AVELUMAB (Bavencio)

INDICATION (ICD10) C44, 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/)
The treatment of previously untreated (with systemic therapy) metastatic Merkel cell carcinoma where all the following criteria are met:
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. Confirmed histological or cytological diagnosis of Merkel cell carcinoma
4. Metastatic disease
5. Treatment naïve to any systemic anti-cancer therapy for Merkel cell carcinoma and in particular has not received any prior treatment with any anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137 or anti-cytotoxic T-lymphocyte-associated antigen-4 [CTLA-4] antibody
6. ECOG performance status of either 0 or 1. Note: a patient with a performance status of 2 or more is not eligible for avelumab
7. If the patient has brain metastases, then these have been treated and are stable
8. Avelumab is to be used as monotherapy only
9. Avelumab is to be continued until loss of clinical benefit or unacceptable toxicity or patient choice to stop treatment. I also confirm that patients with radiological disease progression not associated with significant clinical deterioration (defined as no new or worsening symptoms and no change in performance status for greater than 2 weeks and no need for salvage therapy: all 3 conditions must apply) can continue treatment
10. A formal medical review as to whether treatment with avelumab should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment
11. Treatment breaks of up to 12 weeks beyond the expected cycle length of avelumab are allowed but solely to allow immune toxicities to settle
12. Avelumab will otherwise be used as set out in its Summary of Product Characteristics (SPC).

The treatment of previously treated (with systemic cytotoxic chemotherapy) metastatic Merkel cell carcinoma where all the following criteria are met:
2. The prescribing clinician is 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. Confirmed histological or cytological diagnosis of Merkel cell carcinoma
4. Metastatic disease
5. Has previously been treated with cytotoxic chemotherapy for metastatic Merkel cell carcinoma and has not received any prior treatment with any anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137 or anti-cytotoxic T-lymphocyte-associated antigen-4 [CTLA-4] antibody
6. ECOG performance status of either 0 or 1. Note: a patient with a performance status of 2 or more is not eligible for avelumab
7. If the patient has brain metastases, then these have been treated and are stable
8. Avelumab is to be used as monotherapy only
9. Avelumab is to be continued until loss of clinical benefit or unacceptable toxicity or patient choice to stop treatment. I also confirm that patients with radiological disease progression not associated with significant clinical deterioration (defined as no new or worsening symptoms and no change in performance status for greater than 2 weeks and no need for salvage therapy: all 3 conditions must apply) can continue treatment
10. A formal medical review as to whether treatment with avelumab should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment
11. Treatment breaks of up to 12 weeks beyond the expected cycle length of avelumab are allowed but solely to allow immune toxicities to settle
12. Avelumab will otherwise be used as set out in its Summary of Product Characteristics (SPC)

Avelumab monotherapy for the maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma who have just completed and not progressed on 1st line platinum-containing combination chemotherapy where the following criteria have been met:

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. Has a histologically confirmed diagnosis of urothelial carcinoma.
4. Has locally advanced or metastatic disease.
5. Has recently completed 1st line combination chemotherapy with either the combination of gemcitabine plus cisplatin or gemcitabine plus carboplatin.
- 1st line commenced with gemcitabine plus cisplatin or
- 1st line chemotherapy commenced with gemcitabine plus carboplatin.
6. Has completed at least 4 cycles and no more than 6 cycles of combination chemotherapy with gemcitabine plus cisplatin or gemcitabine plus carboplatin.
7. Had a CT or MR scan after completing this chemotherapy and has been shown to have no evidence of progressive disease compared with the scans performed prior to chemotherapy and with any scans whilst on chemotherapy.
- complete response to treatment at the end of 1st line chemotherapy or
- partial response to treatment at the end of 1st line chemotherapy or
- stable disease at the end of 1st line chemotherapy.

Note: patients who have responded to chemotherapy as demonstrated on an interval scan during chemotherapy but whose scans at the end of chemotherapy show progressive disease are NOT eligible for maintenance avelumab therapy.
8. Will commence treatment with avelumab within 4 to 10 weeks of receiving the last dose of chemotherapy.
9. ECOG performance status score of 0 or 1.
10. Maintenance treatment with avelumab monotherapy will continue until disease progression or symptomatic deterioration or unacceptable toxicity or withdrawal of patient consent or after a maximum of 5 calendar years of avelumab treatment (as measured from cycle 1 day 1 of avelumab administration), whichever of these events occurs first.
11. Has no symptomatically active brain metastases or leptomeningeal metastases.
12. 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 unless the patient has received maintenance avelumab via the EAMS program.
13. Avelumab is being given as monotherapy.
14. A formal medical review as to how treatment with avelumab is being tolerated and whether treatment with avelumab should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment.
15. Where a treatment break of more than 12 weeks beyond the expected 2-weekly cycle length is needed, I will complete a treatment break form to restart treatment, including an indication as appropriate if the patient had an extended break because of COVID 19.
16. Avelumab will otherwise be used as set out in its Summary of Product Characteristics (SPC).

REGIMEN

Day 1 Premedication 30 minutes prior to infusion (see concurrent medication):
Chlorphenamine 10mg IV bolus
Paracetamol 1000mg tablet
AVELUMAB 800mg in 250ml sodium chloride IV infusion over 60 minutes

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 14 days

A medical review as to whether treatment with avelumab should continue or not will need to occur at least by the end of the first 8 weeks of treatment.

Merkel cell - Avelumab is to be continued until loss of clinical benefit or unacceptable toxicity or patient choice to stop treatment. Patients with radiological disease progression not associated with significant clinical deterioration (defined as no new or worsening symptoms and no change in performance status for greater than 2 weeks and no need for salvage therapy: all 3 conditions must apply) can continue treatment.

Urology - Maintenance treatment with avelumab monotherapy will continue until disease progression or symptomatic deterioration or unacceptable toxicity or withdrawal of patient consent or after a maximum of 5 calendar years of avelumab treatment (as measured from cycle 1 day 1 of avelumab administration), whichever of these events occurs first.

ANTI-EMETICS

Minimal emetic risk

CONCURRENT MEDICATION REQUIRED

Avelumab – Ensure premedication give before avelumab for first 4 cycles, then if the fourth infusion is completed without an infusion-related reaction, premedication for subsequent doses should be administered at the discretion of the physician.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Avelumab - neutral

Use 0.2 to 0.22micron in-line filter.
Central or 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

Avelumab	Immune related toxicities - pneumonitis, colitis or hepatitis etc

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Avelumab	-

DOSE MODIFICATIONS

Non-haematological

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

Hepatic impairment
Avelumab
No dose adjustment is needed for patients with mild hepatic impairment. There are insufficient data in patients with moderate or severe hepatic impairment for dosing recommendations.

Renal impairment
Avelumab
No dose adjustment is needed for patients with mild or moderate renal impairment. There are insufficient data in patients with severe renal impairment for dosing recommendations.

REFERENCES
1. D'Angelo, S et al; JAMA Oncol 2018; 4(9):e180077. doi:10.1001/jamaoncol.2018.0077