LONDON CANCER ALLIANCE West and South

Breast Cancer – Oral Vinorelbine weekly in Advanced Breast Cancer

Indication:	Third line or subsequent treatment of Advanced Breast Cancer where anthracyclines have failed or are unsuitable. Patients with progressive breast cancer for whom combination chemotherapy or taxane therapy is deemed inappropriate. NICE CG81
Regimen details:	Monotherapy: Vinorelbine 60mg/m^2 PO weekly After 3rd dose * 80mg/m^2 PO weekly (*See dose escalation guidance under Dose Modification section) Total dose should not exceed 120mg for 60mg/m^2 or 160mg at 80mg/m^2
Administration:	Vinorelbine is available as 20mg, 30mg and 80mg soft capsules. Capsules to be swallowed with water without chewing or sucking the capsule. It is recommended to take oral vinorelbine with food. Oral vinorelbine 80mg/m^2 corresponds to IV vinorelbine 30mg/m^2 Oral vinorelbine 60mg/m^2 corresponds to IV vinorelbine 25mg/m^2
Frequency:	Weekly (max of 18 weeks)
Pre-medication:	Not routinely required
Anti- emetics:	Mild/ Moderate emetogenicity Follow Local Anti-emetic Policy
Supportive medication:	Not routinely required
Extravasation:	Not applicable

Version: 1.0 Supersedes: all other versions	Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries November 2014
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Isabel Munoz	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Lisa Yuen	Date prepared: November 2014 Review Date: November 2016

Regular investigation:	Prior to Cycle 1:	
	FBC	Day 1 (within 14 days)
	LFTs	Day 1 (within 14 days)
	U&E	Day 1 (within 14 days)
	Prior to Cycle 2 onwards:	
	FBC	D1 (within 48 hours)
	LFTs	D1 (within 48 hours)
	U&E	D1 (within 48 hours)
Toxicities:	Myelosupression, ovarian failure/infertility, peripheral neuropathy and neuropathy induced constipation, alopecia (usually mild), GI symptoms	

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥ 1.5	&	≥ 100	100%
< 1.5	or	< 100	Delay until recovered to above these levels then dose as below

Dose escalation	Dose modification
Neutrophil count during 1st three administrations of 60mg/m^2	
> 1.0	Increase to 80mg/m^2 at 4th dose
≥ 0.5 and < 1.0 (1st episode)	Increase to 80mg/m^2 at 4th dose
≥ 0.5 and < 1.0 (2nd episode)	**Continue 60mg/m^2 – do not escalate**
< 0.5	**Continue 60mg/m^2 – do not escalate**
Dose de-escalation	
Neutrophil count from 4th dose onwards	
> 1.0	Continue 80mg/m^2
≥ 0.5 and < 1.0 (1st episode)	Continue 80mg/m^2
≥ 0.5 and < 1.0 (2nd episode)	Delay treatment until recovery, then reduce to 60mg/m^2
< 0.5	Delay treatment until recovery, then reduce to 60mg/m^2
	It is possible to re-escalate the dose after a further 3 administrations with lower dose if well tolerated.

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Non-haematological Toxicities

Renal Impairment

Dose adjustment not required if CrCl ≥ 30ml/min.
If CrCl < 30ml/ml discuss with Consultant.

Hepatic Impairment

Bilirubin		AST / ALT	Dose
< 1.5 x ULN	&	< 5 x ULN	100%
1.5 to 3 x ULN	&	< 5 x ULN	Postpone and reassess in 1 week, consider vinorelbine 50% dose. If toxicity persists for more than 3 weeks, discontinue treatment.
> 3 x ULN			Omit
		> 5 x ULN	Clinical decision, consider 33% dose reduction

Dose modifications for other toxicities as appropriate

	Vinorelbine dose
Grade 1 or 2 neurotoxicity	100% dose
Grade 3 or 4 neurotoxicity	Omit
Grade 3 mucositis	Give 75% dose
Grade 4 mucositis	Omit
Grade 3 or 4 constipation	Omit
Any other grade 3 toxicities	Give 75% dose
Any other grade 4 toxicities	Omit

Location of regimen delivery: Vinorelbine 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: None

Drug interactions: Aprepitant – increased vinorelbine plasma levels
Itraconazole – increased risk of neurotoxicity.
Omeprazole and fluoxetine may inhibit vinorelbine metabolism
Posazonazole and voriconazole- increased vinorelbine plasma levels

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The following table gives the dose required for appropriate ranges of body surface area (BSA)

BSA (m^2)	60mg/m^2 Dose (mg)	80mg/m^2 Dose (mg)
0.95 to 1.04	60	80
1.05 to 1.14	70	90
1.15 to 1.24	70	100
1.25 to 1.34	80	100
1.35 to 1.44	80	110
1.45 to 1.54	90	120
1.55 to 1.64	100	130
1.65 to 1.74	100	140
1.75 to 1.84	110	140
1.85 to 1.94	110	150
≥ 1.95	120	160

Even for patients with BSA ≥ 2m^2 the total dose should not exceed 120mg for 60mg/m^2 or 160mg at 80mg/m^2

References:

www.medicines.org.uk Pierre Fabre 08.2011
SELCN network protocols (PO Vinorelbine), accessed May 09
SWSHCN Protocols. Vinorelbine. Revised Jan 09
NWLCN Breast Cancer protocols Oct 2012
UCLH – Dosage adjustment for Cytotoxics in Hepatic Impairment. January 2009
UCLH – Dosage adjustment for Cytotoxics in Renal Impairment. January 2009
LCA Breast Cancer Clinical Guidelines October 2013

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