VinBLAStine and Methotrexate Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Status
Treatment of advanced aggressive fibromatosis	M72	00554a	Hospital

**If the reimbursement status is not defined [1], the indication has yet to be assessed through the formal HSE reimbursement process.*

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Treatment is to be delivered every 7 days on day 1, 8, and 15 of a 28 day cycle for up to 12 cycles until disease progression or unacceptable toxicity develops.

Day	Drug	Dose	Route	Diluent & Rate	Cycle (28 days)
1,8,15	Methotrexate	30 mg/m^2	IV bolus	N/a	Every 28 days for up to 12 cycles
1,8,15	vinBLAStine[1]	6 mg/m^2	IV infusion	50ml NaCL 0.9% over 10 min	Every 28 days for up to 12 cycles
[1]VinBLAStine is a neurotoxic chemotherapeutic agent. Refer to NCCP Guidance on the Safe Use of Neurotoxic drugs (including Vinca Alkaloids) in the treatment of cancer here					

ELIGIBILTY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to vinBLAStine, methotrexate or any of the excipients.
- Creatinine clearance less than 30 mL/min
- Large third space fluid accumulations (significant ascites, large pleural effusion or other large lobulated fluid accumulations)

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Chest X-ray

Regular tests:

- FBC, renal and liver profile prior to each cycle

Disease monitoring:
Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

Haematological:

Table 1: Dose modification in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Recommended Dose modifications
>0.9	And	>99	100%
0.5-0.9	Or	50-99	50%
<0.5	or	<50	Delay*
*baseline VinBLAStine dose reduced by 25% if chemotherapy delayed by 2 or more weeks			

Renal and Hepatic Impairment:

Table 2: Dose modification in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment			
VinBLAStine	No dose reduction necessary		Bilirubin (micromol/L		AST/ALT (units)	Dose
			26-51	or	60-180	50%
			>51	and	normal	50%
			> 51	and	>180	omit
Methotrexate	Cr Cl (ml/min)	Dose	Bilirubin(micromol/L)		AST (Units)	Dose
	>80	100%	<50	and	<180	100%
	60-80	65%	51-85	or	>180	75%
	45-60	50%	>85			Contra-indicated
	30-45	Clinical Decision				
	<30	Contra-indicated				

Management of adverse events:

Table 3: Dose Modification for Adverse Events

Adverse reactions	Recommended dose modification
Grade >2 Peripheral neuropathy	Dose reduction of vinBLAStine may be required at the discretion of the prescribing consultant
Mucositis	
Grade 1	Dose reduction of methotrexate by 50%
Grade 2	Dose reduction of methotrexate by 100%
Significant third space fluids (ascites, pleural effusions)	Reconsider treatment

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Low (**Refer to local policy).**

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE: Not usually required

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Pleural effusion or ascites**: Methotrexate should be used with caution in patients with pleural effusions or ascites, as methotrexate may accumulate in third space fluid compartments.
- **Extravasation**: vinBLAStine cause pain and tissue necrosis if extravasated **(Refer to local policy)**

DRUG INTERACTIONS:

- Current drug interaction databases should be consulted for more information.
- Drugs which compromise renal function eg. aminoglycosides and CISplatin can decrease clearance of methotrexate and lead to systemic toxicity.
- Concurrent use of non-steroidal anti-inflammatory drugs (NSAIDs) and penicillins reduces renal clearance of methotrexate and these drugs should be avoided when using high dose methotrexate. Cotrimoxazole and ciprofloxacin also interact**.**
- Concomitant administration of drugs that cause folate deficiency may lead to increased methotrexate toxicity.

ATC CODE:

VinBLAStine - L01CA01
Methotrexate - L01BA01

REFERENCES:

1. Skapek SX, Ferguson WS, Granowetter L, et al. vinblastine and methotrexate for desmoids fibromatosis in children: results of a Pediatric Oncology Group phase II trial. J Clin Oncol 2007:25:501-6.
2. Janinis J, Patriki M, Vini L, et al. The pharmacological treatment of aggressive fibromatosis: a systematic review. Ann Oncol 2003:14:181-90.
3. Azzarelli A, Gronchi, Bertullia R, Tesoro JD, Barratti D, Pennacchioli E, et al. Low-dose chemotherapy with methotrexate and vinblastine for patients with advances aggressive fibromatosis. Cancer. 2001:92(5):1259-64
4. The North London Cancer Network, Dose adjustment for cytotoxics in hepatic impairment, Jan 2009.
5. Vinblastine summary of product characteristics accessed January 2019 available at https://www.medicines.org.uk/emc/product/1422/smpc
6. Methotrexate summary of product characteristics Accessed January 2019 Available at www.medicines.org.uk/emc/product/1404/smpc

Version	Date	Amendment	Approved By
1	18/03/2019		Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/