Paclitaxel albumin (Abraxane®)

Indication

Palliative therapy for advanced breast cancer where initial chemotherapy with an anthracycline has failed or is inappropriate, in patients who have a documented severe taxane hypersensitivity despite appropriate pre-medication.

May also be considered as an option for adjuvant or neo-adjuvant treatment of breast cancer in patients who have a documented severe taxane hypersensitivity despite appropriate pre-medication **(Note: this is an unlicensed indication).**

ICD-10 codes

Codes pre-fixed with C50.

Regimen details

Day	Drug	Dose	Route
1	Paclitaxel albumin	260mg/m²	IV infusion

Alternatively may be given weekly as follows **(Note: this dosing regimen is unlicensed)**

Days	Drug	Dose	Route
1, 8, 15*	Paclitaxel albumin	90-120mg/m²	IV infusion

Cycle frequency

21 days
*The weekly schedule may be given on days 1, 8 and 15 every 21 or every 28 days

Number of cycles

Usual maximum 6 cycles

Administration

Paclitaxel albumin is administered as a 5mg/mL infusion over 30 minutes.

It should be administered using an infusion set incorporating a 15µm filter.

Pre-medication

Nil routinely required.

Emetogenicity

This regimen has moderate emetic potential.

Additional supportive medication

Mouthwashes as per local policy
Antiemetics as per local policy
H_2 antagonist or PPI, if required, as per local policy

Extravasation

Paclitaxel albumin – vesicant (Group 5)

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Baseline echocardiogram and ECG if significant cardiac history. Monitor as clinically indicated.

Investigations – pre subsequent cycles

Investigation	Validity period
FBC*	96 hours
U+E (including creatinine)	7 days
LFTs	7 days

* FBC is also required within 48 hours of days 8 and 15.

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	≥ 1.5 x 10^9/L*
Platelets	≥ 100 x 10^9/L
CrCl	≥ 30mL/min
Bilirubin	< 1.5 x ULN
AST/ALT	< 2 x ULN

*For weekly treatments usual criteria to administer is neutrophils ≥ 1.0 x 10^9/L

Dose modifications

- **Haematological toxicity**

For 3 weekly regimen if neutrophils <1.5 x 10^9/L (or <1.0 x 10^9/L if weekly regimen) and/or platelets <100 x 10^9/L delay for 1 week until recovery, then resume at 100% dose. If delayed for > 1 week discuss with consultant, consider dose reduction.

If neutrophils <0.5 x 10^9/L delay until neutrophils >1.5 x 10^9/L (or <1.0 x 10^9/L if weekly regimen) and reduce dose to 220mg/m^2 (or 80% of weekly dose) - discuss with consultant.

If second occurrence delay until neutrophils >1.5 x 10^9/L and reduce dose further to 180mg/m^2 (or 60% of weekly dose).

If > 1 week delay due to neutropenia consider GCSF support.

In the case of febrile neutropenia consider GCSF support.

- **Renal impairment**

Insufficient information regarding dosing in renal impairment. If CrCl < 30mL/min discuss with consultant.

- **Hepatic impairment**

Bilirubin (x ULN)		**AST/ALT** (x ULN)	**Paclitaxel albumin dose**
< 1.5	and	< 2	100%
1.5 – 5	and/or	2 - 10	220mg/m^2 (or 80% of weekly dose)
> 5	and/or	> 10	Discontinue

- **Other toxicities**

Toxicity	Definition	Paclitaxel albumin dose
Neuropathy	Grade 1-2	No dose reduction usually required.
	Grade 3	Withhold until recovery to ≤ grade 1, resume with 220mg/m^2 dose (or 80% of weekly dose). If 2nd occurrence: Withhold until recovery to ≤ grade 1, resume with 180mg/m^2 dose (or 60% of weekly dose).
	Grade ≥ 4	Discontinue or continue with dose reduction as above – consultant decision.

For all other grade ≥ 2 toxicities (except alopecia) withhold until grade ≤ 1 and continue with 220mg/m^2 dose (or 80% of weekly dose). If delayed for > 1 week, discuss with consultant.

For any grade 4 toxicity (except alopecia) withhold and discuss with consultant.

Post-marketing experience has identified rare reports of reduced visual acuity due to cystoid macular oedema. Treatment should be discontinued.

Rare reports of congestive heart failure and left ventricular dysfunction have been observed in patients with underlying cardiac history or previous exposure to cardiotoxic products such as anthracyclines. Patients should be monitored for the occurrence of cardiac events.

If hypersensitivity reaction occurs, treatment should be discontinued immediately and symptomatic treatment should be initiated. The patient should not be re-challenged.

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

- **Rare or serious side effects**

Myelosuppression
Infertility
Teratogenicity
Hypersensitivity reactions
Pneumonitis
Hepatic impairment
Cardiotoxicity

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis, stomatitis
Diarrhoea, constipation
Peripheral neuropathy
Neuropathy
Myalgia, arthralgia
Alopecia
Fatigue
Anorexia

- **Other side effects**

Insomnia, depression, anxiety
Headache, dizziness
Skin reactions
Nail changes
Eye problems

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.

The metabolism of paclitaxel is catalysed, in part, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. Caution should be exercised when administering paclitaxel concomitantly with medicines known to:
inhibit (e.g. ketoconazole and other imidazole antifungals, erythromycin, fluoxetine, gemfibrozil, cimetidine, ritonavir, saquinavir, indinavir, and nelfinavir)
or
induce (e.g. rifampicin, carbamazepine, phenytoin, efavirenz, nevirapine) either CYP2C8 or CYP3A4.

Additional comments

When reconstituted, paclitaxel albumin (Abraxane ®) contains approximately 425 mg sodium per dose. This should be considered if a patient is on a controlled sodium diet.

References

- Summary of Product Characteristics Abraxane (Celgene) accessed 21 July 2016 via www.medicines.org.uk
- Gradishar W, Tjulandin S, Davidson N et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. J Clin Oncol 2005, 23:7794-7803.

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