Australia and New Zealand
Urological Nurses Society INC
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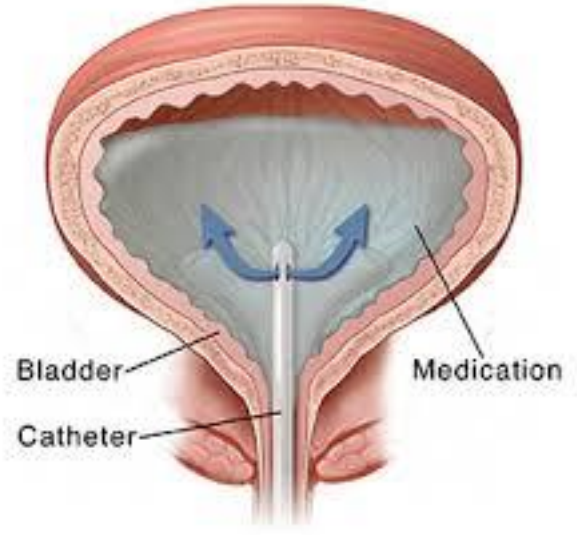
ANZUNS

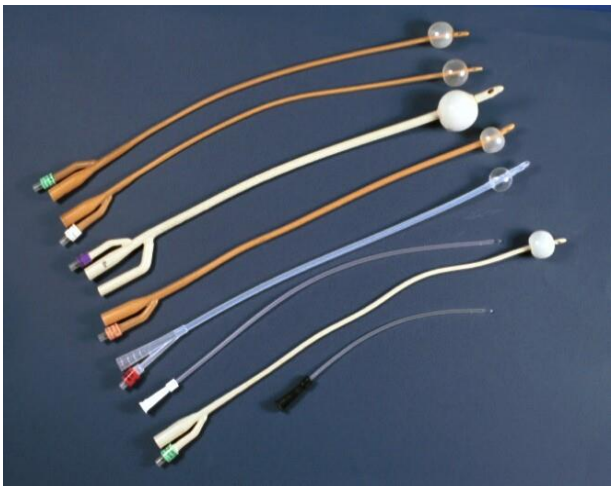
ANZUP
Cancer Trials Group Limited

Intra-vesical therapy for Non-Muscle Invasive Bladder Cancer (NMIBC)

Nursing Guidelines

February 2018





Edited by Kath Schubach

Disclaimer Statement:
Australian and New Zealand Urology Nurses (ANZUNS) have developed this document in collaboration with Australia and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group and The Urological Society of Australia and New Zealand (USANZ).

The information in this document is for health care professionals working with patients requiring intra-vesical therapy. While due care was ensured with the accuracy of the material contained in this guideline, healthcare professionals should refer to existing guidelines within their institutions.
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It is the responsibility of the healthcare professional to ensure they are competent in the administration and management of intra-vesical treatment.

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Introduction

In 2011 the Australia and New Zealand Urological Nurses Society Inc. (ANZUNS) agreed to develop clinical guidelines in this area. Anecdotally there were differences in practice and it was felt we needed a consensus document for our members to access. A project officer was appointed to develop the guidelines and report back at the Darwin conference in April 2012. Trish White edited the first edition and the document was peer reviewed. I would like to acknowledge the work put in by these colleagues on the first edition of these guidelines that have formed the basis for this updated edition.

In 2013 Professor Dickon Hayne commenced the BCG+MMC trial. I was on the Scientific Advisory Committee of Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group as a representative of ANZUNS. There was a discussion of guidelines for intra-vesical therapy. Some urology health professionals were unaware of the ANZUNS intra-vesical guidelines. These guidelines were due to be updated. So I approached the executive committee of ANZUNS and ANZUP to suggest we collaborate in updating the intra-vesical therapy nursing guidelines for NMIBC. This has been a true collaborative project between ANZUNS, ANZUP and USANZ in creating these urology nursing guidelines.

I would also like to acknowledge our international colleagues, European Association of Urology Nurses, British Association of Urology Nurses, & Society of Urologic Nurses Associates for the access to their guidelines and sharing of their resources.

Kath Schubach. MSN Urology Nurse Practitioner
ANZUNS Representative/ANZUP Scientific Advisory Committee
February 2018

Professional Requirements for Nurses Administering Intra-vesical Instillations
The Registered Nurse should be competent in the administration and handling of intra-vesical treatments and have completed training and assessment in a program as per local policy/guidelines. It is also a requirement that they are competent in male and female urethral catheterisation.

New Zealand Nurses should be aware of the National standards for Anti-neoplastic Drug Administration in New Zealand.

https://www.health.govt.nz/system/files/documents/pages/national-nursing-standards-for-antineoplastic-drug-administration-nz.pdf

Supporting evidence for ANZUNS Inc statement on professional requirements

It is recommended Registered Nurses are assessed annually to maintain competency in the administration of cytotoxic or immunotherapeutic medication.

Only registered nurses with specific education and training in the safe handling of anti-cancer medication and related waste management and disposal should administer anti-cancer therapies.

Employers must ensure nurses involved in administering anti-cancer medication have access to education, training and environmental factors such as ease of access, light and space and other resources are addressed as a matter of necessity to ensure minimum professional and safety standards are met.

Employers must ensure that risk assessments have been conducted and recommended processes are in place to enable nurses to maintain their competency and scope of practice in this field.

Cancer Nurses Society of Australia (2010)

New Zealand Nurses Organisation / Cancer Nurses College (2015)

https://eviq.org.au Safe administration of antineoplastic drugs

Definition:
Intra-vesical therapy is the process of instilling a therapeutic agent into the urinary bladder. The agent is instilled using a urethral catheter under a sterile technique.

Abbreviations:

BCG	Bacillus Calmette Guerin
CIS	Carcinoma in situ
LR	Low risk
IR	Intermediate risk
MM	Mitomycin
TURBT	Trans urethral resection of bladder tumour
UTI	Urinary tract infection
NMIBC	Non muscle invasive bladder cancer
PPE	Personal protective equipment
BPH	Benign prostate hyperplasia
BOO	Bladder outlet obstruction
PUNLMP	Papillary urothelial neoplasm of low malignant potential
HG	High grade
LG	Low grade

The following guidelines will discuss the administration of medication instilled into the bladder used to treat non-muscle invasive bladder cancer (NMIBC).

Risk Group Stratification

Risk group stratification	**Characteristics**
Low risk tumours (LG)	Primary, solitary, Ta, G1*, (PUNLMP, LG) <3cm, No CIS
Intermediate risk tumours	All tumours not defined in the two adjacent categories (between the category of low and high risk)
High risk tumours (HG)	Any of the following: T1 tumour G3** (HG) tumour CIS Multiple and recurrent and large (>3cm) Ta, G1, G2 tumours

* Low grade is a mixture of G1 and G2
**High grade is a mixture of some G2 and all G3
CIS=carcinoma in situ
HG=high grade
LG=low grade
PUNLMP=Papillary urothelial neoplasm of low malignant potential

Note: Adapted from EAU Non muscle invasive bladder cancer Guideline 2017 Table 6.3

Indications/ Treatment Recommendations

Within Australia and New Zealand the decision to commence intra-vesical treatment is made by the urological surgeon. It may also be discussed at multidisciplinary meetings.

There are international guidelines to facilitate this decision process provided by The American Urological Association (AUA) and European Association of Urology (EUA). An adequate interval for healing should be allowed (usually 3 or 4 weeks) prior to commencement of induction intra-vesical therapy.

