# Cemiplimab

## Indication
Treatment of locally advanced or metastatic cutaneous squamous cell carcinoma when curative surgery or curative radiotherapy is not appropriate.

(NICE TA598)

## ICD-10 codes
Codes with a prefix C44

## Regimen details

| Day | Drug | Dose | Route |
|---|---|---|---|
| 1 | Cemiplimab | 350mg | IV infusion |

## Cycle frequency
21 days

## Number of cycles
Treatment should be continued until unacceptable toxicity or disease progression, for a maximum of 2 years.

## Administration
Cemiplimab is administered in 100mL sodium chloride 0.9% over 30 minutes. It must be administered via an intravenous line containing a sterile, non-pyrogenic, low-protein binding, in-line or add-on filter (0.2 micron to 5 micron pore size).

Patients should be monitored for infusion related reactions, including nausea, pyrexia, abdominal pain, chills and flushing. For mild to moderate (Grade 1-2) reactions interrupt the infusion and recommence at a slower rate. For severe or life-threatening (Grade 3-4) reactions, permanently discontinue treatment.

## Pre-medication
Nil

## Emetogenicity
This regimen has low emetogenic potential

## Additional supportive medication
Nil required routinely.

## Extravasation
Cemiplimab is neutral (Group 1)

## Investigations – pre first cycle

| **Investigation** | **Validity period** (or as per consultant instructions) |
|---|---|
| FBC | 14 days |
| U+E (including creatinine) | 14 days |
| LFT | 14 days |
| Thyroid function | 14 days |
| Calcium | 14 days |
| Glucose | 14 days |

## Investigations – pre subsequent cycles

| **Investigation** | **Validity period** |
|---|---|
| FBC | 48 hours |
| U+E (including creatinine) | 48 hours |
| LFT | 48 hours |
| Calcium | As clinically indicated |
| Thyroid function* | 48 hours |
| Glucose | 48 hours |

*On alternate cycles.

## 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 | ≤2.5 X ULN or ≤5 X ULN with liver metastases |

## Dose modifications

Dose reductions are not recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability.

- **Haematological toxicity**

Discuss with the consultant if:
WBC <2.0 x $10^9$/L
Neutrophils <1.0 x $10^9$/L
Platelets <75 x $10^9$/L

- **Renal impairment**

No dose adjustment is recommended for patients with mild – moderate renal impairment. There is limited data for cemiplimab in patients with severe renal impairment CrCl <30 mL/min – discuss with consultant.

- **Hepatic impairment**

No dose adjustment is recommended for patients with mild hepatic impairment. Cemiplimab has not been studied in patients with moderate or severe hepatic impairment.

- **Other toxicities**

Management of immune-related adverse reactions may require a dose delay or permanent discontinuation of

treatment and initiation of systemic high-dose corticosteroid or, in some cases, the addition of other immunosuppressive therapy. Dose reduction is not recommended.

**Refer to UKONS and ESMO guidance for treatment of immune related toxicities.**

Early identification and treatment is key.

**<u>Permanently discontinue</u> treatment in patients with the following symptoms:**

| **Toxicity – severe or life threatening** | **Definition** |
|---|---|
| Pneumonitis | Grade 3 or 4<br>or recurrent grade 2 pneumonitis |
| Colitis | Grade 4 or recurrent grade 3 colitis |
| Hepatitis | Grade ≥3 with AST or ALT > 5xULN Or total bilirubin > 3xULN |
| Skin | Grade 4 or **confirmed** Stevens Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN) |
| Nephritis | Grade 3 or 4 |
| Other immune-related adverse reactions | – Grade 4 adverse reaction (excluding endocrinopathies)<br>– Recurrent severe Grade 3 immune-related adverse reaction<br>– Persistent Grade 2 or 3 immune-related adverse reactions lasting 12 weeks or longer (excluding endocrinopathies)<br>– Inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks. |

