IPILIMUMAB

For the treatment of advanced (unresectable or metastatic) melanoma after at least one line of chemotherapy; NICE approved Dec 2012
An option for previously untreated advanced (unresectable or metastatic) melanoma; NICE approved July 2014

Drug/Dosage: Ipilimumab 3mg/kg IV Day 1

Administration: in a minimum of 90ml sodium chloride 0.9% and infused over 90 minutes via a 0.2 - 1.2 micron in-line filter (the PVC-free giving sets used for paclitaxel are appropriate, with a 0.22 micron filter).

If a patient experiences a mild or moderate infusion-related reaction, decrease the rate of infusion and monitor closely. Give any further doses with close monitoring. Premedication with paracetamol and chlorphenamine should be considered for further doses.

If a patient experiences a severe infusion-related reaction, ipilimumab must be discontinued and appropriate treatment given.

Frequency: every 3 weeks for 4 doses
Review for toxicities every 3 weeks, before a dose is due. In addition, it is very important that the patient is educated to immediately report any key signs or symptoms to the treating oncology team (see Comments)
Review for response only after course completed. (The appearance of new lesions, or growth of existing lesions during treatment, is **not** an indicator of lack of response)

Main Toxicities: immune-related reactions may appear during the treatment course, or after the course has completed.
The most common immune-related reactions are: diarrhoea, rash, pruritis, abdominal pain, abnormal hepatic function, hypothyroidism, hypopituitarism, confusion, peripheral neuropathy, blurred vision, eye pain, hypotension, flushing, arthralgia, myalgia

Anti- emetics: mildly emetogenic

Extravasation: non-vesicant

Regular Investigations:		
	FBC	before each dose
	U&Es	before each dose
	LFTs	before each dose, and as indicated
	LDH	before each dose
	Thyroid function*	before each dose
	Cortisol	before each dose

**to avoid treatment delays, use previous results for prescribing purposes, if previous result was within normal limits and no current concerns*

Comments: Patients may be given a supply of loperamide, along with counselling to contact the oncology team in the event of any diarrhoea.

Reason for Update: toxicity management removed; regular investigations reviewed; blood test cut-offs added	Approved by Consultant: Dr M Ajaz
Version: 5	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 4	Date: 11.10.17
Prepared by: S Taylor	Checked by: C Tucker

Patients must be advised to contact the oncology team or the 24 hour hot-line immediately they experience any side effect, as some side effects worsen rapidly. Prompt management of side effects can ensure that the patient continues with treatment.
Each patient should be given a copy of the Yervoy™ patient brochure and alert card (to be carried until 1 year after completion of treatment).

Dose Delays and Toxicity Management:

Any diarrhoea, increased stool frequency, bloody stool, LFT elevations, rash or endocrinopathy must be considered ipilimumab-related and managed appropriately to minimise life-threatening complications.

For detailed guidelines for the management of immune-related adverse events, please refer to the Alliance "Guidelines for Management of Immunotherapy-Related Adverse Events" document.

With regards to blood tests, proceed with next cycle of immunotherapy if:
Platelets ≥ 75 x 10^9/l and Neutrophils ≥ 1.0 x 10^9/l
and
AST/ALT ≤ 3 x ULN
and
Serum creatinine ≤ 1.5 x baseline
and
TSH / free T_4 within range, or no change from baseline

Ipilimumab may be restarted within 12 weeks after the last dose, only if an adverse reaction remains at Grade ≤ 1 and the corticosteroid dose has been reduced to ≤ 10 mg prednisone or equivalent per day.

Renal Impairment: No dose adjustment is required in patients with mild or moderate renal impairment. Ipilimumab clearance is not affected by renal function, but it has not been studied in patients with C&G < 22ml/min.

Hepatic Impairment: If ALT/AST ≥ 5 x ULN or bilirubin > 3 x ULN at baseline, use ipilimumab only with caution, as there is no data on this population.

Reference: Hodi, FS et al; NEJM 2010; 363: 711-723