Suggested intra-vesical treatments according to risk category

Category	Treatment
Low risk	A single dose, instillation of chemotherapeutic agent is recommended immediately following TURBT. It should be administered within 6 hours but can be given up to 24 hours following TURBT. This may be given in theatre or on the ward.
Intermediate risk	Single post-operative instillation of intra-vesical chemotherapy following TURBT may still have value (some institutions will follow this recommendation) +- Induction course of intra-vesical BCG with maintenance is recommended.
High risk	Induction course of intra-vesical BCG with maintenance is recommended.

Note: Adapted from: EAU guidelines on non-invasive urothelial carcinoma of the bladder: update 2014 & Diagnosis and Treatment of Non-Muscle invasive Bladder Cancer: AUA/SUO Guideline 2016. Copyright 2016 American Urological Association Education and Research, Inc.®

Common Treatment Regimes for Non Muscle Invasive Bladder Cancer (NMIBC)

There are various schedules that may be utilised in the treatment of NMIBC. Below are examples of common pathways utilised.

Mitomycin (MM) initial instillation immediately post operatively; within 6 hours but not exceeding 24 hours.

Immediate instillation post op followed by 6 weekly instillations (induction therapy).

Epirubicin may be used post operatively instead of Mitomycin. It is a cheaper alternative however its efficacy has not been proven with any RCT's.

Bacillus Calmette Guerin (BCG) NOT to be instilled immediately post op – to reduce risk of absorption and systemic BCG-osis. It should not be instilled earlier than 2 weeks post TURBT.

Weekly instillations commencing 2 weeks post TURBT and continuing weekly for 6 weeks followed by maintenance dose. It is recommended that maintenance after induction is required for maximum efficacy. There are various schedules used including SWOG (Lamm) protocol administered every week for

3 weeks then every 3 weeks at 3, 6, 9 and 12, for intermediate risk NIMBC who have responded to BCG and continue for 36 months for high risk patients (*Lamm et al 2000, pg1128, Brausi 2011 pg 2160).

Alternatively maintenance can be given monthly for 1 year.
**American Urological Association(AUA) Society of Urologic Oncology (SUO) guideline (2016 pg 18-22)*

Patient preparation prior to commencement of intra-vesical therapy

A medical consent should have been completed before the patient attends the preadmission/pre-treatment appointment.

Before initiating any intra-vesical therapy a thorough patient assessment should be performed. This should include clinical and nursing assessments:

- Allergy status
- Specific urological conditions
- Urinalysis
- Verbal & written education explaining procedure
- Concomitant medications
- Assessment of patient's ability to understand procedure and comply with treatment regime
- Purpose and action of intra-vesical treatment
- Risk and side effect profile of intra-vesical therapy

Patient Safety

- Patients should be instructed if intra-vesical therapy comes in contact with their skin it should be washed off with soap and water immediately
- Hand washing is advised after voiding

Toileting

- Some patients may experience urinary frequency and urgency and there is a potential risk in contamination if the patient is incontinent
- Patients should be instructed to void sitting down
- The toilet lid should be closed before flushing
- Patients having Mitomycin should close the toilet lid and flush twice after use
- Patients having BCG should use 1-2 cups of bleach and close the lid of the toilet, wait 10-15 minutes before flushing
- If sharing a toilet facility it is recommended to clean it with detergent and water after use

Contamination of clothes

- Clothes can be washed normally if contaminated by MM or BCG

Pregnant patients

- It is recommended that pregnancy within 6 months be avoided. Breast-feeding while having treatment is contraindicated

Fertility/Sexual health

- Male patients being treated with BCG have changes in their sperm quality. Patients can have sperm counts below oligospermia levels
- Patients should refrain from sexual intercourse for 48 hours after treatment
- If sexually active a penile sheath /condom is advised during sexual intercourse and should be worn for at least 1 week after intra-vesical therapy has been given
- Male patients should be aware that BCG may increase PSA readings.

Medication pre procedure

Anticholinergic: Can be used in patients with pre-existing storage symptoms but should be used with caution in patients with Benign Prostatic Hyperplasia (BPH), bladder outlet obstruction (BOO) cardiac disease, and acute angle-closure glaucoma.

Analgesics: There is no contraindication with intra-vesical therapies and the use of non-steroidal anti-inflammatories. However caution should be taken if patients have pre-existing gastric ulcer or in patients taking anti-coagulant therapy.

Antibiotics: There is currently no evidence to suggest that patients having con-current antibiotic treatment decrease the effectiveness of either MMC or BCG. However patients who are taking antibiotics should discuss with the Consultant before starting or delaying treatment with intra-vesical therapy.

Diuretics: Patients taking diuretics should discuss with the Consultant, as this should be individually assessed. Ideally delaying the diuretic and restricting fluid intake prior to treatment will aid in the decrease of urine production and assist patients to hold intra-vesical therapy in their bladder.

Urinary alkalisation: Oral sodium bicarbonate 1.3gram tablets taken the night before and morning of the procedure and 30 minutes prior to treatment may optimise the effectiveness of Mitomycin instillation, however this is not mandated.

Note: Information adapted from Evidenced based Guidelines for Best Practice in Urological Health Care Intra-vesical instillation (2015 pg. 37-38) European Association of Urology Nurses

Intra-vesical Chemotherapy

In Australia and New Zealand there are various drugs used for intra-vesical chemotherapy. These drugs are; Mitomycin, Doxorubicin, Epirubicin and Gemcitabine, these are discussed further in the appendices.

Pharmacological Optimisation for Mitomycin therapy

- Drug concentration 40mg in 40 mls sterile water
- Alkalinise urine if patient can tolerate
- Patient to refrain from oral fluids for 4 hours before and during treatment
- Ensure bladder is empty after catheterisation
- Use 2 hour dwell time with patients if they can tolerate it

**Nat Rev Urol. 2014 Apr; 11 (4): 220-30. doi: 10.1038/nrurol.2014.52. Epub 2014 Mar 11. Optimizing intravesical Mitomycin C therapy in non-muscle-invasive bladder cancer*

This section of guideline will provide procedures for:

Single Postoperative Dose of Intra-vesical Chemotherapy - (Mitomycin)

This may be administered immediately at the completion of TURBT, in absence of perforation, and then completed treatment in recovery. Alternatively, it may be the Registered Nurse's responsibility to administer the intra-vesical therapy in the designated setting (Should ideally be given within 6 hours post op, and no longer than 24 hours).

