

**Systemic Anti Cancer Treatment Protocol**

**Docetaxel / Capecitabine  
Advanced Breast Cancer**

**PROTOCOL REF: MPHADOCABR  
(Version No: 1.0)**

**Approved for use in:**

**Metastatic Breast Cancer:** Criteria, very fit patients only PS 0-1

Visceral crisis disease that requires doublet treatment

**Dosage:**

Drug	Dosage	Route	Frequency
Docetaxel	75 mg/m <sup>2</sup> day 1	IV	Every 21 days, for 6 cycles
Capecitabine	1000mg/m <sup>2</sup> twice daily for 14 days from day 1 of cycle	Oral	

**Supportive treatments:**

Dexamethasone tablets 8mg twice daily for 3 days starting 24 hours before docetaxel  
(To reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions)

Loperamide 2mg when required after each loose stool

Domperidone 10mg tablets, up to three times a day when required

**Notes - capecitabine**

Tablets should be taken 12 hours apart

Swallow whole with water within 30 minutes of a meal

Do not add doses missed due to toxicity onto the end of the cycle. Continue according to the treatment plan and stop taking on the originally scheduled day.

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## Extravasation risk:

Docetaxel: exfoliant.

## Administration:

Day	Drug	Dose	Route	Diluent and rate
1	Docetaxel	75mg/m <sup>2</sup>	IV Infusion	Sodium chloride 0.9% 250mL over 60 minutes
1 to 14	Capecitabine	1000mg/m <sup>2</sup> twice daily	Oral	Every 12 hours

If oral dexamethasone has not been taken then an intravenous dose of 8mg can be administered on the day of treatment, in addition to the oral dose of 8mg

## Main Toxicities:

<b>Haematological</b>	Neutropenia, thrombocytopenia and anaemia.
<b>Gastrointestinal</b>	Nausea, vomiting, stomatitis, diarrhoea
<b>Cardiotoxicity</b>	Capecitabine: myocardial infarction, angina, dysrhythmias, cardiogenic shock, sudden death and electrocardiographic changes (including very rare cases of QT prolongation).
<b>Dermatological</b>	Alopecia, normally reversible, although can be permanent following docetaxel. Capecitabine can cause hand-foot syndrome (PPE) Severe skin reactions such as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis. Capecitabine should be permanently discontinued in patients who experience a severe skin reaction.
<b>Ocular</b>	Watery eyes, gritty and irritated
<b>Dermatological</b>	Docetaxel: Brittle, chipped and ridged nails
<b>Gastrointestinal</b>	Mucositis, nausea and vomiting
<b>Hypersensitivity reactions</b>	Reactions may occur within a few minutes following the initiation of treatment with docetaxel, facilities for the treatment of hypotension and bronchospasm should be available.  If hypersensitivity reactions occur, minor symptoms such as flushing or localised rash with or without pruritus do not require interruption of therapy. However, severe reactions, such as severe

	hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate treatment. Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel.
<b>Nervous system</b>	Docetaxel: peripheral neuropathy is very common
<b>Musculoskeletal</b>	Arthralgia, myalgia common with docetaxel

### Investigations and Treatment Plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Comments
Medical Assessment	X		X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X		X	X	X	X	X	Every cycle
U&E & LFT	X		X	X	X	X	X	Every cycle
Informed Consent	X							
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X		X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle

### Dose Modifications and Toxicity Management:

#### Haematological Toxicity:

Proceed on day 1 if-

Plt $\geq 100 \times 10^9/L$	ANC $\geq 1.0 \times 10^9/L$
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Delay 1 week on day 1 if-

Plt $\leq 99 \times 10^9/L$	ANC $\leq 0.9 \times 10^9/L$
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## Non-haematological toxicities

### Hepatic Impairment:

Docetaxel
If Bilirubin >22µmol/L +/-or ALT/AST >3.5 times ULN with ALP > 6 times ULN, docetaxel should not be used unless strictly indicated.
ALT +/-or AST > 1.5 times ULN and ALP > 2.5 times ULN – give 75mg/m <sup>2</sup>

**Renal Impairment:** Before every cycle, calculate CrCl using Cockcroft and Gault formula.

Creatinine Clearance (mL/min)	Capecitabine Dose
> 50	Give 100% dose
30 to 49	Give 75%
< 29	Omit

**Capecitabine dose adjustment guidelines (according to CTCAE) for side effects including diarrhoea, vomiting, mucositis and PPE:**

### Capecitabine dose reduction schedule (3-weekly cycle) – table ref SPC;

Toxicity grades*	Dose changes within a treatment cycle	Dose adjustment for next cycle/dose (% of starting dose)
• <i>Grade 1</i>	Maintain dose level	Maintain dose level
• <i>Grade 2</i>		
-1st appearance	Interrupt until resolved to grade 0-1	100%
-2nd appearance		75%
-3rd appearance		50%
-4th appearance	Discontinue treatment permanently	Not applicable
• <i>Grade 3</i>		
-1st appearance	Interrupt until resolved to grade 0-1	75%
-2nd appearance		50%
-3rd appearance		Discontinue treatment permanently

• <i>Grade 4</i>		
-1st appearance	Discontinue permanently <i>or</i> If physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	50%
-2nd appearance	Discontinue permanently	Not applicable

**Note that severe diarrhoea and/or severe mucositis early in capecitabine treatment can be the first presenting toxicity due to DPD enzyme deficiency, in which case potentially fatal neutropenia can quickly follow.**

## References

Superior survival with capecitabine plus docetaxel

JCO 2002 20(12) 2812-23

O'Shaughnessy et al

SPC for Capecitabine (Actavis) available via Electronic Medicines Compendium at <http://www.medicines.org.uk/emc/>

Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH  
(Version 3 - updated January 2009)

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