

NATIONAL CANCER CONTROL PROGRAMME

Oncology Medication Safety Review

Implementation Resources

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

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Glossary and Definitions

- **Chemotherapy drugs** - any systemic anti cancer treatment
- **Cytotoxic** - chemicals that are directly toxic to cells preventing their replication or growth
- **Dispensing** - is the activity of preparing the dose and placing 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.
- **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, vinORELBbine and vinflunine.

Abbreviations

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

1. Introduction

Neurotoxins¹⁻³, such as vinca alkaloids¹ or proteasome inhibitors² chemotherapy should **only** be administered intravenously or subcutaneously (in the case of some proteasome inhibitors). Many patients receiving these drugs also receive other medication via an intrathecal route as part of their treatment protocol. Accidental administration of neurotoxins into the cerebrospinal fluid can result in death (1-4). Since 1968, this error has been reported in a variety of international settings at least 55³ times (2). There have been repeated warnings over time and extensive labelling requirements and standards have been published (2, 5-9). However, errors related to the accidental administration of vinCRISTine via a spinal route continue to occur (3).

This document should be read in conjunction with the NCCP Oncology Medication Safety Review (10). The ITC Project Board has produced the following documents which should be read in conjunction with this document:

- Guidance on the Safe Use of Intrathecal Chemotherapy in the Treatment of Cancer
- NCCP Guidelines for the assessment of competency for the provision of intrathecal chemotherapy.
- NCCP Criteria for Acting as an Assessor of Competence – Intrathecal Chemotherapy.

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

2. Development of recommendations

A Project Board was convened to complete the NCCP action relating to recommendation 71 of the NCCP Oncology Medication and Safety review⁴ (10), where the NCCP was to lead on the development of national policies for intrathecal chemotherapy and the preparation of neurotoxins for the treatment of cancer. The terms of reference are provided at Appendix 1 and membership details are provided at Appendix 2. The resulting recommendations have been drawn up to ensure the safe administration of neurotoxins by the intravenous and subcutaneous route.

The draft version of this document was made available for consultation for a period of four weeks and the consultation process was notified to key stakeholders. Comments received during the consultation feedback were considered by the Project Board and incorporated, as appropriate, into the final document.

3. Implementation of Recommendations

The recommendations are for implementation locally, in conjunction with the general recommendations of the NCCP Oncology Medication Safety review report on chemotherapy (10), to ensure the safety and quality of the chemotherapy services.

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

⁴ 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.

4. NCCP recommendations on neurotoxic drug preparation

The working group identified a number of key recommendations in relation to the safe delivery of neurotoxic drugs used in the treatment of cancer.

Recommendations	
Neurotoxin Rec. 1	A local protocol ⁵ covering all aspects of preparation and labelling of neurotoxic drugs must be in place.
Neurotoxin Rec. 2	Neurotoxic drugs for administration to adults and adolescents should be dispensed in a 50mL minibag, where possible ⁶ , to be given over 5-15 minutes.
Neurotoxin Rec. 3	<p>Neurotoxic drugs for administration to paediatrics should be supplied in minibags where drug stability allows.</p> <p>Where syringes must be used for the administration then:</p> <ul style="list-style-type: none"> ○ The neurotoxic drug must not be prepared or administered on the same day that intrathecal chemotherapy is scheduled for that patient. ○ The neurotoxic drug must be prepared in a <u>large volume</u> (10-20ml) syringe⁶

⁵ 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 3) or identified through local risk assessment or international best practice.

⁶ 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.

Neurotoxin Rec. 4	Negative labelling, i.e. “Not foruse.”) must be AVOIDED.
Neurotoxin Rec. 5	There should be judicious use of colour and design on the label, outer packaging and delivery bags to differentiate syringes/minibags containing Neurotoxic drugs from other preparations.
Neurotoxin Rec. 6	<p>All Neurotoxic drugs dispensed in syringes or minibags are labelled with the following auxiliary label, as appropriate:</p> <div data-bbox="570 596 1360 884" style="border: 1px solid black; padding: 10px; margin: 10px 0; text-align: center;"> <p>WARNING NEUROTOXIC DRUG</p> <p>PROTEASOME INHIBITOR</p> <p>CYTOTOXIC</p> <p>FOR INTRAVENOUS OR SUBCUTANEOUS USE ONLY</p> </div> <div data-bbox="570 936 1360 1224" style="border: 1px solid black; padding: 10px; margin: 10px 0; text-align: center;"> <p>WARNING NEUROTOXIC DRUG</p> <p>VINCA ALKALOID</p> <p>CYTOTOXIC</p> <p>FOR INTRAVENOUS USE ONLY</p> </div> <p><i>The auxiliary labels are placed directly on the syringe barrel or minibag 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.</i></p>