Equipment

- Personal protective equipment (PPE) for the nurse: impervious protective gown, sterile gloves, eye protection, mask N95
- Urinary catheterisation pack
- Catheter valve (if available) and using indwelling catheter
- Medication in a prefilled syringe
- Cytotoxic rubbish bags and labels
- Incontinent sheets or plastic draw sheets
- Cytotoxic spill kit to be available at all times
- Small gauge intermittent catheter or indwelling catheter if needed (for a course of MMC)

Single Postoperative Dose of Intra-vesical Chemotherapy - (Mitomycin)

Procedure	Rationale
Prior to Surgery	
Provide written information on procedure stating reasons for treatment Gain informed consent Outline risks, side effects and potential complications of both surgery and chemotherapy medication to be used	Shows patient has a good understanding and is well informed of procedure
Check allergies	Prevent medication reaction
Order prescribed medication	Must be available on day of surgery, preferably within six hours of surgery
Withhold diuretics prior to surgery if requested by Urologist; this is an individual requirement and may differ	To prevent over-distension of bladder causing discomfort while patient retaining chemotherapy
Complete normal preoperative preparation	
Immediately Prior to Administration of Chemotherapy	
Check operation record, prescription and allergies	To identify any potential complications i.e. extensive resection or specific surgeon instructions and to prevent medication errors
Confirm patient identity to comply with National Safety and Quality Health Standards (NSQHS) & Health Quality & Safety Commission New Zealand (HQSC)	Two nurses to check identity and prescription prior to administration of chemotherapy
If possible nurse in a private room	To prevent risk of contamination and provide privacy
Assess urine colour and consistency – if frank, moderate or heavy haematuria is present, treatment should be delayed until it lessens and symptomology investigated	It is important not to proceed with chemotherapy with heavy haematuria in the postoperative patient as it could be an indicator of bladder perforation following TURBT and may lead to systemic absorption or extravasation Heavy haematuria also has the potential to clot and block the catheter Always consult with the Urologist if unsure whether to proceed

Procedure	Rationale
Assess temperature and if febrile consult with Urologist for confirmation to proceed	To reduce the risk of administering treatment when the patient is systemically unwell
Assess pain level Simple analgesia such as paracetamol can be considered If uncomfortable, anticholinergic medication may prevent bladder spasm, which could cause catheter bypassing/ leakage	Check any increase in pain is not due to a blocked catheter
If bladder irrigation in place, turn it off but do not disconnect tubing. If not in place you may set up continuous bladder irrigation (CBI) tubing, and sodium chloride 0.9%	Ensure urine is light rose or no visible haematuria when turning bladder washout off; to ensure patency of catheter
Empty catheter drainage bag and record output	Maintain accurate intake and output records in these patients
Assemble required equipment as above Ensure spill kit is available	
Instillation Procedure	
Place protective sheet under penis and above scrotum, or in females tuck it around the labia	To prevent skin contamination in case of spillage
Wash hands and don personal protective equipment	To maintain sterility and to protect yourself from cytotoxic contamination
Place sterile fenestrated sheet on top of incontinent sheet	To maintain sterility
Cleanse catheter connection with prescribed solution as per local policy	
Disconnect catheter from drainage bag and keep tip sterile If available attach catheter valve to assist in controlled instillation	Prevent infection Catheter valve reduces the risk of spillage
Attach the medication container to the end of valve, open the valve	
Slowly instil medication, DO NOT USE FORCE If painful you should STOP IMMEDIATELY	Slow instillation allows you to assess patient for discomfort that could be bladder spasm or potential extravasation

Procedure	Rationale
Either turn off valve or use a catheter clamp to prevent leakage while removing medication container	If not using a valve there is a risk of spillage at this point
Dependant on postoperative instructions either: Remove catheter, OR leave catheter in situ with the valve in the off position, reconnect drainage bag, leave sterile guard over genital area and apply cytotoxic sticker to the top of guard Alert colleagues of potential for contamination	See catheter removal selection below If catheter remains in-situ leave valve closed and attach catheter bag to avoid contamination To ensure staff safety
Dispose of contaminated waste in cytotoxic bag according to local policy	Cytotoxic waste is properly disposed preventing contamination of environment
Apply cytotoxic label to catheter drainage bag	To alert colleagues of potential for contamination
Patient to stay in bed for one hour while medication is in place	Movement is encouraged to help to distribute the intra-vesical agent throughout the bladder
Ensure patient comfortable and call button within reach, assess patient frequently for pain, as they may not be able to tolerate a full hour. Periodically check for leakage	Patient may not be aware of leakage if spinal anaesthesia has been given
Any bypassing or leakage requires immediate action; remove protective guards, pads or protective sheets and wash patient's skin thoroughly with soap and water Environmental spills should be treated as per local policy	Prevent contamination from spillage on patients skin Refer to local cytotoxic policy, spill kit should be available at all times
Two hours following instillation (or at time tolerated preferably minimum of 1 hour)	
Unclamp catheter and attach closed urinary drainage bag, ensure urine freely flowing	Reduces risk of urine spillage and ensure patency of drainage system
If any haematuria or clots blocking catheter a manual bladder irrigation may be required or a small volume from continuous bladder washout to ensure patency; use cytotoxic precautions	To ensure patency of catheter
Ensure bladder is empty. Once the bladder is empty, remove drainage bag containing urine and remove and place in cytotoxic rubbish bag and dispose of according to local policy	Measure output Reduces risk of spillage and contamination of environment

Procedure	Rationale
Apply new sterile drainage bag	To prevent spillage, overflow
Document chemotherapy administration on medication chart	
Ongoing assessment of patient for pain and continue postoperative care	To ensure any adverse effects are noted immediately
If catheter is to be removed (depending on individual patient assessment)	
Cytotoxic protective equipment to be worn	Prevent contamination
Place protective sheeting underneath patient	
Remove catheter slowly; you may wish to use a gauze square at the meatus to prevent urine flicking from the tip Dispose of as per local cytotoxic policy Wash patient's genital area with soap and water	Prevent contamination
Patient may need bedside commode, pan or urinal if they have decreased mobility or are at risk of incontinence getting to toilet	Prevent spillage of chemotherapy
Advise caution with handling urine for six hours following treatment • Patient to sit to void • Flush toilet twice • Advise patient to wash the genital area well with soap and water.	Prevent spillage/contamination of environment
Assess success of trial without catheter as per local policy	Increase in pain could be due to either urinary retention or bladder perforation
Encourage fluids up to 2-3L in the following 24hrs	To help flush medication out of the body
Urine samples should not be sent to a laboratory in the next 72 hours unless urgent Any samples must be clearly marked as cytotoxic and caution needs to be taken by laboratory staff to prevent contamination	Prevent potential contamination in laboratory services

Procedure for a Course of Intra-vesical Chemotherapy

Definition

Patients with non-invasive bladder cancer are often managed with TURBT then may be prescribed course of intra-vesical chemotherapy. Regimes vary depending on the histopathology of tumour. The aim is to achieve disease control and a decrease or eradication of tumours.

Contraindications

- It is not to be given within two weeks of surgery if bladder injury sustained e.g. perforation
- History of allergy or adverse reaction to medications
- Specific medication contraindications are available in the appendices.