**<u>Withhold</u> treatment in patients with the following symptoms and refer to UKONS and ESMO guidance on treatment of immune mediated toxicities for full actions and advise:**

| Toxicity – severe or life threatening | Definition | Action |
|---|---|---|
| Pneumonitis | Grade 2 | Withhold.<br>Treat with initial dose of 1 /kg/day prednisone or equivalent followed by a taper.<br>Resume if pneumonitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent. |
| Colitis | Grade 2 or 3 | Withhold.<br>Treat with initial dose of 1 /kg/day prednisone or equivalent followed by a taper.<br>Resume if colitis or diarrhoea improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent. |
| Hepatitis | Grade 2 with AST or ALT >3 and ≤5xULN<br>or<br>total bilirubin >1.5 and ≤3xULN | Withhold.<br>Treat with initial dose of /kg/day prednisone or equivalent followed by a taper.<br>Resume if hepatitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent or returns to baseline AST or ALT after completion of corticosteroid taper. |
| Hypothyroidism | Grade 3 or 4 | Withhold if symptoms.<br>Initiate thyroid hormone replacement as clinically indicated.<br>Resume when hypothyroidism returns to Grade 0 to 1 or is otherwise clinically stable. |
| Hyperthyroidism | Grade 3 or 4 | Withhold if symptoms.<br>Initiate symptomatic management as clinically indicated.<br>Resume when hypothyroidism returns to Grade 0 to 1 or is otherwise clinically stable. |
| Hypophysitis | Grade 2-4 | Withhold if symptomatic.<br>Resume if hypophysitis improves and hormone replacement is established. |
| Adrenal insufficiency | Grade 2-4 | Withhold.<br>Hormone (hydrocortisone) replacement should be commenced. |

| | | |
|---|---|---|
| Type 1 diabetes | Grade 3 or 4 | Withhold.<br>Initiate treatment with anti-hyperglycaemics as clinically indicated.<br>Resume when returns to Grade 0 to 1 or is otherwise clinically stable. |
| Skin | Grade 2 lasting longer than 1 week,<br>Grade 3<br>or<br>**suspected** Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) | Withhold<br>Treat with initial dose of 1 /kg/day prednisone or equivalent followed by a taper.<br>Resume if improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent. |
| Nephritis | Grade 2 | Withhold<br>Treat with initial dose of 1 /kg/day prednisone or equivalent followed by a taper.<br>Resume if improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent. |
| Other immune-related adverse reactions | Grade 3 clinical signs or symptoms of an immune-related adverse reaction not described above. | Withhold.<br>Initiate symptomatic management. Resume if other immune-related adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent. |

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

- **Serious side effects**

Pneumonitis
Colitis
Hepatitis
Thyroid disorders
Hypophysitis
Adrenal insufficiency
Nephritis
Infusion related reactions
Vasculitis
ITP
Peripheral neuropathy, Guillain Barre syndrome, encephalitis

- **Frequently occurring side effects**

Skin disorders
Stomatitis
Diarrhoea
Fatigue
Arthralgia, arthritis
Decreased appetite
Hyperglycaemia
Abdominal pain
Anorexia

- **Other side effects**

Headache
Raised transaminases

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

**Corticosteroids or immunosuppressants**: use of systemic corticosteroids or immunosuppressants before starting cemiplimab, 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 cemiplimab to treat immune-related adverse reactions.

## Additional comments

Patients must be provided with a Patient Alert Card before they start treatment.

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

## References


- http://www.swscn.org.uk/guidance-protocols/cancer-protocols/ accessed 9 Jul 2020
- National Institute for Health and Clinical Excellence TA384. Accessed 27 November 2019 via www.nice.org.uk
- Summary of Product Characteristics Cemiplimab via www.medicines.org.uk
- Migden, M et al ; PD-1 Blockade with Cemiplimab in Advanced Cutaneous Squamous-Cell Carcinoma NEJM 2018 ; 379 : 341 - 351


**THIS PROTOCOL HAS BEEN DIRECTED BY DR BOARD, DESIGNATED LEAD CLINICIAN FOR MELANOMA**

**RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE**

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