NIVOLUMAB (Opdivo)

INDICATION (ICD10) C15, C34, C43, C49, C64

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (NIV1) (NIV4) (NIV5) (NIV6) (NIV7) (NIV8a) (NIV8b) (NIV8c) (NIV15) (NIV17)

1. Nivolumab monotherapy for the treatment of PD-L1 (TPS) ≥1%) positive stage IIIB, IIIC or IV NON-SQUAMOUS locally advanced or metastatic disease non-small cell **lung** cancer 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. 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 (CTL-4) antibody unless the patient discontinued or completed checkpoint inhibitor immunotherapy as part of adjuvant/neoadjuvant/maintenance therapy without disease progression and at least 6 months elapsed between the date of the last immunotherapy treatment and the date of first diagnosis of relapse with recurrent or metastatic disease. No symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1. (TA713)
2. Nivolumab monotherapy for the treatment of stage IIIB, IIIC or IV SQUAMOUS locally advanced or metastatic non-small cell **lung** cancer 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. 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 (CTL-4) antibody unless the patient discontinued or completed checkpoint inhibitor immunotherapy as part of adjuvant/neoadjuvant/maintenance therapy without disease progression and at least 6 months elapsed between the date of the last immunotherapy treatment and the date of first diagnosis of relapse with recurrent or metastatic disease. No symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1. (TA655)
3. Nivolumab monotherapy for the treatment of recurrent or metastatic squamous-cell carcinoma of the **head and neck** not amenable to local therapy with curative intent (surgery and/or radiation therapy with or without chemotherapy) after disease has progressed or recurred during or within 6 months of the last dose of previously received platinum-based chemotherapy. No symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1. (TA736)
4. Nivolumab monotherapy for the adjuvant treatment of newly diagnosed and completely resected stage III or completely resected stage IV malignant **melanoma**. Treatment naïve to systemic therapy for malignant melanoma and in particular has not previously received any BRAF V600 inhibitors or MEK inhibitors and is treatment naïve to systemic therapy for malignant melanoma. PS 0 or 1. (TA684)
5. Nivolumab monotherapy (with or without initial combination treatment with ipilimumab) for unresectable or advanced malignant **melanoma.** At the time of starting nivolumab, is treatment-naïve to systemic therapy or has/had previously only received BRAF/MEK-targeted therapy or ipilimumab monotherapy or both BRAF/MEK-targeted treatment and ipilimumab monotherapy and not received prior treatment with any anti-PD-1, anti-PD-L1, anti-PD-L2 or anti-CD137 treatments unless the patient has received adjuvant immunotherapy with nivolumab or pembrolizumab in which case the patient must have relapsed after the discontinuation of such adjuvant immunotherapy.. PS fit to receive treatment with immunotherapy. (form a) (TA684)
6. Nivolumab monotherapy for treating unresectable or advanced malignant **melanoma**) with stable disease or a response state to treatment with nivolumab for melanoma and has received 2 or more years of nivolumab (including any doses given with ipilimumab) **(discontinuation form b**) (TA684)**.**
7. Nivolumab monotherapy for treating unresectable or advanced malignant **melanoma** progressive non-resectable or metastatic melanoma and not received any other systemic therapy in the time between the date of elective discontinuation of nivolumab and this

application to re-start nivolumab. Has a sufficient PS to be fit to receive treatment with immunotherapy. (restart form c) (TA684).

8. Nivolumab for previously treated with only 1 or 2 previous lines of antiangiogenic therapy unresectable locally advanced or metastatic **renal cell** carcinoma with has a clear cell component or is a papillary RCC. PS Karnofsky 70 or more. (TA417)
9. Nivolumab monotherapy for treatment of adult patients with unresectable locally advanced or recurrent or metastatic squamous cell carcinoma of the **oesophagus** previously treated with a fluoropyrimidine and platinum-based combination chemotherapy. No symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1. (TA707)
10. Nivolumab monotherapy as adjuvant treatment for those with completely resected oesophageal or **gastro-oesophageal** carcinoma who have residual pathological disease at surgery following prior neoadjuvant platinum based chemoradiotherapy (the primary treatment intent at the outset of therapy was to treat with the sequence of chemoradiotherapy followed by surgical resection). Has undergone surgery for M0 disease and that the tumour has been completely resected i.e. the patient has had a R0 resection for M0 disease and this application for adjuvant nivolumab is less than 16 weeks since surgical resection of the tumour and still has M0 disease within last 4 weeks. PS 0 or 1. (TA746)

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REGIMEN 28 day SC
Day 1 NIVOLUMAB 1200mg subcutaneous over 3 to 5 minutes

REGIMEN 28 day IV
Day 1 NIVOLUMAB 480mg in 100ml sodium chloride IV infusion over 30 minutes

CYCLE FREQUENCY AND NUMBER OF CYCLES
Lung - every 28 days until progression for up to 26 cycles (2 years) (unlicensed frequency)
Head and neck - every 28 days until progression (unlicensed frequency)
Melanoma adjuvant – every 28 days up to 13 cycles (12 months)
Melanoma metastatic - every 28 days until disease progression or intolerance. For the monotherapy phase following ipilimumab nivolumab combination, the first dose of nivolumab should be administered 6 weeks after last dose of nivolumab and ipilimumab combination.
Oesophagus, gastro-oesophageal adjuvant – every 28 days up to 13 cycles (12 months)
Oesophagus metastatic – every 28 days until disease progression (unlicensed frequency)
Renal – every 28 days until disease progression.

Can be given 2 weekly SC or IV if necessary (see SPC for details including 2 weekly dose)

ANTI-EMETICS
None required

CONCURRENT MEDICATION REQUIRED
None required

ADMINISTRATION

Nivolumab	SC administer in the abdomen or thigh over 3 to 5 minutes. Alternate injection sites.

EXTRAVASATION AND TYPE OF LINE / FILTERS
Nivolumab IV - neutral

IV use low protein binding 0.2 to 1.2micron in-line or add-on filter.
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
Thyroid function baseline, then every cycle
Random cortisol baseline, then every cycle
Random glucose every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Nivolumab	Immune related toxicities - pneumonitis, colitis or hepatitis etc

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC)

Nivolumab	-

DOSE MODIFICATIONS

Non-haematological

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

Hepatic impairment

Nivolumab
Data from patients with moderate or severe hepatic impairment are too limited to draw conclusions. Nivolumab should be administered with caution in patients with moderate or severe hepatic impairment ie bilirubin >1.5xULN and any AST.

Renal impairment

Nivolumab
Data from patients with severe renal impairment (CrCl <30ml/min) are too limited to draw conclusions.

REFERENCES

1. Borghaei, H; NEJM 2015; 373: 1627 – 1639 (NSCLC)
2. Ferris, R et al; NEJM 2016; 375: 1856 1867 (H&N)
3. Weber, J et al; Lancet Oncology 2015; 16 (4): 375–384 (melanoma)
4. Robert, C et al; NEJM 2015; 372 (4): 320–330 (melanoma)
5. Weber, J et al; NEJM 2017; 377: 1824–1835 (adjuvant, melanoma)
6. Motzer, R et al; NEJM 2015; 373; 1803–1813 (rcc)