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/m² 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)
Prior to Day 1 (all cycles):

- **FBC**
- **LFTs**
- **U&Es**

**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

<table>
<thead>
<tr>
<th>Neutrophils (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5 &amp; ≥ 100</td>
<td>75 - 99</td>
<td>100% dose</td>
</tr>
<tr>
<td>1.0 – 1.5 or 75 - 99</td>
<td>75 - 99</td>
<td>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 &gt;1 delay.</td>
</tr>
</tbody>
</table>

- 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

<table>
<thead>
<tr>
<th>Creatinine Clearance (ml/min)</th>
<th>Capecitabine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>100%</td>
</tr>
<tr>
<td>30-50</td>
<td>Give 75% dose</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Omit</td>
</tr>
</tbody>
</table>

Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.
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.

<table>
<thead>
<tr>
<th>Bilirubin (treatment-related elevation)</th>
<th>ALT / AST (treatment-related elevation)</th>
<th>Capecitabine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 3 x ULN</td>
<td>&gt; 2.5 x ULN</td>
<td>Omit until recovers and discuss with consultant</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>CTC Grade</th>
<th>1\textsuperscript{st} Appearance Dose</th>
<th>2\textsuperscript{nd} Appearance Dose</th>
<th>3\textsuperscript{rd} Appearance Dose</th>
<th>4\textsuperscript{th} Appearance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>delay* then 100%</td>
<td>delay* then 75%</td>
<td>delay* then 50%</td>
<td>discontinue</td>
</tr>
<tr>
<td>3</td>
<td>delay* then 75%</td>
<td>delay* then 50%</td>
<td>discontinue</td>
<td>discontinue</td>
</tr>
<tr>
<td>4</td>
<td>discontinue or delay* then 50%</td>
<td>discontinue</td>
<td>discontinue</td>
<td>discontinue</td>
</tr>
</tbody>
</table>

*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.
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:

Stockley’s Drug Interactions accessed 1st April 2008 from www.medicinescomplete.com
DC Talbot et al (2002); British Journal of Cancer, Vol 86:pp1367-1372
JL Blum et al (2001); Cancer, Vol 92:pp1759-1768
JL Blum et al (1999); JCO, Vol 17:pp485-493
SELCN capecitabine in metastatic breast cancer protocol
Mount Vernon capecitabine protocol – breast cancer
NWLCN Breast Regimen Version 7 01
UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009
UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009
LCA Breast Cancer Clinical Guidelines October 2013
Breast Pathway Group – Capecitabine in Advanced Breast Cancer

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Second check by: Lisa Yuen
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