Equipment- as per instillation single instillation of Mitomycin

Procedure	Rationale
Prior to Treatment	
Ensure patient has medical consent Provide written information on procedure stating reasons for treatment Outline risks, side effects and potential complications of both surgery and chemotherapy medication to be used	Shows patient has a good understanding and is well informed of procedure
Check allergies and no prior adverse reaction to chemotherapy	Prevent medication reaction
Order prescribed medication	Must be available on day of treatment to avoid delays
Withhold diuretics prior to treatment if requested by Urologist, this is an individual requirement and may differ	To prevent over distention of bladder causing discomfort while patient retaining chemotherapy. To prevent dilution of chemotherapy agent
Obtain MSU prior to commencing 6 week treatment Full ward test of urine on day of treatment	To rule out urinary tract infection and allow time to treat if urine positive
Immediately Prior to Administration of Chemotherapy	
Check prescription and allergies	Prevent medication error and ensure treatment plan has not altered

Procedure	Rationale
Confirm patient identity according to comply with Australian National Standards and Health Quality & Safety Commission New Zealand	Two nurses to check identity and prescription prior to administration of chemotherapy
Assess patient for suitability to continue with procedure: Urine: colour, haematuria, clarity, dysuria General assessment: has there been any change in symptoms since previous treatment e.g. elevated temperature or rash	If UTI suspected, withhold treatment and send MSU for culture and sensitivity and treat as per local policy. It may be safe to proceed but always consult Urologist if unsure If uncomfortable, anti-cholinergic medication may prevent bladder spasm which could cause leakage
Assess if patient will be able to retain chemotherapy or will a temporary catheter be required	To maximise amount of time chemotherapy will be able to be retained in the bladder
Assemble required equipment as above and ensure it is located conveniently	
Instillation Procedure	
Place protective sheet under penis and above scrotum, or in females tuck it around the labia	To prevent skin contamination in case of spillage
Wash hands and don protective equipment	To maintain sterility and to protect yourself from cytotoxic contamination
Prepare sterile field and equipment	
Place sterile guard on top of protective sheet	To maintain sterility
Clean genital area with skin preparation fluid e.g. normal saline/chlorhexidine	Decrease risk of infection
Instil lignocaine/lubricating gel if prescribed and wait two to three minutes before proceeding with catheterisation	Increase patient tolerability of treatment
Insert small gauge intermittent catheter, or indwelling catheter if plan is to leave it in situ for treatment Follow your local catheterisation policy	Maintain aseptic technique to decrease risk of infection
Ensure catheter is within bladder and drain all urine	To improve medication efficacy

Procedure	Rationale
Observe for evidence of haematuria	If signs of traumatic catheterisation present then remove catheter and abandon treatment as this would increase the risk of systemic absorption If only slight haematuria then safe to proceed
Attach the medication container to the end of catheter and slowly instil medication, DO NOT USE FORCE If painful you should STOP IMMEDIATELY	Slow instillation allows you to observe patient for discomfort that could be bladder spasm or potential extravasation Movement is encouraged to help to distribute the intra-vesical agent throughout the bladder
Dependant on patient requirements either: - Remove catheter carefully, OR - Leave catheter in situ and clamped	
If any leakage occurs wash thoroughly with soap and water	
Dispose of contaminated waste in cytotoxic bag according to local policy	Prevents contamination of environment
Any leakage requires immediate action; remove protective guards, pads or protective sheets and wash patient's skin thoroughly with soap and water Environmental spills should be treated as per local policy	Prevent injury from spillage Refer to local cytotoxic policy, spill kit should be available at all times Warn colleagues of potential for contamination
Ensure the patient is aware of the length of time the medication needs to stay in the bladder	Patient may mobilise in the department Some allow the patient to go home at this point and void there; reduces risk of contamination
Encourage patient to drink 400mL of water half an hour before designated time to void or drain IDC	To ensure bladder contains urine sufficient to void
Two hours following instillation (or time tolerated preferably 1 hour minimum)	
The patient should be encouraged to void sitting down on a designated toilet for the first 6 hours after treatment. The toilet should be double flushed after each use. Advise patient to wash the genital area well with soap and water after voiding.	Prevent spillage or contamination

Procedure	Rationale
Document administration on drug chart in patient record	Provides accurate documentation of administered treatment Continuity of treatment
Encourage patient to drink 2-3L for 24 hrs Avoid caffeine and alcohol as this may cause further irritation to the bladder	Helps to flush medication from the body
Ensure patient knows how to seek advice for any unexpected symptoms	Ensures prompt attention for timely treatment
Urine samples should not be sent to a laboratory in the next 72hrs unless urgent Any samples must be clearly marked as cytotoxic and caution needs to be taken by laboratory staff to prevent contamination	Prevent potential contamination in laboratory services
Before the patient leaves make sure he/she is aware of their ongoing treatment plan.	Ensure ongoing continuity of treatment
Patients with catheter left in situ following instillation	
If the catheter has been left in for treatment period, after instillation it can be clamped spigot or flip-flo valve turned off for designated time. An incontinence pad and net pads can be fitted to prevent major spillage Remove spigot, clamp or open flip-flo valve and empty urine into drainage bag and remove catheter and proceed with instructions in above section, or apply leg bag if catheter is to remain in place Dispose of all equipment into cytotoxic waste rubbish bag as per local policy Inform patient of cytotoxic precautions	Prevent contamination Provides patient with information to prevent contamination of environment

This guideline has been developed from information in the following documents: *ADHB*,** 2012, *BAUN*, 2011, *WA Cancer and Palliative Care Network* 2010, *EAUN,* 2015, *WDHB*, 2010, *SUNA,* 2017

Management of spillage/contamination of cytotoxic medication

A chemotherapy spill kit should be available at all times and contain personal protective equipment (PPE) (long sleeved gown, overshoes, goggles, gloves, and absorbent pads/granules, bleach).

Prevention of leakage or spills should be a priority when administering intra-vesical chemotherapy. If contact does occur with the patient's skin, immediately place absorbent cloth over the area then wash immediately with soap and water and reapply barrier cream. Place the cloth in cytotoxic waste bag.

All clinical equipment should be disposed of according to local cytotoxic waste policy including heavily contaminated linen, gowns etc.

Contamination of:

Eyes/mucous membranes: irrigate with copious amounts of sodium chloride 0.9%, (do not use sodium bicarbonate). Remove eye contacts prior to irrigation if wearing these; seek medical advice, report incident. Observe eyes for several days for signs of corneal injury.

Ingestion: seek immediate medical advice

Linen: change immediately and dispose of in cytotoxic bag

Clothes: remove immediately and deal with skin contamination then wash clothes on hot cycle.

Incidents should be reported according to the protocol at your place of employment.

Other methods of administering intra-vesical cytotoxics

There are other methods using device-assisted therapies for the administration of cytotoxics such as Mitomycin. These therapies include hyperthermia and electromotive therapy drug administration but these therapies are currently considered experimental.

EAU guidelines 2017

Side effects of Mitomycin (MM)

MM-local	Side effect	Nursing intervention	Possible complication
Chemical cystitis	Dysuria Urgency Frequency	Increase oral fluid intake Simple analgesia Assess post void residual Consider anticholinergic if not contraindicated Cystitis remedies Reduce caffeine, etc. Discussion with consultant re: • Dose reduction • Dwell time	Urinary tract infection Epididymitis/orchitis May reduce efficacy of treatment
Skin toxicity	Erythema	Remove exposing agent Wash skin with copious amounts of soap and water Use barrier cream to protect skin	Necrosis of skin Contact dermatitis
MM-systemic Myelosuppression	Rash Fatigue Malaise High temperature	Stop instillation; may need to change to different chemotherapy drug Thorough assessment of patient Seek medical advice	Neutropenia (rare)
Intraperitoneal extravasation	Pain Evacuation of agent	Seek medical advice Will require urgent cystogram; may require surgery to repair injury	
Extraperitoneal extravasation	Pain	Seek urgent medical advice Requires catheter drainage Imaging required to evaluate injury	Abscess formation Fistula formation Bowel obstruction

Note: Table adapted from British Association of Urological Nurses 2010 pg. 17

Intravesical Immunotherapy

Bacillus Calmette-Guerin (BCG)

Intravesical immunotherapy is used as a treatment for intermediate and high-risk non-muscle invasive bladder tumours and carcinoma in situ. It is used for reducing recurrence and preventing or delaying progression of disease *(Chang, Boorjian, Chou, Clark, Daneshmand, Konety, Pruthi, Quale, Ritch, Seigne, Skinner, Smith, & McKieran, 2016).*

Action
It is a freeze-dried preparation of an attenuated strain of *Mycobacterium bovis.* When administered into the bladder as a cancer therapy, BCG promotes a local acute inflammatory and sub-acute granulomatous reaction with macrophage and leukocyte infiltration in the urothelium and lamina propria of the urinary bladder. The local inflammatory effects are associated with an elimination or reduction of non-muscle invasive cancerous lesions of the urinary bladder. The exact mechanism of action is unknown.

