NATIONAL CANCER CONTROL PROGRAMME

Guidance on the Safe Use of

Neurotoxic drugs (including Vinca Alkaloids)

in the Treatment of Cancer

Version	Date	Amendment	Approved By
1	Nov 15	Initial Report	NCCP Oncology Medication Safety Review Implementation Steering Committee
2	Feb 16	Following further discussion, the decision was made that the use of minibags for neurotoxic drugs should also be implemented in the paediatric setting where supporting stability exists. Appendix 3 was updated.	NCCP Oncology Medication Safety Review Implementation Steering Committee
3	Nov 2020	Recommendation 4 - the phrasing of negative labelling amended Appendix 1 - Terms of Reference updated to reflect the review of national guidance and development of e-learning module. Appendix 2 - new project board group membership added	NCCP Intrathecal Chemotherapy Project Group 2020
4	Feb 2025	HSE logo updated Removal of 'Oncology Medication Safety Review Implementation Resources' from cover page Footer updated with title of document Replaced 'hospital group' with 'health region' throughout document Applied Tallman lettering to drugs names where appropriate Glossary – inclusion of anthracyclines NCCP SACT Model of Care included Removal of Development of Recommendations section Rec. 2 – Updated to incorporate Rec. 3; additional detail included for dispensing of minibag or syringe	NCCP Intrathecal Working Group 2024

		Rec. 3 – Retired as use of minibags now implemented in paediatric setting for vinca alkaloids, syringes for vinca alkaloids no longer in use; moved stability detail from Rec 3 in to Rec. 2 Rec. 4 – Inclusion of the use of positive labelling Rec. 5 – updated; remove use of colour from guidance Rec. 6 – retired as content incorporated into Rec 5 Rec. 7 – retired as content incorporated into Rec 5 Rec. 8 – retired as content incorporated into Rec 5 Appendix 1 & 2 removed – Project Group Membership and Terms of Reference New Appendix 1 – Inclusion of anthracyclines in list of drugs to be treated as neurotoxic New Appendix 2 – sample warning labels updated; vinca alkaloid label, neurotoxic drug label; warning and route of administration remains	

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Glossary and Definitions

- **Anthracyclines** - a group of chemotherapeutic agents, e.g. DAUNOrubicin, DOXOrubicin. These agents are administered intravenously and are neurotoxic.
- **Chemotherapy drugs** - any systemic anticancer treatment
- **Cytotoxic** - chemicals that are directly toxic to cells preventing their replication or growth
- **Dispensing** - is the activity of preparing the dose and placing it in packaging for transport.
- **Intrathecal chemotherapy -** intrathecal chemotherapy or intra-ventricular chemotherapy which is injected into the intrathecal cavity of the spinal cord.
- **Neurotoxin -** A substance that damages, destroys, or impairs the functioning of nerve tissue e.g. vinca alkaloids, proteasome inhibitors, anthracyclines.
- **Proteasome inhibitor** – a neurotoxic chemotherapeutic agent which is usually administered intravenously or subcutaneously, depending on the type of drug. Bortezomib is an example of proteasome inhibitor.
- **Vinca alkaloid** – a neurotoxic chemotherapeutic agent which is always administered intravenously. The following drugs are examples in the class of drugs referred to as vinca alkaloids: vinCRIStine, vinBLAStine, vindesine, vinorelbine and vinflunine.

Abbreviations

HSE	Health Service Executive
IMSN	Irish Medication Safety Network
ITC	Intrathecal Chemotherapy
NCCP	National Cancer Control Programme
Rec.	Recommendation

1. Introduction

Neurotoxic chemotherapy (neurotoxins[1-3]), such as vinca alkaloids[1] or proteasome inhibitors[2] or anthracyclines[3] should **only** be administered intravenously or subcutaneously (in the case of some proteasome inhibitors). Many patients receiving these drugs also receive other medication via the intrathecal route as part of their treatment protocol. Accidental administration of neurotoxins into the cerebrospinal fluid can result in death (1-5). Since 1968, this error has been reported in a variety of international settings at least 55[4] times (2). There have been repeated warnings over time and extensive labelling requirements and standards have been published (2, 6-10). However, errors related to the accidental administration of vinCRIstine via a spinal route continue to occur (3-10).

