Indication	The first line treatment of locally advanced or metastatic transitional cell urothelial cancer which has PD-L1 expression at a level of >/= 5% in patients who are ineligible for cisplatin-based chemotherapy and meet commissioning criteria. For locally advanced or metastatic transitional cell urothelial cancer previously treated with platinum-based chemotherapy and meeting commissioning criteria. For previously platinum-treated locally advanced/ metastatic non squamous or squamous non-small cell lung cancer which has been prospectively determined 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. If the tumour is EGFR positive or ALK positive, the patient should also, where appropriate, have received a targeted treatment. For untreated metastatic NSCLC which has PD-L1 expression on at least 50% of tumour cells or in at least 10% of tumour-infiltrating immune cells and does not have an epidermal growth factor receptor (EGFR) mutation, anaplastic lymphoma kinase (ALK) gene rearrangement or a ROS1 gene rearrangement. Via project Orbis: Adjuvant treatment of completely resected stage IIB or IIIA or N2 only IIIB NSCLC which has PD-L1 expression at a level of >/= 50% which has not progressed on adjuvant platinum-based chemotherapy (maximum 4 cycles). Patients must not have 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. NB: Patient must have commenced adjuvant platinum-based chemotherapy within 12 weeks of resection of the NSCLC and no more than 12 weeks must have elapsed since the start of the last cycle of adjuvant platinum-based chemotherapy.
Treatment Intent	Palliative Adjuvant (NSCLC only)
Frequency and number of cycles	Schedule 1: Every 21 days Schedule 2: Every 28 days **1st line treatment of locally advanced or metastatic transitional cell urothelial cancer & untreated metastatic NSCLC:** Continue until disease progression or excessive toxicity or patient choice to discontinue. **Locally advanced or metastatic transitional cell urothelial cancer previously treated with platinum-based chemotherapy & previously treated NSCLC:** Continue until progressive disease or unacceptable toxicity up to a maximum treatment duration of 2 years of uninterrupted treatment or 35 administrations with Atezolizumab if given 3 weekly, or a maximum of 26 administrations if given 4 weekly, whichever is later. Treatment breaks of up to 12 weeks beyond the expected cycle length are allowed but solely to allow immune toxicities to settle.

	Adjuvant treatment of NSCLC: Continue until progressive disease, unacceptable toxicity or patient choice or up to a maximum treatment duration of 1 year (maximum of 13 x 4-weekly cycles or 18 x 3-weekly).

Monitoring parameters pre-treatment	• Monitor FBC, U&Es, and LFTs at each cycle.
	• Thyroid function and 9am cortisol level must be assessed at baseline then at least 6-8 weeks.
	• Monitor for signs and symptoms of myocarditis. Carry out ECG as clinically indicated.
	• Dose reductions are not recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability.
	• Renal - no dose adjustment is required in patients with mild or moderate renal impairment (30-89ml/min). No recommendation for patients with severe (<30ml/min) renal impairment as data is too limited.
	• Hepatic impairment (prior to treatment, for immune related hepatitis see below) - no dose adjustment is required for patients with mild hepatic impairment (bilirubin ≤ ULN and AST > ULN or bilirubin > 1.0 × to 1.5 × ULN and any AST). No data is available to make a recommendation in patients with moderate or severe hepatic impairment (bilirubin > 1.5 × to 3 × ULN and any AST or bilirubin > 3 × ULN and any AST).
	• Infusion-related reactions – reduce infusion rate or interrupt treatment if Grade 1 or 2 infusion-related reaction. Atezolizumab may be continued with close monitoring; premedication with antipyretic and antihistamines should be considered. Permanently discontinue in patients with Grade 3 or 4 infusion related reactions.
	• Immune- related reactions:
	  ○ Reactions include myocarditis, pneumonitis, colitis, hepatitis, pancreatitis, adrenal insufficiency, meningoencephalitis, hyperthyroidism, hypothyroidism, hypophysitis, diabetes, rash, arthralgia, musculoskeletal pain, neuropathies, myasthenic syndrome and Guillain-Barre syndrome.
	  ○ Atezolizumab must be permanently discontinued for any Grade 3 immune-related adverse reaction that recurs and for any Grade 4 immune-related adverse reactions, except for endocrinopathies that are controlled with replacement hormones
	  ○ If corticosteroids are used to treat an immune related reaction they should be tapered over at least 1 month. Treatment should not be resumed while the patient is receiving immunosuppressive doses of corticosteroids (>10mg prednisone) or other immunosuppressive therapy. Prophylactic antibiotics should be used where appropriate to prevent opportunistic infections in patients receiving immunosuppressive therapy.
	  ○ See guidelines for management of immune-related adverse reactions following immunotherapy:
	  ○ http://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/
	• Drug interactions:
	  ○ The use of systemic corticosteroids or immunosuppressants before starting atezolizumab should be avoided. However, systemic corticosteroids or other immunosuppressants can be used to treat immune-related adverse reactions after starting atezolizumab.
	  ○ Patients should not receive the flu vaccine unless the benefit outweighs the risk and after discussion between consultant and patient.
	• Patients experiencing fatigue should be advised not to drive and use machinery.

	• Use with caution in patients with any history of or concurrent brain metastases, active autoimmune disease, or medical conditions requiring systemic immunosuppression, after careful consideration of the potential risk-benefit. • The patient should be provided with the Tecentriq® Patient Alert card with each prescription (to be carried until at least 5 months after the last dose of treatment).
Reference(s)	SPC accessed online 10.11.21 CDF v1.193 accessed online 10.11.21 BT form for NSCLC accessed online 10.11.21

NB For funding information, refer to CDF and NICE Drugs Funding List

Schedule 1: Repeat every 21 days

Day	Drug	Dose	Route	Infusion Time	Administration Details
Day 1	Metoclopramide	20mg	PO		
	Atezolizumab	**1200mg**	IV	1st dose over 60 mins. If tolerated, all subsequent infusions over 30 mins	diluted in 250ml 0.9% sodium chloride
TTO	Drug	Dose	Route	Directions	
	Metoclopramide	10mg	PO	up to 3 times a day for 3 days, then 10mg up to 3 times a day as required (max. 30mg per day including 20mg pre-chemo dose) Do not take for more than 5 days continuously.	
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if specified.	

Schedule 2: Repeat every 28 days

Day	Drug	Dose	Route	Infusion Time	Administration Details
Day 1	Metoclopramide	20mg	PO		
	Atezolizumab	**1680mg**	IV	1st dose over 60 mins. If tolerated, all subsequent infusions over 30 mins	diluted in 250ml 0.9% sodium chloride
TTO	Drug	Dose	Route	Directions	
	Metoclopramide	10mg	PO	up to 3 times a day for 3 days, then 10mg up to 3 times a day as required (max. 30mg per day including 20mg pre-chemo dose) Do not take for more than 5 days continuously.	
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if specified.	