Principles
Used in patients with a diagnosis of non muscle invasive transitional cell carcinoma and Carcinoma in-situ (CIS).

The aim is to reduce risk of progression and increase disease free survival.

Contraindications (also see manufacturers instructions in appendices)

BCG should **not** be administered within two weeks of TURBT or bladder biopsy, or in patients with active tuberculosis or a prior history of tuberculosis, HIV positive, currently having radiotherapy or chemotherapy.

Check patient is cognitively able to follow pre and post treatment procedures or they must have a person with them who can supervise them.

Check for a history of rheumatic fever or artificial valve replacements, as cardiologist may prefer to have antibiotic cover for procedure.

Check allergies and check they have not had any prior adverse reactions to intra-vesical chemotherapy, immunotherapy or seasonal influenza vaccinations.

Check they are not on concurrent immunosuppressant therapy.

Contraindicated in nursing mothers and children.

Procedure for a course of Intra-vesical Immunotherapy

Equipment

- Personal protective equipment for the nurse: impervious protective gown, sterile gloves, eye protection, mask N95
- Catheterisation pack
- Lignocaine/lubricating gel
- Skin preparation fluid e.g. Chlorhexidine/normal saline
- Small gauge intermittent catheter or indwelling catheter if needed. Catheter size selection is based on the patients clinical assessment but aim for smallest possible gauge
- Catheter valve
- BCG in prefilled syringe, with cap applied if available or can be reconstituted and administered using a closed reconstitution system such as Method for Easy Reconstitution and Convenient Instillation (MERCI)
- Connection device to attach BCG syringe to catheter to minimise spillage
- Skin barrier cream
- Hazardous rubbish bags
- Protective sheets or plastic draw sheets
- Cytotoxic spill kit to be available at all times
- Bleach (a commercial household product is adequate)

Procedure	Rationale
Prior to Treatment	
Ensure medical consent completed Provide written information on procedure stating reasons for treatment Outline risks and side effects of BCG	Shows patient has a good understanding and is well informed of procedure
Check allergies and no prior adverse reaction to chemotherapy	Prevent medication reaction
Order prescribed BCG	Must be available on day of treatment and BCG should be administered within two hours of mixing
Patient to refrain from oral fluids for 4 hours prior to treatment and withhold diuretics (if requested by Urologist); this is an individual requirement and may differ	To prevent dilution of the drug and over distension of bladder causing discomfort while patient retaining chemotherapy

Procedure	Rationale
Obtain MSU the week prior to commencing 6 week treatment Dipstick urine on day of treatment	To rule out urinary tract infection and allow time to treat if urine positive If UTI suspected withhold treatment and send for culture and sensitivity Treat with antibiotics as per local policy
Immediately Prior to Administration of BCG	
Check prescription and allergies	Prevent medication error and ensure treatment plan has not altered
Confirm patient identity Two nurses to check identity and prescription prior to administration of BCG	Ensures compliance with Australian National Standards and Health Quality & Safety Commission New Zealand
Assess patient for suitability to continue with procedure: Urine: colour, haematuria, clarity, dysuria General assessment: has there been any change in symptoms since previous treatment e.g. elevated temperature or rash	If uncomfortable, anticholinergic medication may prevent bladder spasm which could cause leakage Specifically no haematuria in the 24hrs prior to instillation
Assess if patient will be able to retain medication or will a temporary indwelling catheter be necessary	To maximise amount of time BCG will be able to be retained in the bladder Patients with high residuals need catheterising for two hours, then draining before IDC removed as they have delayed emptying and a longer dwell time of BCG can lead to severe flu like symptoms
Assemble the required equipment as above and ensure it is located conveniently	Efficiency and reduce risk of spillage or contamination

BCG Instillation Procedure	
Procedure	**Rationale**
Place protective sheet under penis and above scrotum, or in females tuck it around the labia	To prevent skin contamination in case of spillage
Wash hands and don protective equipment	To maintain sterility and to protect yourself from cytotoxic contamination
Prepare sterile field and equipment	
Place sterile guard on top of protective sheet	To maintain sterility
Clean genital area with skin preparation e.g. chlorhexidine/normal saline	Decrease risk of infection
Instil lignocaine/lubricating gel and wait before proceeding with catheterisation	Increase patient tolerability of treatment
Insert intermittent catheter, or indwelling catheter if plan is to leave it in situ for treatment Follow your local catheterisation policy	Maintain aseptic technique to decrease risk of infection
Ensure catheter is within bladder and drain all urine	To improve medication efficacy
Observe for evidence of haematuria If signs of traumatic catheterisation present then remove catheter and abandon treatment	Traumatic catheterisation increases the risk of systemic absorption
Attach the medication container to the end of catheter according to manufacturer instructions and slowly instil medication; DO NOT USE FORCE If painful you should STOP IMMEDIATELY	Slow instillation allows you to observe patient for discomfort that could be bladder spasm or potential extravasation
Dependant on patient requirements either: - Remove catheter carefully OR - Leave catheter in situ and clamped After instillation spigot, an incontinence pad and net pads can be fitted to prevent major spillage	Movement is encouraged to help to distribute the intra-vesical agent throughout the bladder

Procedure	Rationale
If any leakage occurs wash thoroughly with solution or soap and water	To prevent contamination of skin
Dispose of contaminated waste in a hazardous bag according to local policy	To prevent environmental contamination
Environmental spills should be treated as per local policy	Prevent injury from spillage Refer to local cytotoxic policy; spill kit should be available at all times Warn colleagues of potential for contamination
Ensure the patient is aware of the length of time the BCG needs to remain in the bladder	Patient may mobilise in the department Some allow the patient to go home at this point and void there Patient must never forcibly retain BCG solution as this can lead to systemic side effects
Encourage patient to drink 400mL of water half an hour before designated time to void or drain IDC	
Two hours following instillation (or time tolerated preferably minimum of 1 hour)	
Encourage to void sitting down on a designated toilet and advise following every void over first six hours, pour two cups of undiluted bleach into toilet and leave for 15-20 minutes then flush Advise patient to wash the genital area well with soap and water after voiding	Prevent contamination
Document administration on drug chart in patient record	Provides accurate documentation, continuity of treatment
Encourage patient to drink 2-3L/24hrs for one week and avoid tea, coffee, alcohol and cola drinks as they may increase bladder irritation	To avoid irritation in urinary bladder
Ensure patient knows how to seek advice for any unexpected symptoms to allow timely treatment	To promote timely intervention