Neurotoxin Rec. 7

All injections of Neurotoxic drugs will be supplied in a sealed 'neurotoxic drug transport bag'. This bag should be labelled as followed, as appropriate, either in a pre-printed format or as an attached label.

WARNING NEUROTOXIC DRUG
PROTEASOME INHIBITOR
CYTOTOXIC
FOR INTRAVENOUS OR SUBCUTANEOUS USE ONLY

WARNING NEUROTOXIC DRUG
VINCA ALKALOID
CYTOTOXIC
FOR INTRAVENOUS USE ONLY

NOTE: The label should reference VINCA ALKALOIDS or NEUROTOXIC DRUG or PROTEASOME INHIBITORS, as appropriate.

Neurotoxin Rec. 8

All neurotoxins dispensed in syringes or minibags are labelled with a pharmacy dispensing label containing the patient and dose details as described in Appendix 10 of the NCCP Oncology Medication Safety review⁷.

A copy of this label will also be affixed to the 'neurotoxic drug transport bag'.

⁷ Available: www.hse.ie/nccponcsafetyreview

Appendix 1. NCCP ITC Project Board Terms of Reference

Background

The Intrathecal Chemotherapy Project Group was originally convened to develop and agree a national guidance document for the use of intrathecal chemotherapy. The ITC Project Board was a sub-group of the NCCP Oncology Medication Safety Implementation Steering Group. The Project Group was then disbanded following the completion of the national guidance document. It was agreed that the Project Group could be re-convened as required to review the guidance in place as required and also to consider any additional projects relating to the area of intrathecal chemotherapy.

A second Intrathecal Chemotherapy Project Group was convened in 2020 to oversee the development and roll out of a formal education programme on the use of intrathecal chemotherapy (ITC).

Membership

1. The composition of the Group will be determined by the NCCP.
2. The Chair/s of the Group will be appointed by and report to the Director of the NCCP.
3. Membership will be for the duration of the project.
4. Additional members may be co-opted to the group from time to time

Objective

1. To review and refresh the national guidance as required, considering any new evidence of relevance to the recommendations contained.
2. To advise, approve and ensure that the e-learning module content is aligned to the NCCP Guidance on the Safe Use of Intrathecal Chemotherapy in the Treatment of Cancer and is suitable for use by all hospitals. UHW have agreed to develop the content and incorporate the feedback of the editorial board.

Frequency of meetings

It is envisaged that the Group will meet approximately three times and the work of the group will conclude when the e-learning programme is finalised.

Secretariat

The Secretariat to the Group will be provided by NCCP.

Appendix 2. Members of NCCP ITC Project Board

Project Group Membership 2014

Role of group	Name and professional title
NCCP	Dr Maccon Keane, Clinical Lead, Medical Oncology Ms Patricia Heckmann, NCCP Chief Pharmacist Ms Ciara Mellett, Medical Oncology Programme Manager
Consultant medical oncologist (ISMO rep.)	Dr. Cliona Grant, Consultant Medical Oncologist, St. James's Hospital.
Consultant haemato-oncologist – paediatrics	Aengus S. O'Marcaigh, Consultant Paediatric Haematologist, Crumlin.
Nursing Representatives	Ms. Lorna Cosgrave, CNM2, Beaumont Hospital. Ms. Teresa Meenaghan, RANP in Haematology, Galway Ms. Lorna Storey, RANP, Paediatric Haematology, Crumlin Ms. Frieda Clinton, RANP, Paediatric Haematology Oncology, Crumlin
Pharmacy Representatives	Ms AnnMarie de Frein – Chief II Pharmacist SVUH Ms. Keira McQuaid – Oncology Pharmacist, Beacon Hospital Mr. Nuno Silva – Chief II Pharmacist St. Vincent's Private Hospital

