PEMBROLIZUMAB (Keytruda) PACLITAXEL

INDICATION (ICD10) C50

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (PEMB18)

1. The treatment of previously untreated locally advanced unresectable or metastatic triple negative breast cancer in patients with PD-L1 expression test results of immune cell (IC) <1% and a combined positive score (CPS) of 10 or more. PS 0 or 1. (TA801)

REGIMEN (SC) (pembrolizumab before chemotherapy)

Days 1, 8 and 15 (pembrolizumab before chemotherapy on days both administered)

Premedication 30 minutes prior to infusion**:

Dexamethasone	8mg IV bolus
Chlorphenamine	10mg IV bolus
PACLITAXEL	90mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes

Day 1 PEMBROLIZUMAB 790mg subcutaneous* (4.8ml) over 2 minutes every 42 days

*Into the thigh or abdomen, avoiding the 5cm area around the navel

REGIMEN (IV) (pembrolizumab before chemotherapy)

Days 1, 8 and 15 (pembrolizumab before chemotherapy on days both administered)

Premedication 30 minutes prior to infusion**:

Dexamethasone	8mg IV bolus
Chlorphenamine	10mg IV bolus
PACLITAXEL	90mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes

Day1 PEMBROLIZUMAB 400mg in 100ml sodium chloride IV infusion over 30 minutes every 42 days

diluent and diluent volume for dose prescribed as per national standardised product specification
** If no hypersensitivity reactions after the first two doses, remove pre-medication with dexamethasone and chlorphenamine from dose 3 onwards (off-label).

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days
Pembrolizumab every 42 days until disease progression up to maximum 2 years
Paclitaxel until disease progression or unacceptable toxicity
(if one drug needs to be discontinued due to toxicity, the other may continue)

ADMINISTRATION

Pembrolizumab SC - withdraw the required volume using a transfer needle (18-21G recommended). To avoid needle clogging, change the needle to a 25-30G, 13 mm hypodermic injection needle immediately prior to SC injection.
Do not administer other medicinal products for injection at the same site as the pembrolizumab.

ANTI-EMETICS

Low risk days 1, 8 and 15

CONCURRENT MEDICATION REQUIRED

Paclitaxel	Ensure premedication given before paclitaxel
Pembrolizumab	None required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Paclitaxel – vesicant
Pembrolizumab IV – neutral

Administer paclitaxel via polyethylene lined or DEHP free administration set with ≤0.22micron filter
Administer pembrolizumab IV via low protein binding 0.2 to 5micron in-line or add-on filter

Central line
Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC every dose. U&E and LFTs every dose (unless no concerns on day 1, then every cycle).
Neutrophils x 10^9/L ≥1.0 day 1 (if not delay), ≥1.0 days 8 and 15 (if not omit clinician discretion)
Platelets x 10^9/L ≥100 day 1 if not delay), ≥100 days 8 and 15 (if not omit paclitaxel clinician discretion)
Thyroid function* baseline, then every pembrolizumab cycle
Random cortisol baseline, then every pembrolizumab cycle (or as specified in Trust guideline)
Random glucose every pembrolizumab cycle
Hba1c baseline
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Paclitaxel	(2% risk of severe hypersensitivity) Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.
Pembrolizumab	Immune related toxicities - pneumonitis, colitis or hepatitis etc Pembrolizumab SC skin reactions at site of administration route

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Paclitaxel	DOACs to be used with caution, need dose modifications or to be avoided eg apixaban Clopidogrel interacts with paclitaxel, potentially increasing the concentration of paclitaxel. Paclitaxel is catalysed, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. inhibitors (eg erythromycin, fluoxetine, gemfibrozil) use with caution. inducers (eg rifampicin, carbamazepine, phenytoin, phenobarbital, efavirenz, nevirapine) use with caution.
Pembrolizumab	-

DOSE MODIFICATIONS

Non-haematological

Paclitaxel

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration

If grade ≥2 neuropathy, consider giving 75% paclitaxel dose

If grade >3 peripheral neuropathy is >grade 3 omit further paclitaxel

Pembrolizumab

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

If the drug-related toxicity does not resolve to grade 0-1 within 12 weeks after onset of toxicity, discontinuation is recommended.

Hepatic impairment

Paclitaxel

In the absence of Gilbert's syndrome:

Transaminase <10xULN and bilirubin ≤1.25xULN	no dose reduction
Transaminase <10xULN and bilirubin 1.26-2xULN	Clinician discretion
Transaminase <10xULN and bilirubin 2·01-5xULN	Clinician discretion
Transaminase ≥10xULN or bilirubin >5xULN	contraindicated

Pembrolizumab

No dose adjustment is needed

Renal impairment

Paclitaxel

No dose adjustment is needed

Pembrolizumab

No dose adjustment is needed

REFERENCES

1. SPC
2. Blueteq criteria