Procedure	Rationale
Urine samples should not be sent to a laboratory in the next 72hrs unless urgent Any samples must be clearly marked as infectious and caution needs to be taken by laboratory staff to prevent contamination	Prevent potential contamination in laboratory services
Before the patient leaves make sure he/she is aware of their ongoing treatment plan	Ensure continuity of treatment
Patients with catheter left in situ following BCG instillation	
If the catheter has been left in for the treatment period, spigot for two hours An incontinence pad and net pads can be fitted to prevent major spillage After two hours remove spigot and empty urine into drainage bag. Remove catheter and proceed with instructions in above section, or apply leg bag if catheter is to remain in place Dispose of all equipment into hazardous waste rubbish bag as per local policy	To prevent spillage or contamination

***This guideline has been developed from information in the following documents: ADHB, 2012, BAUN, 2011, WA Cancer and Palliative Care Network 2010, EAUN, 2015, WDHB, 2010, SUNA, 2017*

Common Side Effects of Intra-vesical immunotherapy

Common Symptoms	Nursing Management
Cystitis, dysuria	Encouraged oral fluids (if not contraindicated) Regular simple analgesia Suggest decrease caffeine intake Urinary alkaliser
Lower urinary tract symptoms Frequency, urgency	Full ward test urine Increase oral intake Assess post void residual Consider anti-cholinergic if not contraindicated Discussion with consultant to consider Dose reduction, withhold treatment for a week Reduced dwell time Short course of antibiotics NB This management may have potential reduction of efficacy
Haematuria	Increase oral fluids Exclude UTI Discuss with consultant Omit treatment
Flu like symptoms	Regular paracetamol Increase oral fluids
Fever	Regular paracetamol Increase fluids Seek medical advice if >24 hours
Common Symptoms	**Nursing Management**

Urinary Tract Infection	MSU for culture and sensitivity Inform Consultant Treat UTI as appropriate Frequently used antibiotics include: Fluoroquinolones, macrolides, tetracyclines and aminoglycosides are contraindicated and can render the BCG ineffective GPs need to be informed of this potential problem
Granulomatous prostatitis Epididymo-orchitis	Seek medical advice May require antibiotics STOP treatment
Arthralgia/ arthritis Joint pain/ vomiting	Seek medical advice

Note: Table modified from EAUNS guidelines 2015 pg.42 & BAUN 2011 pg. 17

Management of spillage/contamination

Prevention of spills should be a priority when administering BCG. If contact does occur with the patient's skin, immediately place an absorbent cloth over the area then wash immediately with soap and water. Place the cloth in a hazardous waste bag.

Chemotherapy spill kit should be available at all times and contain protective clothing (long sleeved gown, overshoes, goggles, gloves, and absorbent pads/granules, bleach).

All clinical equipment should be disposed of according to the local hazardous waste policy including heavily contaminated linen, gowns etc.

Contamination of:

Skin: Mop up excess with absorbent pad, irrigate with sodium chloride 0.9%, and wash with soap and water, report the incident according to local policy

Eyes/mucous membranes: Irrigate with copious amounts of sodium chloride 0.9%, remove contacts prior to irrigation if wearing them, and seek medical advice, report incident according to local policy

Ingestion: Seek immediate medical advice

Linen: Change immediately and launder as soiled linen

Clothes: Remove immediately and deal with skin contamination then wash clothes on hot cycle in dilute bleach solution

BCG/Interferon Combination Therapy

Indications

- Patients who are at high risk of disease recurrence and/or progression after failing BCG treatment
- Patients who are BCG intolerant or refractory
- Patients where BCG alone is inappropriate due to co-morbidities and is unfit for or refuse cystectomy

Method of Action

- Treatment interferes with cancer cells and stops growth and division
- Stimulates the immune system by encouraging killer T cells and other cells to attack cancer cells
- Encourages cancer cells to send out chemicals that attract immune system cells to them

Treatment

- Six-week induction course of Interferon alpha 2b plus reduced dose of BCG followed by maintenance doses at three, six and twelve month intervals
- Instillation and instructions are same as for BCG although because Interferon is water-soluble patients are advised only to drink as their thirst dictates in the first 24 hours

Side Effects Similar to BCG although patients get more flu-like symptoms, especially joint pain. (ADHB)

Further Reading: The Journal of Urology Vol 166, Issue 4, October 2001, Pages 1300 – 1305

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Edited by Trish White, Nurse Practitioner, Hawkes Bay, New Zealand

Peer review
Jean Bothwell, Clinical Nurse Specialist, Urology Waitemata District Health Board, Auckland, New Zealand

Melinda Fieldsend, Urology Nurse Practitioner (Candidate), Urology & Continence Department Mater Health Services, South Brisbane, Queensland, Australia

Marco Hake, Clinical Nurse Consultant Urology/ Continence/ Stomal Therapy
WACHS-Great Southern Health Service, Albany Hospital, Western Australia

Marianne Lyon, BCG Nurse Specialist & Clinic Nurse, OneSixOne Medical Group, Auckland, New Zealand

Billy Allan, Chief Pharmacist, Hawke's Bay District Health Board, Hastings, New Zealand

Jeff Albaugh, USA

Lucinda Poulton, President of British Association of Urological Nurses (BAUN)

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Edited by Kath Schubach, Urology Nurse Practitioner, Victoria, Australia

Peer Review
Gregory Bock, Urology Cancer Nurse Coordinator, WA Cancer and Palliative Care Network, Australia;

Erica Botha, Urology Clinical Nurse Consultant, Fiona Stanley Hospital, WA, Australia;

Cynthia Hawks, Clinical Nurse, Fiona Stanley Hospital, WA, Australia;

Michelle Walsh, Clinical Nurse, Day Medical Procedure Unit, Fiona Stanley Hospital, WA, Australia;

Victorian Urological Nurses, Bladder Cancer Special Interest Group, VIC Australia;

Andrea Nixon, President ANZUNS, New Zealand;

Trish White, Nurse Practitioner, Hawkes Bay, New Zealand;

Karina So, Urology Clinical Nurse Consultant, Concorde Hospital, Sydney, Australia;

Michelle Roberts, Urology Clinical Nurse Consultant, Mater Private Hospital, QLD, Australia;

Anne Woollett, Clinical Trials Project Manager, ANZUP Cancer Trials Group, Sydney, Australia;

Acknowledgement of reviewers, continued

Professor Dickon Hayne MBBS MD FRCS (Eng) FRCS (Urol)
Professor of Urology, UWA Medical School, University of Western Australia
Head of Urology, Fiona Stanley Hospital
Lead Clinician, Urology Tumour Collaborative, WACPCN
Chair, Bladder Cancer Subcommittee, Member Scientific Advisory Committee, ANZUP Cancer Trials Group

Professor Shomik Sengupta FRCS (Urol)
Leader, Genitourinary Oncology Special Advisory Group, USANZ
Board Director, Bladder Subcommittee Deputy-Chair, Member Scientific Advisory Committee, ANZUP Cancer Trials Group
Honorary Clinical Associate Professor, Austin Dept of Surgery, The University of Melbourne
Executive Committee member & Urologic Cancer Committee Chair, Clinicians Network, Cancer Council Victoria

Associate Professor Peter Grimison
Staff Specialist Medical Oncology, Chris O'Brien Lifehouse, Camperdown NSW
Visiting Medical Officer at Royal Prince Alfred and Dubbo Base Hospitals
Clinical Associate Professor, University of Sydney
Member, Australian Government Pharmaceutical Benefits Advisory Committee
Chair, Germ Cell Cancer Subcommittee, Member Scientific Advisory Committee, ANZUP Cancer Trials Group

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Appendix 1

Drugs commonly used for intra-vesical chemotherapy in Australia and New Zealand.