Project Group Membership 2020

Role of group	Name and professional title
Chair	Prof. Patrick Thornton, Consultant Haemato-oncologist, Beaumont
NCCP	Ms Patricia Heckmann, Assistant National Director, NCCP & Chief Pharmacist Ms Anne Marie De Frein, NCCP Deputy Chief Pharmacist Ms Elizabeth Breen, NCCP Chief II Pharmacist Ms Tracy Folliard, NCCP Project Manager Systemic Therapy
NCCP Medical Oncology Advisor	Prof. Maccon Keane, Consultant Medical Oncologist at Galway University Hospital.
Consultant medical oncologist (ISMO rep.)	Dr. Deirdre O'Mahony, Consultant Medical Oncologist, Bons Secours, Cork
Consultant haemato-oncologist – paediatrics	Prof. Aengus S. O'Marcaigh, Consultant Paediatric Haematologist, Children's Health Ireland at Crumlin (CHI at Crumlin).

HSE Quality Improvement	Ms Ciara Kirke, Medication Safety National Lead, Quality Improvement Lead, HSE
Nursing Representatives	Ms. Rachel Fox, Beaumont Hospital Ms. Lorna Storey, Paediatric Haematology ANP, CHI at Crumlin
Pharmacy Representatives	Ms Catriona Collins, Pharmacist, Galway University Hospital Ms Nessa Fahy, Pharmacist, Galway University Hospital Mr Enda Molloy, Pharmacist, CHI at Crumlin

Appendix 3. 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.

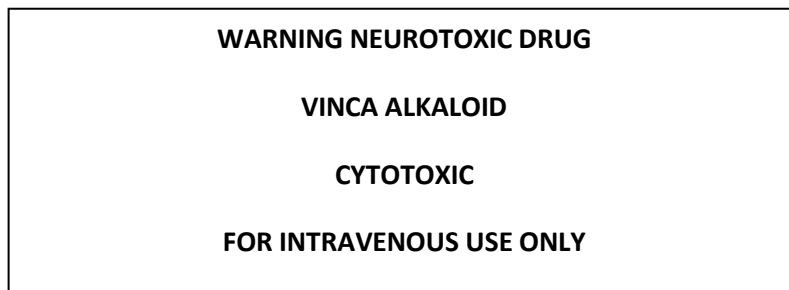
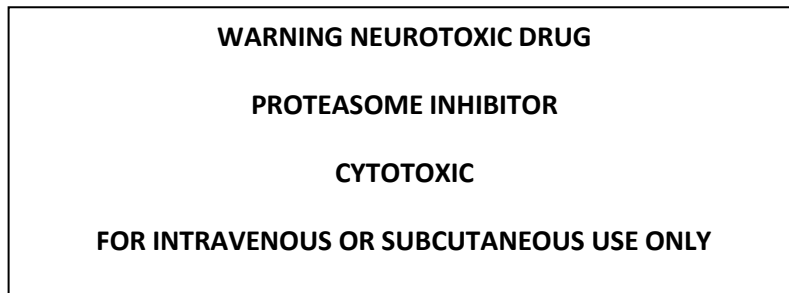
1. Vinca Alkaloids e.g. vinCRISTine, vinBLASStine, vindesine, vinORELBine and vinflunine
2. Proteasome inhibitors e.g. bortezomib, carfilzomib.

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

Appendix 4. Sample labels

Label 1: Sample label for neurotoxic drug transport bag labels.

This may be in a pre-printed format or as an attached label. The colour of the transport bag should be selected to differentiate the contents from other minibag infusions.



Bibliography

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2. World Health Organization. Information Exchange System. Alert 115. 2007.
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4. EMA. Recommendations to prevent administration errors with Velcade (bortezomib). 2012.
5. ISMP. Death and neurological devastation from intrathecal vinca alkaloids: Prepared in syringes = 120; Prepared in minibags = 0. 2013.
6. ISMP. IV vincristine survey shows safety improvements needed. 2006.
7. Woods K. The Prevention of Intrathecal Medication Errors; A report to the Chief Medical Officer. In: DOH, editor. 2001.
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10. NCCP. NCCP Oncology Medication Safety Review Report. 2014.
11. NCCP. NCCP Guidelines on the Safe Use of Intrathecal Chemotherapy in the treatment of cancer. 2020.