



Government of **Western Australia**
Department of **Health**

Guidelines for the administration of intravesical cytotoxic and immunotherapeutic drugs within the hospital setting

These guidelines for practice have been produced by the
WA Cancer and Palliative Care Network November 2010



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Suggested citation:

Department of Health, Western Australia. Guidelines for the administration of intravesical cytotoxic and immunotherapeutic drugs within the hospital setting. Perth: Health Networks Branch, Department of Health, Western Australia; 2010.

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This package has been developed by the WA Cancer and Palliative Care Network Urology Tumour Collaborative

The local implementation, training and evaluation of clinical staff remains the responsibility of the employing authority.

Date produced: November 2007

Date first reviewed: May 2008

Date reviewed: November 2010

Date for next review: November 2012

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Legislative Requirements

This policy applies to registered nurses and medical practitioners who have been trained and assessed as competent in delivering intravesical bladder cancer treatment.

The patient's treating clinician prior to commencement of any treatment should obtain informed verbal consent. This will be reinforced by the administering practitioner prior to commencing treatment.

Medical Requirements

Intravesical chemotherapy and immunotherapy can be used in the treatment of non-muscle invasive bladder cancer either:

1. As an ablative therapy for the treatment of carcinoma in situ
2. As an adjuvant therapy to reduce the recurrence rates of non-muscle invasive bladder tumours.

The most commonly used agents are BCG (Bacillus Calmette-Guérin) and Mitomycin C. It is theorised that BCG stimulates an inflammatory response that promotes malignant cell kill by immunocompetent cells. Mitomycin C, on the other hand, inhibits the synthesis of DNA.

This treatment is given to patients with non-muscle invasive bladder tumours.

Urine Cultures

Urine culture is required within the week prior to administration. If the urine has a positive culture, the treatment will be suspended and the patients will be prescribed the appropriate antibiotic.

Patients having intravesical therapy should have urine culture collected and reviewed prior to commencement of treatment.

Information regarding administration of Mitomycin C in the presence of a urinary infection is limited and is therefore a clinical decision to proceed.

In patients having BCG therapy, if urine microscopy subsequently identifies either

- Leukocytes $>100 \times 10^6/L$.
- Bacteria growth or a specific organism identified.

Or if the patient has macroscopic haematuria, then treatment should be deferred until clearance is achieved. Should there be any concerns with interpreting urine culture results then the microbiologist is to be consulted.

Coupled with a urinary tract infection, BCG not only can induce BCG cystitis but also can cause more severe adverse genitourinary tract effects. Antibiotics can also diminish BCG efficacy as BCG bacilli are sensitive to a wide range of antibiotics.

Side Effects

Ensure potential side effects are explained to and understood by the patient. Both agents may cause a chemical cystitis resulting in frequency, dysuria and occasional mild haematuria. These symptoms usually subside within 24 to 48 hours. Persistent symptoms may indicate a urinary tract infection and should be investigated. Any patients who develop persistent side effects should be discussed with the patient's treating Urologist prior to receiving any further treatments. BCG sepsis is an infrequently occurring, but potentially fatal effect from BCG treatment. This is discussed in further detail below.

BCG contraindications and considerations

Intravesical BCG should not be administered for the following reasons:

- within 14 days of bladder surgery
- following traumatic catheterisation
- if the patient has visible haematuria
- if pregnant or lactating
- if suffering from active TB (Tuberculosis)
- if currently taking immunosuppressants and/or bone marrow suppressants and/or radiotherapy treatment
- in the presence of a urine infection
- any previous allergies or adverse reactions to BCG.

Any patient having BCG treatment carries a small but potentially fatal risk of developing BCG sepsis. Any patients who are suspected of developing BCG sepsis should be investigated and treated as follows:

1. The patient should be admitted into hospital and blood cultures taken for BCG.
2. If BCG sepsis is suspected anti-tuberculosis therapy should be commenced in consultation with a microbiologist or physician.
3. The patient would not necessarily need transferring to a tertiary centre from a rural centre, but advice should be sought from an infectious disease physician.

Intravesical BCG is a live, attenuated mycobacteria and therefore has the potential risk for transmission. The preparation, handling and disposal should bring with it the same precautions of other biohazardous materials. It is recommended that the BCG agent be reconstituted and prepared in a certified biological cabinet, and used within 2 hours of making. When a biological cabinet is not available for the mixing of BCG, a closed system reconstitution kit should be used to eliminate the risk of aerosol exposure. The use of a closed system should adhere to the manufacturer's specific instructions.

Mitomycin contraindications and considerations

Intravesical Mitomycin C should not be administered for the following reasons:

- within 14 days of bladder surgery if bladder perforation was sustained.
- history of hypersensitivity or idiosyncratic reaction to Mitomycin
- if the patient is thrombocytopenic
- if the patient has coagulation disorders or an increase in tendency to bleed related to other causes
- any previous allergies or adverse reactions to Mitomycin.