Information obtained from both New Zealand and Australian licensing agencies – Medsafe in New Zealand and the Therapeutic Goods Administration in Australia.

The recommended dosages are the manufacturer's instructions. Dose may vary according to local policy.

Mitomycin

Action: Mitomycin is an antibiotic isolated from the broth of Streptomyces caespitosus, which has been shown to have anti-tumour activity.

Dosage: For the treatment of bladder tumours the reconstituted 40mg dose is further diluted to 40mL (this may vary amongst institutions, common dose usually 30mg-40mg in 40 mls) with sterile water for injection and immediately instilled directly into the bladder via a catheter and retained in the bladder as long as possible, preferably two hours. This can be given as either a single post-operative dose or weekly dose for six weeks according to local policy.

Specific Recommendations: Watch for the following potential side effects: Genitourinary irritation, including dysuria, cystitis, nocturia, increased frequency of micturition, haematuria, and other symptoms of local irritation, rash and pruritus on hands and genital area. Reports of bladder fibrosis/contraction, which in rare cases have required cystectomy, have been received post marketing. Bladder necrosis and penile necrosis have been reported following intravesical administration. *(Omegapharma 2016)*
This drug is light sensitive and only stable for 24 hours.

Mitomycin consumer medication information:

https://www.nps.org.au/medical-info/medicine-finder/Mitomycin-omegapharm-powder-for-infusion

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2016-CMI-01767-1&d=2018012916114622483

Epirubicin

Action: The mechanism of action of epirubicin hydrochloride has not been fully elucidated but is probably related to its ability to bind DNA. Cell culture studies have shown cell penetration, localisation in the nucleus and inhibition of nucleic acid synthesis and mitosis. In bladder cancer, Epirubicin is indicated in the prophylaxis of recurrence after transurethral resection of stage T1 papillary cancers and stage Ta multifocal papillary cancers (Grade 2 and 3).

Dosage: For the treatment of papillary transitional cell carcinoma of the bladder, a therapy of 8 weekly instillations of 50 mg (in 25 to 50mL of saline solution) is recommended. In the case of local toxicity (chemical cystitis) a dose reduction up to 30 mg is advised. For carcinoma *in situ*, depending on the individual tolerability of the patient, the dose may be increased up to 80 mg.

For prophylaxis of recurrences after transurethral resection of superficial tumours, 4 weekly administrations of 50 mg followed by 11 monthly instillations at the same dosage are recommended.

Specific Recommendations: Generally, the instillate should be retained in the bladder for one hour. To avoid undue dilution with the urine, the patient should be instructed not to drink any fluid in the twelve hours prior to instillation.

Contraindications for intravesical use are:

- Invasive tumours that have penetrated the bladder wall,
- Urinary infections,
- Inflammation of the bladder,
- Catheterisation problems

(Hospira , 2011)

Epirubicin hydrochloride consumer medication information:

http://www.nps.org.au/medical-info/medicine-finder/epirubicin-actavis

Doxorubicin

Action: Doxorubicin is an anti-euplastic antibiotic, which may act by forming a stable complex with DNA and interfering with the synthesis of nucleic acids. Doxorubicin administered intravesically can be used for the treatment of superficial bladder tumours or as prophylaxis to reduce recurrence after trans-urethral resection.

Dosage: The recommended doxorubicin dose for topical intra-vesical treatment of superficial bladder cancer is 30 to 50 mg in 25 – 50mL of saline solution per instillation, with the optimal concentration being in the 1.0 mg/mL range. In the case of local toxicity (chemical cystitis), the dose should be instilled in 50-100 ml of saline solution.

Specific recommendations: Generally, the instillation should be retained in the bladder for 1-2 hours. To avoid undue dilution with urine, the patients should be instructed not to drink any fluid in the twelve hours prior to instillation (this should limit urine production to approximately 50 ml/hour). The patient should be instructed to void at the end of the instillation. Instillations can be repeated at intervals, which can vary from one week to one month, depending on whether the treatment is therapeutic or prophylactic. The systemic absorption of doxorubicin following intra-vesical instillation is very low.

Contraindications for intra-vesical use are:

- Invasive tumours that have penetrated the bladder wall;
- Urinary infections;
- Inflammation of the bladder;
- Catheterisation problems (e.g. due to massive intra-vesical tumours).
- Hematuria

(Pfizer, NZ. 2011)

Doxorubicin consumer medication information:
http://www.nps.org.au/__data/assets/pdf_file/0015/16116/pfcadrii10707.pdf

Gemcitabine

Action: Gemcitabine is a pyrimidine analog that blocks the synthesis of nucleotides and disrupts the synthesis or function of DNA and RNA. It has an anti tumour activity on the cells acting on the specific cell cycle phase (Bullock & Manias).

Dosage: The recommended gemcitabine dose for intravesical treatment of superficial bladder cancer is 2000mg in 50 – 100mL of saline solution per instillation. Induction dose is given weekly for six weeks with a dwell time of 1-2 hours. A maintenance dose is given monthly for ten months. Common side effects are chemical cysistitis and dysuria.

Specific recommendations: Gemcitabine is used in patients that have failed BCG therapy or patients that have had recurrent superficial bladder cancer.

Contraindications for intravesical use are:

- Invasive tumours that have penetrated the bladder wall;
- Urinary infections;
- Inflammation of the bladder;
- Catheterisation problems (e.g. due to massive intravesical tumours)
- Hematuria

http://www.auspharmacist.net.au, retrieved June 2017
http://www.bccancer.bc/cadrug-database-site/Drug%20, retrieved June 2017

Appendix 2

Drugs commonly used for intravesical immunotherapy in Australia and New Zealand

Bacillus Calmette-Guerin (BCG)

Action: It is a freeze dried preparation of an attenuated strain of *Mycobacterium bovis.* When administered into the bladder as a cancer therapy, BCG promotes a local acute inflammatory and sub-acute granulomatous reaction with macrophage and leukocyte infiltration in the urothelium and lamina propria of the urinary bladder. The local inflammatory effects are associated with an elimination or reduction of non-muscle invasive cancerous lesions of the urinary bladder. The exact mechanism of action is unknown.

Contraindications:

- Known allergy
- 14 days since TURBT or traumatic catheterisation
- Traumatic catheterisations
- Haematuria in previous 24 hours prior to instillation
- Immunosuppressed patients should not receive as risk of systemic infection
- Congenital or acquired immune deficiencies, (whether due to a concurrent disease such as acquired immune deficiency, leukaemia, lymphoma) or immunosuppressive therapy e.g. corticosteroids, cancer
- Therapy (cytotoxic drugs, radiation, etc) because of the risk of disseminated BCG infection
- Patients with urinary tract infection should not receive BCG
- If patient has a fever, cause should be found and treated prior to administration of BCG
- Patients with active tuberculosis should not receive BCG

http://www.ebs.tga.gov.au, retrieved June 2017
(Merck Sharp & Dohme (NZ) Ltd, 2016)

Appendix 3

BCG Shortage

In 2014 there was a worldwide shortage of BCG and USANZ issued the following guidelines in response, they may be useful in case of future shortages of BCG.

