjuvant chemotherapy for NSCLC and has since had disease progression
-was previously treated with neoadjuvant chemotherapy for NSCLC and has since had disease

progression
-this patient was previously treated with concurrent chemo-radiotherapy for NSCLC and has since had disease progression
8. ECOG performance status (PS) of 0 or 1 and would otherwise be fit for platinum-based chemotherapy.
9. No symptomatically active brain metastases or leptomeningeal metastases.
10. Atezolizumab will be administered as monotherapy at a dose of either 1200mg 3-weekly or 1680mg 4-weekly.
11. Has not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody.
12. Atezolizumab will be stopped at disease progression or unacceptable toxicity or withdrawal of patient consent, whichever occurs first. Note: there is NO stopping rule for atezolizumab in this indication and hence patients continuing to benefit from atezolizumab after 2 years of treatment can continue if the patient and clinician agree. Note: once atezolizumab is stopped for disease progression or unacceptable toxicity or withdrawal of patient consent, atezolizumab cannot be re-started.
13. A formal medical review as to how atezolizumab is being tolerated and whether atezolizumab should continue or not will be scheduled to occur at least by the end of the second 3- or 4-weekly cycle of treatment.
14. When a treatment break of more than 3 months beyond the expected 3- or 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of Covid-19.
15. Atezolizumab will otherwise be used as set out in its Summary of Product Characteristics.

The first line treatment of locally advanced or metastatic urothelial cancer in patients who are ineligible for cisplatin-based chemotherapy where all the following criteria are met:
2. Fully aware of the management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies and hepatitis.
3. Histologically or cytologically documented transitional cell carcinoma of the urothelial tract
4. Disease that is either locally advanced (ie T4b any N or any T N2-3 disease) or metastatic (any T any N M1 disease)
5. Not received previous chemotherapy for inoperable locally advanced or metastatic urothelial cancer
6. EITHER not received previous adjuvant chemotherapy, neoadjuvant chemotherapy or chemo-radiotherapy OR, if previously treated with platinum-based chemotherapy whether as adjuvant chemotherapy or as neoadjuvant chemotherapy or with chemo-radiotherapy, has relapsed more than 12 months since completing the platinum-based chemotherapy** Patients meeting this criterion are eligible to be considered as treatment naïve for locally advanced/ metastatic disease but must satisfy all other criteria
7. ECOG performance status (PS) of 0, 1 or 2. Note: treatment of patients of performance status 2 should only proceed with caution as there is limited safety data on PS 2 patients with urothelial cancer treated with atezolizumab.
8. Ineligible for platinum-based chemotherapy, due to one or more of the following: impaired renal function (EDTA-assessed glomerular filtration rate >30 and <60mls/min), hearing loss of 25dB as assessed by formal audiometry, NCI CTCAE grade 2 or worse peripheral neuropathy, ECOG PS 2
9. Has undergone PD-L1 testing
10. A PD-L1 expression of ≥5% has been recorded and the measurement used for PD-L1 testing is defined as the presence of discernible PD-L1 staining of any intensity in tumour infiltrating immune cells covering ≥5% of tumour area occupied by tumour cells, associated intra-tumoural and contiguous peri-tumoural desmoplastic stroma
11. Not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody
12. No symptomatically active brain metastases or leptomeningeal metastases

13. Atezolizumab is being given as monotherapy and will commence at a fixed dose of 1200mg every 3 weeks or 1680mg every 4 weeks
14. A formal medical review as to whether treatment with atezolizumab should continue or not will be scheduled to occur at least by the end of the third cycle of treatment
15. To be treated until disease progression and loss of clinical benefit or excessive toxicity or patient choice, whichever is the sooner.
16. Treatment breaks of up to 12 weeks beyond the expected cycle length are allowed but solely to allow immune toxicities to settle. Where treatment is interrupted any restart and continuation of drug must be in line with the treatment break policy outlined in Specialised Services Circular (SSC) 1918.
17. Atezolizumab will otherwise be used as set out in its Summary of Product Characteristics