Mitomycin C can be absorbed through the bladder mucosa and may rarely cause depression of the peripheral blood count. If the patient is unwell their full blood count should be checked to ensure the blood cell count is within normal limits.

Mitomycin C is a vesicant and therefore it is recommended that it is reconstituted and prepared in a cytotoxic class 2 or 3 cabinet. The preparation, handling and disposal should bring with it the same precautions of other cytotoxic materials. Refer to manufacturer's full prescribing information for storage. Where a closed system is used for reconstitution and dilution, adhere to manufacturer's specific instructions.

Both single instillations and courses of intravesical agents are to be prescribed in the appropriate section of the medication chart on an as required basis. Requests for dispensing of these medications should be made to the hospital pharmacy no later than ONE WEEK prior to date required allowing adequate time for ordering and drug preparation.

Safety Information

Any practitioner who is intending to give intravesical treatment requires appropriate training and assessment. This assessment includes both a theoretical and practical component. All practitioners are to be able to demonstrate a thorough understanding of non-muscle invasive bladder cancer, associated health and safety issues regarding handling of cytotoxic and immunotherapeutic agents as well demonstrating safe practical skills relating to their administration.

Nurses, who are already certified as competent to administer chemotherapy but are unfamiliar with intravesical treatments, should complete the self directed learning package prior to undertaking any clinical practice. This is available as a separate WA Cancer and Palliative Care Network document.

All nurses administering intravesical cytotoxic drugs should be annually assessed and their assessor should record this as part of their performance management.

All clinical areas which are to be administering or caring for patients who have received intravesical chemotherapy / immunotherapy should be in possession of, and be competent to use a cytotoxic drug spillage kit. Spills should be reported in accordance to local hospital policy.

Protective clothing and gloves are to be worn by all personnel handling or administering cytotoxic substances. Avoid contact of cytotoxic drugs with the eyes and skin as they can

cause severe damage. Extra care should be taken therefore when reconstituting, diluting, administering and disposing of these drugs. ALL personnel handling the cytotoxic drugs should wear gloves, aprons and eye protection. These should be disposed of into 2 CYTOTOXIC waste bags sealed with adhesive tape or bag ties following completion of the intervention along with any other materials used in the treatment process. Two waste bags are used in case of leakage. This should be disposed of in accordance to local hospital policy.

Patients having this treatment should be nursed in areas which have a designated toilet which can be isolated from use by others for the duration of the treatment.

Nursing Management

All patients (and their carers, where appropriate) should be provided with the opportunity to discuss all aspects of the treatment prior to commencement of therapy and be provided with written information. Patients should be aware of all potential side effects including when and how to seek medical advice in order to have these side effects investigated and managed.

Where patients are prescribed diuretics as part of their regular medications, the need to withhold these must be verified with the patient's Urologist, as this is a patient specific issue.

All medication should be checked prior to administration paying specific attention to the following details:

- ensure the medication dispensed and dosage correlates with that written on the patient's prescription sheet
- date and time of expiry
- date and time the treatment is to be given
- patient's name, address, hospital number and date of birth.
- allergies to medication and other substances.

It is advisable for patients to refrain from drinking tea and coffee prior to treatment due to their diuretic effect, and also to reduce the volume of fluid intake for 4 hours prior to the delivery of the treatment to prevent dilution and improve tolerance. It is not necessary to fast for this treatment.

Procedural Information

Part A) Procedure for the instillation of a single post operative dose of intravesical chemotherapy agent

Patients should receive the single agent instillation ideally within 6 hours surgery but not exceeding 24 hours post TURBT procedure. Mitomycin treatment can be given to patients who have haematuria (providing there are no clots). It is the responsibility of the nurse administering the treatment to check with the patient's treating clinician if they are unsure whether or not to proceed with the treatment due the haematuria.

Procedure requirements:

1. Personal protective equipment
2. 1 plastic backed protective sheets
3. Medication as charted
4. 2 cytotoxic waste bags
5. "Cytotoxic" label
6. Cytotoxic spillage kit
7. Flip-flo catheter valve or 2 catheter clamps
8. Plastic draw sheet and linen draw sheet
9. Plastic jug
10. Bicarbonate of Soda solution (8.4%).
11. 2 Cytotoxic waste bags
12. Adhesive tape or bag ties.

Administration procedure:

A catheter is already insitu in patients who are having this treatment post operatively. These patients have been identified as the largest group of patients who are at risk of spillage, these guidelines minimise the risk of spillage / contamination.

