LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Capecitabine in Advanced Breast Cancer

Indication:	Monotherapy for the treatment of advanced breast cancer after failure of taxanes and an anthracycline-containing chemotherapy regimen or for whom further anthracycline therapy is not indicated. NICE TA62
Regimen details:	Capecitabine 1000-1250 mg/m^2 twice daily PO Days 1 to 14, followed by 7 day rest period
Administration:	Capecitabine tablets orally twice daily, swallow whole with water within 30 minutes after a meal and approximately 12 hours apart. Capecitabine is available as 500mg and 150mg tablets.
Frequency:	Days 1 to 14, every 21 days, for 6 to 8 cycles. Responding patients may be continued on treatment at the discretion of the treating physician
Pre-medication:	Not required
Anti- emetics:	Low emetogenicity Follow local anti-emetic policy
Supportive medication:	Diarrhoea can be managed with loperamide Mouthcare as per local policy
Extravasation:	Not applicable
Regular investigation:	Prior to Cycle 1: FBC Day 1 (within 14 days) LFTs Day 1 (within 14 days) U&Es Day 1 (within 14 days)

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Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Wendy Ng	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Lisa Yuen	Date prepared: November 2014 Review Date: November 2016

Prior to Day 1 (all cycles):	
FBC	Day 1 (within 72 hours)
LFTs	Day 1 (within 72 hours)
U&Es	Day 1 (within 72 hours)

Toxicities: Diarrhoea, nausea, vomiting, stomatitis, skin reactions and hand and foot syndrome (palmar-plantar erythrodysesthesia)
Cardiotoxicity: Cardiac arrhythmias, angina pectoris, myocardial infarction, heart failure and cardiomyopathy have been reported in patients receiving capecitabine. Caution must be exercised in patients with history of significant cardiac disease, arrhythmias and angina pectoris

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥ 1.5	&	≥ 100	100% dose
1.0 – 1.5	or	75 - 99	Discuss with Consultant – treatment can be considered on medical advice. Or consider treatment delay for 1 week. Repeat FBC - If recovered to above these levels, resume treatment at 100% dose. Consider dose reduction for >1 delay.

- Dose reduction and / or delay is more appropriate in the advanced setting - seek Consultant advice
- If platelets persistently < 100 x 10^9/L on Day 1 despite dose delay - seek Consultant advice and consider dose reduction by 25%

Non-haematological Toxicities

Renal Impairment

Creatinine Clearance (ml/min)	Capecitabine Dose
> 50	100%
30-50	Give 75% dose
<30	Omit

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Hepatic Impairment

In the absence of safety and efficacy data in patients with hepatic impairment, capecitabine use should be carefully monitored in patients with mild to moderate liver dysfunction, regardless of the presence or absence of liver metastasis.

Bilirubin (treatment-related elevation)		ALT / AST (treatment-related elevation)	Capecitabine Dose
> 3 x ULN	**or**	> 2.5 x ULN	Omit until recovers and discuss with consultant

Dose modifications for other toxicities as appropriate

Refer to tables below for dose modifications for diarrhoea, nausea, vomiting, stomatitis, and hand-foot syndrome (palmar-plantar erythrodysesthesia)

CTC Grade	1st Appearance Dose	2nd Appearance Dose	3rd Appearance Dose	4th Appearance Dose
0-1	100%	100%	100%	100%
2	delay* then 100%	delay* then 75%	delay* then 50%	discontinue
3	delay* then 75%	delay* then 50%	discontinue	discontinue
4	discontinue or delay* then 50%	discontinue	discontinue	discontinue

*interrupt treatment until resolved to Grade 0-1

Chest pain typical of myocardial ischaemia requires cessation of capecitabine and should be investigated.

Location of regimen delivery:	Capecitabine to be supplied to the patient for oral self-administration. Ensure that the patient has an information pack and the treatment plan. Suitable for home delivery
Comments:	Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced metabolism of capecitabine. Ensure patient is informed of action to take if signs of toxicity (e.g. severe mucositis, diarrhoea) develop within the first few days of treatment, as this is often an early indication of DPD deficiency.

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Severe skin reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported during treatment with capecitabine. Some cases were fatal. Capecitabine should be discontinued if a serious skin reaction occurs, and the reaction should be treated promptly

Capecitabine contains anhydrous lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Drug interactions:

Significant interactions below. For full details consult product literature/reference texts.
Allopurinol: avoid concomitant use (reduced efficacy of capecitabine)
Folinates: avoid concomitant use (enhanced capecitabine toxicity)
Phenytoin: monitor plasma phenytoin levels (increase phenytoin level)
Warfarin/coumarin anticoagulants: switched to low molecular weight heparin (altered coagulation parameters and/or bleeding including death)

References:

Accord Healthcare Ltd. Summary of Product characteristics: capecitabine 26/09/2013. Available at www.medicines.org.uk [accessed 06/03/14]
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