This guidance completes the NCCP action relating to recommendation 71 of the NCCP Oncology Medication and Safety review[5] (11), where the NCCP was to lead on the development of national policies for intrathecal chemotherapy and the preparation of neurotoxins.

This document should be read in conjunction with the following documents:

- NCCP Oncology Medication Safety Review
- NCCP Systemic Anticancer Therapy (SACT) Model of Care
- Guidance on the Safe Use of Intrathecal Chemotherapy in the Treatment of Cancer
- NCCP Guidance for the assessment of Competency for the Provision of Intrathecal Chemotherapy

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[1] VinCRIStine, which is an example of a vinca alkaloid, is a widely used chemotherapeutic agents which is neurotoxic and must only be administered intravenously

[2] Proteasome inhibitors are widely used chemotherapeutic agents which are neurotoxic and must only be administered intravenously or subcutaneously, depending on the nature of the agent.

[3] Anthracyclines are widely used chemotherapeutic agents which are neurotoxic and must only be administered intravenously

[4] There have been additional reports of this error since this publication was available.

[5] The NCCP Oncology Medication Safety review was conducted across the 26 hospitals in Ireland involved in the administration of systemic cancer therapy in adults and children. The aim of this review was to assess the oncology medication policies and practices in day units nationally, from a patient safety and quality perspective.

All of these documents are available on the NCCP website at:

https://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/safetyreview/

2. Implementation of Recommendations

These recommendations are for implementation locally, in conjunction with the general recommendations of the NCCP Oncology Medication Safety review report on chemotherapy(11) and NCCP Systemic Anticancer Therapy Model of Care(12), to ensure the safety and quality of the chemotherapy services.

The NCCP recommends that hospitals collaborate within the health region or cancer network structure, to share good practice pertaining to systemic anticancer therapy provision and to develop and implement national policies and practices for anticancer medication.

3. NCCP recommendations on neurotoxic drug preparation

A number of key recommendations were identified in relation to the safe delivery of neurotoxic drugs used in the treatment of cancer.

Recommendations	
Neurotoxin Rec. 1	A local protocol[6] covering all aspects of preparation and labelling of neurotoxic drugs must be in place.
Neurotoxin Rec. 2	Vinca alkaloids must be dispensed in a minibag, where drug stability allows[7], to be given over 5-15 minutes or greater. For other neurotoxic drugs where this dispensing in a minibag is not feasible, the neurotoxic drug must be prepared in a large volume (10-20ml) syringe. Where a large volume syringe is not possible, e.g. bortezomib subcutaneous, the dilution requirement may be omitted but all other

[6] This protocol must define the drugs to be treated as neurotoxins for the purpose of this policy. These drugs may be as identified by the NCCP (see Appendix 1) or identified through local risk assessment or international best practice.

[7] Stability information will be required. Vinca alkaloids have the required stability. Other neurotoxic drugs may not. Where stability does not allow for the required dilution then the dilution requirement may be omitted but all other recommendations with regard to packaging, labelling, storage and delivery must be followed.