GUIDELINES FOR THE MANAGEMENT OF UROTHELIAL CARCINOMA OF THE BLADDER DURING A SUPPLY SHORTAGE OF BCG FOR INTRAVESICAL USE

Management decisions will need to be individualised for each patient, depending on factors such as age, general health, tumour characteristics, previous treatment & responses and patient preferences.

Thorough counselling of patients is essential, especially if potentially sub-optimal management being used.

If there is a LIMITED supply of BCG (Bacillus Calmette-Guérin): prioritise which patients receive the available BCG;

- Patients with primary CIS as highest priority (alternative intravesical therapy being inferior to BCG);
- Patients enrolled on the BCG-MMC trial
- Patients with high-grade &/or T1 disease OVER those with multiple or recurrent low-grade Ta disease, (induction rather than maintenance – consider using intravesical chemotherapy for maintenance, although data limited); maximise the number of patients who can be treated;
- Half or third dose treatment if practically feasible (vials may only be utilised on same day);
- Utilise intravesical chemotherapy, early cystectomy or close observation with periodic cystoscopy and resection as alternatives (as detailed below) as required.

If there is NO availability of BCG:

- Utilise intravesical chemotherapy as an alternative (equivalent efficacy for papillary disease in terms of progression & survival, not as effective in reducing recurrence or in the treatment of primary CIS) where possible;
- Consider close observation with periodic cystoscopy and resection (maybe appropriate for frail or elderly patients, less aggressive disease, lack of prior treatment failure);
- Consider radical treatment by early cystectomy or chemo-radiation (maybe appropriate for younger patients, high-grade &/or T1 disease, prior failed BCG therapy).

Acknowledgements: Approach for Consideration to Address Shortage of Bacillus Calmette-Guérin (BCG) | Bladder Cancer Canada 2014. Available at: http://bladdercancercanada.org/en/news/approach-for-consideration-to-address-shortage-of- bacillus-calmette-guerin.

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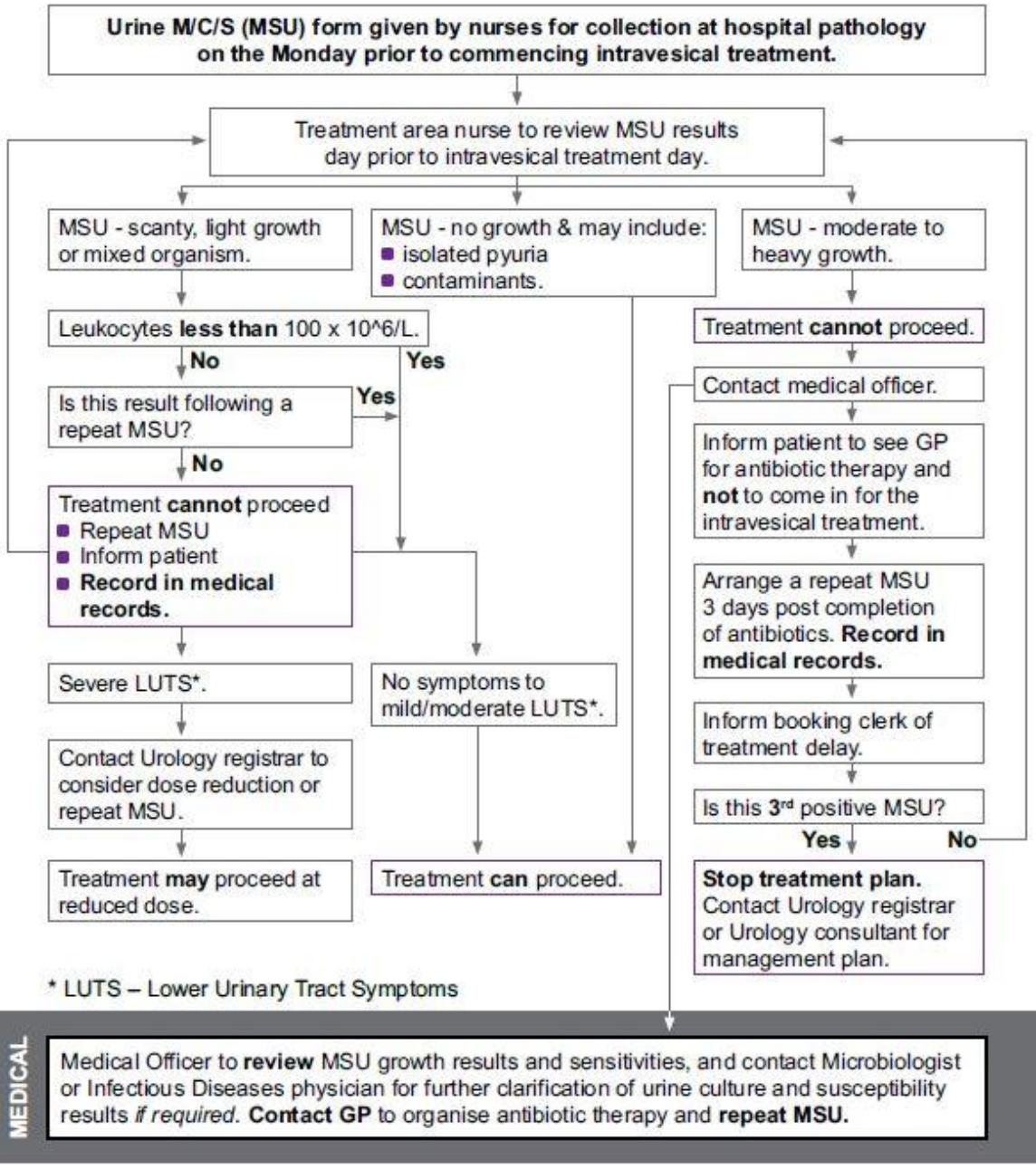
Appendix 4 WA Cancer and Palliative Care Network, (2010). Reproduced with permission from WA Cancer & Palliative Care Network, Government of Western Australia Department of Health

Government of **Western Australia**
Department of **Health**
WA Cancer and Palliative Care Network

Intravesical treatment clearance to proceed algorithm



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Appendix 5

One Six One Medical Group

BCG Interferon Protocol

Policy for BCG+Interferon alpha-2b Use

Prior BCG Failure-non-tolerant

INDUCTION

6 weeks 1/3 strength BCG+Interferon alpha-2b 50mu
Reduce to 1/10th BCG for Symptoms if needed

↓

Cysto+Cytology at 6 weeks after last treatment

↓ **6 WEEKS**

Maintenance Cycle ❶
1/3 BCG+50mu Interferon alpha-2b x 1
1/10 BCG +50 mu Interferon alpha -2b x 2
***(Weekly treatment)**

↓

Cysto+cytology 6 weeks after treatment

↓

Cysto+Cytology 3 months from Prior cysto

↓**6 Months from last Instillation**

Maintenance Cycle ❷
1/3 BCG+50mu Interferon x1
1/10 BCG + 50mu Interferon x2
***(Weekly treatment)**

↓

Cysto+Cytology at 6 weeks at 6 weeks after last treatment

↓

Cysto+Cytology at 3 months prior Cystoscopy

↓**6 Months from last Instillation**

Maintenance Cycle ❸
1/3 BCG+50mu Interferon x1
1/10 BCG + 50mu Interferon x2
***(Weekly treatment)**

↓

Cysto+Cytology at 3,6,9 months from Prior cysto

↓

Observe Cytology at 6-12 months

*Futher dose reduction to 1/10,1/100 and 1 week delays permitted for severe symptoms.