Nivolumab (Head & Neck)

Indication

Metastatic or unresectable recurrent squamous cell carcinoma of the head and neck in patients whose disease has progressed **within 6 months of last dose of platinum chemotherapy**.

Performance status 0-1.

(NICE TA736)

ICD-10 codes

Codes prefixed with C00-13.

Regimen details

Day	Drug	Dose	Route
1	Nivolumab	480mg every 4 weeks*	IV infusion

*NB. 240mg, two-weekly is also an option but the 4 weekly schedule is preferred unless there are clinical reasons for using 2 weekly treatment

Cycle frequency

Every 28 days

Number of cycles

Continued until disease progression or unacceptable toxicity.

Administration

Nivolumab may be administered without dilution or in sodium chloride 0.9% or glucose 5% at a concentration between 1-10mg/mL over 30 minutes. Nivolumab should be administered via an infusion set with an in-line sterile, non-pyrogenic, low protein binding filter (pore size 0.2 – 1.2µm).

Patients should be monitored (blood pressure, pulse and temperature) every 30 minutes during the infusion for infusion related reactions. For mild to moderate reactions, decrease the infusion rate and closely monitor. Premedication with paracetamol and chlorphenamine should be used for further doses. For severe infusion related reactions discontinue treatment.

Pre-medication

Nil

Emetogenicity

This regimen has low emetogenic potential

Additional supportive medication

Loperamide should be supplied to be used if required.
Antiemetics as per local policy, if required.

Extravasation

Neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFT	14 days
Thyroid function	14 days
Glucose	14 days
Calcium	14 days
Cortisol	14 days

Investigations – pre each subsequent cycle

Investigation	**Validity period** (or as per local policy)
FBC	7 days
U+E (including creatinine)	7 days
LFT	7 days
Thyroid function	7 days
Glucose	7 days
Cortisol	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophil count	≥ 1.0 x 10^9/L
Platelets	≥ 75 x 10^9/L
Creatinine Clearance (CrCl)	≥ 30mL/min
Bilirubin	≤ 1.5 x ULN
ALT/AST	< 3 x ULN
Alkaline Phosphatase	< 5 x ULN

Dose modifications

- **Haematological toxicity**

Discuss with the consultant if:
Neutrophils <1.0 x 10^9/L
Platelets <75 x 10^9/L

- **Renal impairment**

No dose modifications required in mild-moderate renal impairment. Use with caution in severe renal impairment.

- **Hepatic impairment**

Nivolumab has not been studied in moderate to severe hepatic impairment. Use with caution if bilirubin > 1.5 x ULN – consultant decision. See below for management of hepatitis during treatment.

- **Other toxicities**

Patients must be advised to seek specialist advice if they experience side effects as these can worsen rapidly. Immune reactions may occur during or after completion of treatment. ESMO Clinical Practice Guidelines for management of immunotherapy toxicities can be found here.

Toxicity	Definition	Action
Colitis	Grade 1	Continue and closely monitor
	Grade 2-3	Withhold until symptoms resolve to ≤ grade 1
	Grade 4 or recurrent grade 3	Permanently discontinue nivolumab
Pneumonitis	Grade 1	Continue and closely monitor
	Grade 2	Withhold until symptoms resolve to ≤ grade 1
	Grade 3-4 or recurrent grade 2	Permanently discontinue nivolumab
Nephritis	Grade 2 or 3 (creatinine 1.5-6 x ULN)	Withhold until symptoms resolve to ≤ grade 1
	Grade 4 (creatinine > 6 x ULN)	Permanently discontinue nivolumab
Endocrine	Symptomatic hypophysitis	Withhold until symptoms resolve to ≤ grade 1
	Type 1 diabetes with grade > 3 hyperglycaemia (glucose > 13.9 mmol/L) or ketoacidosis	Withhold until ≤ grade 2 May consider recommencing after corticosteroid taper or discontinue.
	Hyperthyroidism ≥ grade 3	Withhold until ≤ grade 2 May consider recommencing after corticosteroid taper or discontinue.
	Hypothyroidism	Continue and manage with replacement therapy
Hepatitis	AST/ALT 3-5 x ULN or Bilirubin > 1.5-3 x ULN	Withhold until resolves to ≤ grade 1
	AST/ALT > 5 x ULN or Bilirubin > 3 x ULN	Permanently discontinue nivolumab
	If liver metastasis with baseline AST/ALT 3-5 x ULN: - If AST/ALT increases ≥ 50% for ≥ 1 week	Permanently discontinue nivolumab
Infusion-related reactions	Grade 3-4	Permanently discontinue nivolumab
Skin reactions	Grade 3 or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	Withhold until resolves to ≤ grade 1
	Grade 4 or confirmed SJS or TEN	Permanently discontinue nivolumab
Other immune-related adverse reactions	Grade 3 or 4 myocarditis Grade 3 or 4 encephalitis Grade 3 or 4 Guillain-Barre syndrome	Permanently discontinue nivolumab

Nivolumab should be permanently discontinued if:
- Grade 4 toxicity (except for endocrinopathies that are controlled with replacement hormones)
- Corticosteroid dosing cannot be reduced to ≤10 mg prednisolone or equivalent per day within 12 weeks
- Treatment-related toxicity does not resolve to Grade 0-1 within 12 weeks after last dose
- Any event occurs a second time at Grade ≥ 3 severity

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Immune reactions may occur during or after completion of treatment.
Colitis
Hepatitis
Peripheral neuropathy
Hypopituitarism
Hypothyroidism
Uveitis
Glomerulonephritis
Cardiac events
Thromboembolism
Interstitial lung disease

- **Frequently occurring side effects**

Pruritus
Rash
Nausea and vomiting
Diarrhoea
Fatigue
Decreased appetite
Hyperglycaemia
Abdominal pain
Anorexia

- **Other side effects**

Tumour pain
Headache
Raised transaminases

Significant drug interactions – for full details consult product literature/ reference texts

Anticoagulants: increased risk of haemorrhage – avoid or closely monitor.

Corticosteroids: use of systemic corticosteroids at baseline, before starting nivolumab, should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of the agent. However, systemic corticosteroids or other immunosuppressants can be used after starting nivolumab to treat immune-related adverse reactions.

Additional comments

Women of child bearing potential should use effective contraception during treatment and for at least 4 months after the last dose.

References

- National Institute for Health and Clinical Excellence TA736. Accessed 21 September 2023 via www.nice.org.uk
- Summary of Product Characteristics Nivolumab (Bristol Myers Squibb) accessed 21 September 2023 via www.medicines.org.uk
- Ferris, R.L et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. N Engl J Med 2016; 375:1856-1867

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