Atezolizumab for locally advanced or metastatic urothelial cancer previously treated with platinum-based chemotherapy where all the following criteria are met (TA525):
2. Fully aware of the management of and the treatment modifications that may be required for the immune-related adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies and hepatitis
3. Histologically or cytologically documented transitional cell carcinoma of the urothelial tract
4. Disease is either locally advanced (i.e. T4b any N or any T N2-3 disease) or metastatic (any T any N M1 disease)
5. Either not received previous adjuvant chemotherapy, neoadjuvant chemotherapy or chemo-radiotherapy, or if previously treated with platinum-based chemotherapy whether as adjuvant chemotherapy or as neoadjuvant chemotherapy or with chemo-radiotherapy, has relapsed ≤ 12 months since completing the platinum-based chemotherapy** Patients meeting this criterion are eligible to be considered as previously treated for locally advanced/ metastatic disease (and can answer “Yes” to criteria 6 below) but must satisfy all other criteria
6. Been disease progression during or following previous platinum-based combination chemotherapy for inoperable locally advanced or metastatic urothelial cancer
7. ECOG performance status (PS) score of 0 or 1
8. Not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PDL2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody unless it was received as part of the atezolizumab compassionate use programme for this indication and the patient meets all other criteria listed here
9. Atezolizumab is being given as monotherapy and will commence at a fixed dose of1200mg every 3 weeks or 1680mg every 4 weeks
10. A formal medical review as to whether treatment with atezolizumab should continue or not will be scheduled to occur at least by the end of the third cycle of treatment
11. To be treated until disease progression and loss of clinical benefit or excessive toxicity or patient choice, whichever is the sooner
12. Will receive a maximum treatment duration of 2 years of uninterrupted treatment (i.e. a maximum of 35 administrations if given every 3 weeks, or a maximum of 26 administrations if given every 4 weeks) with atezolizumab, whichever is later*.*Where treatment is interrupted any restart and continuation of drug must be in line with the treatment break policy outlined in Specialised Services Circular (SSC) 1918.
13. No symptomatically active brain metastases or leptomeningeal metastases
14. Atezolizumab will otherwise be used as set out in its Summary of Product Characteristics

REGIMEN 21 day
Day 1 ATEZOLIZUMAB 1200mg in 250ml sodium chloride 0.9% IV infusion

CYCLE FREQUENCY AND NUMBER OF CYCLES
Lung (previously treated) - every 21 days up to a maximum 2 years (35 cycles)
Lung (previously untreated) - every 21 days until progression
Urothelial (previously treated with cisplatin) - every 21 days up to a maximum 2 years (35 cycles)
Urothelial (first line metastatic ineligible for cisplatin) - every 21 days until progression

REGIMEN 28 day
Day 1 ATEZOLIZUMAB 1680mg in 250ml sodium chloride 0.9% IV infusion

CYCLE FREQUENCY AND NUMBER OF CYCLES
Lung (previously treated) - every 28 days up to a maximum 2 years (35 cycles)
Lung (previously untreated) - every 28 days until progression
Urothelial (previously treated with cisplatin) - every 28 days up to a maximum 2 years (26 cycles)
Urothelial (first line metastatic ineligible for cisplatin) - every 28 days until progression

Atezolizumab - The initial dose of Atezolizumab 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.

For the first infusion, the patient's vital signs (heart rate, respiratory rate, blood pressure, and temperature) should be determined within 60 minutes before, during (every 15 minutes), and 30 minutes after the infusion.
For subsequent infusions, vital signs should be monitored within 60 minutes before infusion and at the end of the infusion. Patients will be informed about the possibility of delayed post-infusion symptoms and instructed to contact their study physician if they develop such symptoms.
Inflammation of the lung (pneumonitis) new or worsening cough, shortness of breath, and chest pain.

ANTI-EMETICS
Low risk

CONCURRENT MEDICATION REQUIRED
None required

EXTRAVASATION AND TYPE OF LINE / FILTERS
Atezolizumab – neutral

Use of 0.2-5micron filter is optional
Peripheral line

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Random blood glucose every cycle
Thyroid function baseline and every 1 to 2 cycles
Random cortisol baseline and every 1 to 2 cycles
Baseline weight

MAIN TOXICITES AND ADVERSE REACTIONS

Atezolizumab	Immune mediated pneumonitis Immune mediated hepatitis Immune mediated colitis Immune mediated endocrinopathies

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Atezolizumab	-

DOSE MODIFICATIONS
Non-haematological
Atezolizumab
Immune-related adverse reactions refer to TV immune-oncology agent immune related adverse event clinical guideline for dose modifications.

Infusion-related reactions

Grade 1 or 2	Reduce infusion rate or interrupt. Treatment may be resumed when the event is resolved
Grade 3 or 4	Permanently discontinue Atezolizumab

Hepatic impairment
Atezolizumab
No dose adjustment is needed for patients with mild hepatic impairment. Atezolizumab has not been studied in patients with moderate or severe hepatic impairment.

Renal impairment
Atezolizumab
No dose adjustment is needed for patients with renal impairment.

REFERENCES
1. Rittmeyer, A et al; Lancet 2017; 289 (10066): 255–265 (NSCLC)
2. Balar, A et al ; Lancet 2017; 389 (10064): 67–76 (bladder)