Weekly Paclitaxel

Indication
Second line treatment of locally advanced or metastatic gastric/gastro-oesophageal junction adenocarcinoma.

ICD-10 codes
Codes pre-fixed with C15 and C16.

Regimen details

Day	Drug	Dose	Route
1, 8, 15	Paclitaxel	80mg/m²	IV infusion

Note: no treatment on day 22

Cycle frequency
28 days

Number of cycles
Usually treat for up to 6 cycles depending upon response. For patients who are tolerating treatment well, additional cycles may be administered until unacceptable toxicity or disease progression.

Administration
Paclitaxel is administered in a 250-500mL sodium chloride 0.9% non-PVC infusion bag with a 0.22 micron in-line filter over 1 hour.
Blood pressure and pulse should be monitored regularly (e.g. every 30 minutes) during paclitaxel infusion.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of paclitaxel. Facilities for the treatment of hypotension and bronchospasm **must** be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of paclitaxel and appropriate therapy should be initiated.

Pre-medication
30 minutes prior to each infusion:

Ranitidine 50mg IV slow bolus
Chlorphenamine 10mg IV slow bolus
Dexamethasone 8mg IV slow bolus

Emetogenicity
This regimen has moderate emetic potential.

Additional supportive medication
Mouthwashes as per local policy
H_2 antagonist or PPI, if required, as per local policy

Extravasation

Paclitaxel – vesicant (Group5)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local practice)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local practice)
FBC	24 hours – prior to each dose
U+E (including creatinine)	96 hours – prior to day 1 only
LFTs	96 hours – prior to day 1 only

Standard limits for administration to go ahead

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

Investigation	**Limit**
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Bilirubin	< 1.5 x ULN
AST/ALT	< 5 x ULN

Dose modifications

- ### Haematological toxicity

If neutrophils < 1.0 x 10^9/L and/or platelets < 100 x 10^9/L delay for 1 week then resume at 100% dose. If delayed for > 1 week discuss with consultant.

In the case of febrile neutropenia (neutrophils < 0.5 × 10^9/L and fever > 38.5°C requiring IV antibiotics) reduce paclitaxel to 60mg/m^2 for all future doses.

- ### Renal impairment

No dose modifications required.

- ### Hepatic impairment

Paclitaxel is not recommended in severe hepatic impairment. If bilirubin < 1.5 x ULN and AST/ALT < 5 x ULN proceed with 100% dose. For more severe hepatic impairment, treatment may only proceed on consultant's decision, at a reduced dose with weekly monitoring of LFTs.

- ### Other toxicities

Toxicity	**Definition**	**Paclitaxel dose**
Neuropathy	Grade 2	Reduce to 60mg/m^2 for all subsequent doses.
	Grade ≥ 3	Discontinue

For all other grade ≥ 2 toxicities (except alopecia) withhold until grade ≤ 1 and continue with 60mg/m^2 dose. If delayed for > 1 week, discuss with consultant.

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

- **Rare or serious side effects**

Myelosuppression
Infertility
Teratogenicity
Hypersensitivity reactions
Pulmonary fibrosis
Electrolyte disturbances
Arrhythmias
Cardiac failure

- **Frequently occurring side effects**

Nausea and vomiting
Mucositis, stomatitis
Myelosuppression
Diarrhoea, constipation
Peripheral neuropathy
Oedema
Phlebitis
Myalgia, arthralgia
Alopecia
Fatigue

- **Other side effects**

Taste changes
Headache
Abdominal pain

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

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Clozapine: increased risk of agranulocytosis

Paclitaxel is a CYP 2C8/9 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

Additional comments

Nil

References

- Summary of Product Characteristics Paclitaxel (Hospira) accessed 3 April 2019 via www.medicines.org.uk
- NICE Clinical Guideline 83 – Second-line palliative chemotherapy for locally advanced or metastatic oesophago-gastric cancer. Accessed via www.nice.org.uk
- Wilke, H., at al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. Lancet Oncol. 2014 Oct;15(11):1224-35

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