1. Assess for pain prior to commencing. It may be advisable to give antispasmodic medication 20 minutes prior to instillation post surgery as this may assist the patient's tolerance to the drug, for example, buscopan or oxybutinin.
2. Assemble equipment on trolley.
3. Place both plastic and linen draw sheet underneath patient's buttocks.
4. Switch off bladder washout but don't dispose of it.
5. Empty catheter bag and update fluid balance chart.
6. A plastic backed sheet should be placed under the catheter connection and across the patient to prevent the spillage of any chemotherapy onto the patient or bedding if there is a leak.

- 7a. **If flip-flo catheter valves are available:** Disconnect catheter from drainage bag. Attach the flip-flo catheter valve to the catheter. Attach the Mitomycin container to the end of the flip-flo valve. Open the valve and the drug is then introduced. The catheter should be left in situ and the flip-flo valve closed with the Mitomycin container attached. This ensures a closed circuit and avoids spillage whilst the patient retains the treatment.
- 7b. **Alternative, if flip-flo catheter valves are not available:** Attach catheter clamps. Disconnect catheter from drainage bag. Attach the Mitomycin container to the end of the catheter and remove clamps. The drug is then introduced and the catheter is re clamped. The clamped catheter should be left in situ with the Mitomycin container attached. This ensures a closed circuit and avoids spillage whilst the patient retains the treatment.
8. All efforts should be made to ensure the cytotoxic drug does not come into contact with the skin, clothing or other surfaces. Should the Mitomycin come into contact with the patient's skin at the time of administration, the skin should be washed down with Bicarbonate of Soda solution (8.4%). For other spillages, an absorbent cloth should be placed over the spillage, which is then disposed of into the cytotoxic waste bag. The area should then be washed thoroughly with copious amounts of soap and water.
9. Following insertion of intravesical chemo -therapeutic agents, the patient should lie prone for 15 minutes and should then be allowed to move freely to ensure the drug has the opportunity to bathe all parts of the bladder mucosa. The drug needs to remain in the patient's bladder for at least 1 hour (to a maximum of 2 hours).
10. Following completion of the treatment, the Mitomycin should be drained from the patient's bladder, by attaching a catheter drainage bag, opening up the flip-flo valve or removing clamps, and allowing the Mitomycin to drain into the sealed bag. The bladder irrigation can then be recommenced if requested by the treating clinician.
11. The catheter drainage bag should be clearly labelled with a 'cytotoxic' label to ensure other staff members are aware of the potential contamination risk.
12. The nurse should always check with the patient's treating clinician prior to removing the patient's catheter following treatment. If appropriate, the patient's catheter can then be removed at this stage. This ensures containment of the waste products, which can then be disposed of.
13. ANY clinical equipment, which has come into contact with cytotoxic material, should be disposed of into 2 cytotoxic waste bags, labelled and secured closed with cytotoxic tape and disposed of in accordance with local hospital policy.
14. Caution is to be exercised when handling urine in the 6 hours following treatment. The toilet should be flushed twice. The patient and his carers should also be made aware of the need to exercise caution and the reason for this.
15. The patient should be encouraged to drink 2-3 litres of fluid for the first 24 hours following treatment to encourage elimination of absorbed drugs.
16. Urine samples should not routinely be sent to the laboratory within 72 hours of treatment. If necessary, the specimen should be clearly labelled. Caution should be taken with samples as these could potentially be contaminated. It is not necessary to use these precautions for other samples, as the treatment is local and so should not be present in any other system.

Part B) Procedure for the instillation of a course of intravesical chemotherapeutic / immunotherapeutic agents using pre mixed medication

Procedure requirements:

1. Personal protective equipment
2. 1 plastic backed protective sheets
3. Medication as charted
4. 2 cytotoxic waste bags for disposal of clinical waste
5. "Cytotoxic" label and tape
6. Cytotoxic spillage kit
7. Urethral catheter
8. Standard equipment required for insertion of a urethral catheter
9. Plastic draw sheet and linen draw sheet
10. Bicarbonate of Soda solution (8.4%) – for patients having Mitomycin
11. Bleach – for patients having BCG treatment.

Administration procedure:

1. Assemble equipment on trolley as above.
2. Place both plastic and linen draw sheet underneath patient's buttocks.
3. Insert urethral catheter as per policy and drain bladder.
4. A plastic backed sheet should be placed under the catheter connection and across the patient to prevent the spillage of any chemotherapy or BCG onto the patient or bedding if there is a leak.
5. Attach the Mitomycin / BCG container to the catheter.
6. Insert drug.
7. Remove catheter carefully and advise the patient they are to retain liquid in bladder for up to two hours following instillation.
8. All efforts should be made to ensure the intravesical drugs do not come into contact with the skin, clothing or other surfaces. Should the Mitomycin come into contact with the patient's skin at the time of administration, the skin should be washed down with Bicarbonate of Soda solution (8.4%). For other spillages, including BCG, an absorbent cloth should be placed over the spillage, which is then disposed of into the cytotoxic waste bag. The area should then be washed thoroughly with copious amounts of soap and water.
9. Following insertion of intravesical therapeutic agents, the patient should lie prone for 15 minutes and should then be allowed to move freely to ensure the drug has the opportunity to bathe all parts of the bladder mucosa. The drug needs to remain in the patient's bladder for at least 1 hour (to a maximum of 2 hours).