Recommendations	
	recommendations must be followed.
Neurotoxin Rec. 3	Rec. 3 retired as incorporated into Rec. 2
Neurotoxin Rec. 4	Positive labelling should be used to ensure associations between the product and its intended use. Vinca alkaloids must be clearly labelled with the intended route of administration. For example, ''FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES.'' The use of negatively worded labels such as ''Not for …….use'' must be avoided as the inclusion of the word ''intrathecal'' may actually promote administration by this route. Negative labelling, i.e. "Not for ……use.") must be AVOIDED.
Neurotoxin Rec. 5	There should be judicious use of prominent text to include warnings on the patient product label and any auxiliary label for the product and outer packaging to differentiate syringes/minibags containing neurotoxic drugs from other preparations. All neurotoxic drugs are labelled with a pharmacy dispensing label containing the patient and dose details as described in Appendix 10 of the NCCP Oncology Medication Safety review[8]. See below for warnings that must be included on the patient product label and/or any auxiliary label/pre-printed outer packaging for vinca alkaloids: **WARNING** **NEUROTOXIC DRUG** **FOR INTRAVENOUS USE ONLY** **FATAL IF GIVEN BY ANY OTHER ROUTE** See below for warnings that must be included on the patient product label and/or any auxiliary label/pre-printed outer packaging for other neurotoxic drugs:

[8] Available: www.hse.ie/nccponcsafetyreview

Recommendations	
	WARNING **NEUROTOXIC DRUG** **FOR INTRAVENOUS USE ONLY** **WARNING** **NEUROTOXIC DRUG** **FOR SUBCUTANEOUS USE ONLY** Patient product labels and any auxiliary labels are placed directly on the infusion bag or syringe barrel so that they are clearly visible to the person administering the drug. This should be done regardless of whether the patient is also scheduled to receive additional medication(s) by the intrathecal route. Labels are also available in Appendix 2.
Neurotoxin Rec. 6	Recommendation retired as incorporated into Rec. 5
Neurotoxin Rec. 7	Recommendation retired as incorporated into Rec. 5
Neurotoxin Rec. 8	Recommendation retired as incorporated into Rec. 5

Appendix 1. List of drugs to be treated as neurotoxic

The list of drugs below should be treated as neurotoxic for the purpose of this policy. Local policies may require additional drugs to be treated as neurotoxic based on local risk assessment, clinical trial requirements or international best practice.

1. Vinca Alkaloids e.g. vinCRIStine, vinBLAStine, vindesine, vinORELBine and vinflunine
2. Proteasome inhibitors e.g. bortezomib, carfilzomib
3. Anthracyclines e.g. DAUNOrubicin, DOXOrubicin

This list may not be exhaustive and will be updated intermittently.

Appendix 2. Sample labels

Label 1: Sample labels for neurotoxic drug products and outer packaging.

This may be in a pre-printed format or as an attached label.

Vinca alkaloids:

WARNING

NEUROTOXIC DRUG

FOR INTRAVENOUS USE ONLY

FATAL IF GIVEN BY ANY OTHER ROUTE

Other neurotoxic drugs:

WARNING

NEUROTOXIC DRUG

FOR INTRAVENOUS USE ONLY

WARNING

NEUROTOXIC DRUG

FOR SUBCUTANEOUS USE ONLY

Bibliography

1. DOH. **HSC 2008/001 Updated national guidance on the safe administration of intrathecal chemotherapy**. 2008.
2. World Health Organization. Information Exchange System. Alert 115. 2007.
3. World Health Organization. Patient Safety Workshop

Learning from Error. 2008.
4. EMA. Recommendations to prevent administration errors with Velcade (bortezomib). 2012.
5. Liu H TR, Liu GL, Yan H, Kaye AD. Inadvertent intrathecal injections and best practice management. 2017. p. 11-22
6. ISMP. Death and neurological devastation from intrathecal vinca alkaloids: Prepared in syringes = 120; Prepared in minibags = 0. 2013.
7. ISMP. IV vincristine survey shows safety improvements needed. 2006.
8. Woods K. The Prevention of Intrathecal Medication Errors; A report to the Chief Medical Officer. In: DOH, editor. 2001.
9. ISMP. Medication Safety Alert Worth Repeating Preventing wrong route vinCRIStine errors. 2010.
10. IMSN. Briefing document: Vinca alkaloids –administration via intravenous minibag only. 2010.
11. Heckmann P, McCarthy T, Walsh O, Hanan T. NCCP Oncology Medication Safety Review Report. HSE; 2014.
12. NCCP. Systemic Anti-Cancer Therapy Model of Care. 2022.