10. ANY clinical equipment, which has come into contact with cytotoxic material, should be disposed of into 2 cytotoxic waste bags, labelled and secured closed with cytotoxic tape and disposed of in the clinical waste for incineration.
11. Following completion of the treatment, the patient should be advised to void into the designated toilet.
12. For patients who have been given BCG. The toilet should not be flushed. Two cups of bleach should be poured into the toilet bowl and left for 20 minutes prior to flushing. Patients should be advised to continue to use bleach in the toilet bowl with each void for 6 hours following treatment.
13. Bleach is NOT required for patients who have had Mitomycin however there will be traces of Mitomycin in the urine for up to six hours following treatment. Caution is to be exercised when handling urine in the 6 hours following treatment. The toilet should be flushed twice. The patient and their carers should also be made aware of the need to exercise caution and the reason for this.
14. The patient should be encouraged to drink 2-3 litres of fluid for the first 24 hours following treatment to encourage elimination of absorbed drugs.
15. Urine samples should not routinely be sent to the laboratory within 72 hours of treatment. If necessary, the specimen should be clearly labelled. Caution should be taken with samples as these could potentially be contaminated. It is not necessary to use these precautions for other samples, as the treatment is local and so should not be present in any other system.
16. The patient should be given instructions on after care, their next appointment and contact details should they encounter any problems prior to leaving the department.

Part C) Procedure for the instillation of a course of intravesical BCG using a closed system reconstitution kit

Procedure requirements:

1. Personal protective equipment
2. 1 plastic backed protective sheets
3. Medication as charted
4. 2 cytotoxic waste bags for disposal of clinical waste
5. "Cytotoxic" label and tape
6. Cytotoxic spillage kit
7. Standard equipment required for insertion of a urethral catheter
8. Plastic draw sheet and linen draw sheet
9. Bleach
10. Foley Catheter
11. Closed system reconstitution equipment as per manufacturer's instructions.

Administration procedure:

1. Assemble equipment on trolley as above.
2. Reconstitute BCG using closed system equipment as per manufacturers' instructions. BCG should always be given within 2 hours of mixing.
3. Place both plastic and linen draw sheet underneath patient's buttocks.
4. Insert urethral catheter as per policy and drain bladder
5. A plastic backed sheet should be placed under the catheter connection and across the patient to prevent the spillage of any chemotherapy or BCG onto the patient or bedding if there is a leak.
6. Instil BCG into patient's bladder in adherence to the manufacturer's instructions for using closed system products.
7. Remove catheter carefully and advise the patient they are to retain liquid in bladder for up to two hours following instillation.
8. All efforts should be made to ensure the intravesical drugs do not come into contact with the skin, clothing or other surfaces. Should the BCG come into contact with the patient's skin at the time of administration, an absorbent cloth should be placed over the spillage, which is then disposed of into the cytotoxic waste bag. The area should then be washed thoroughly with copious amounts of soap and water.

9. Following insertion of intravesical therapeutic agents, the patient should lie prone for 15 minutes and should then be allowed to move freely to ensure the drug has the opportunity to bathe all parts of the bladder mucosa. The drug needs to remain in the patient's bladder for at least 1 hour (to a maximum of 2 hours).
10. ANY clinical equipment, which has come into contact with cytotoxic material, should be disposed of into 2 cytotoxic waste bags, labelled and secured closed with cytotoxic tape and disposed of in the clinical waste for incineration.
11. Following completion of the treatment, the patient should be advised to void into the designated toilet.
12. The toilet should not be flushed. Two cups of bleach should be poured into the toilet bowl and left for 20 minutes prior to flushing. Patients should be advised to continue to use bleach in the toilet bowl with each void for 6 hours following treatment.
13. The patient should be encouraged to drink 2-3 litres of fluid for the first 24 hours following treatment to encourage elimination of absorbed drugs.
14. Urine samples should not routinely be sent to the laboratory within 72 hours of treatment. If necessary, the specimen should be clearly labelled. Caution should be taken with samples as these could potentially be contaminated. It is not necessary to use these precautions for other samples, as the treatment is local and so should not be present in any other system.
15. The patient should be given instructions on after care, their next appointment and contact details should they encounter any problems prior to leaving the department.

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