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## CPG C6

### CLINICAL MANAGEMENT OF GENITAL WARTS

**GUIDELINE STATUS:** FINAL 14/05/2008

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## SCOPE OF PRACTICE

### TARGET POPULATION

- Clients with a presumptive clinical diagnosis of uncomplicated Human Papilloma Virus (HPV) genital warts from clinical examination
- Clients with confirmed uncomplicated genital warts

### EXCLUSION CRITERIA

- Clients who are pregnant or breast feeding requesting Aldara
- Clients with complications of infection including genital ulceration, treatment reaction, diabetes mellitus, HIV infection and other immunological conditions
- Clients with ongoing symptoms unresponsive to treatment

## GUIDELINE OBJECTIVES AND ANTICIPATED OUTCOMES

- Provide treatment for clients with genital warts
- Identification of individual STI risk and provision of appropriate screening
- Identify public health risks to control infections by:
  - Provision of STI education and information
  - Identification and exploration of sexual risk taking behaviour
  - Partner notification and treatment

## BACKGROUND

### CONDITION DESCRIPTION

Warts are benign epidermal tumors produced by the human papillomavirus (HPV) infection of the skin and mucous membranes.<sup>1,2</sup> There are around 60 different types of HPV that cause warts, each type preferring a specific skin location. The incubation period varies from 1 to 3 months and possibly up to several years.<sup>1,2,3</sup>

Warts are spread by direct or indirect contact. Impairment of the epithelial barrier function, by trauma (including mild abrasions), maceration or both, greatly predisposes the individual to inoculation of the virus, and is generally assumed to be required for infection at least in fully keratinised skin. Warts can also spread by autoinoculation. Whether a wart will develop as a result of inoculation with infected materials will depend on the amount of virus present and the immunity of the individual towards the virus.<sup>2,3,4,5</sup>

Most warts will resolve spontaneously without trace within 6 –18 months, although in some individuals warts can be present for 3 – 5 years and in a minority of clients they can persist for longer.<sup>5,6,7</sup>

**EPIDEMIOLOGY**

Up to 75% of sexually active adults may experience genital wart virus infection, commonly occurring between 18-28 years of age. Of these people 15% will develop genital warts <sup>3,4</sup> The period of inoculation and the presentation of symptoms vary with each client. Some will experience extended latency periods before presenting with symptoms. <sup>4,5,6</sup>

**SEQUELAE**

Genital warts are self limiting and usually resolve completely. Clients with anal warts may experience anal bleeding and discomfort on defecation. <sup>1,4</sup> The psychological impact of genital warts may be significant. Having genital warts may effect sexual self esteem, self confidence, sexual function and relationships. Where psychological distress is apparent, referral for counselling may be appropriate. <sup>5,7,8</sup>

**INVESTIGATIONS AND DIAGNOSTIC**

- No routine diagnostic test exists for subclinical warts
- Warts are diagnosed by visual examination





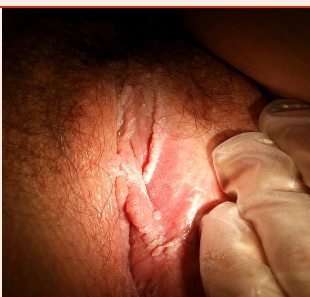
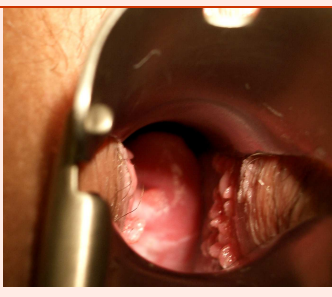
	LOCATION	CLINICAL PICTURES	
<b>PENILE</b>	<ul style="list-style-type: none"> <li>• MEATUS</li> <li>• SHAFT</li> <li>• BASE</li> <li>• SCROTUM</li> </ul>		
<b>ANAL</b>	<ul style="list-style-type: none"> <li>• INTRA ANAL</li> <li>• EXTERNAL ANAL</li> </ul>		
<b>VAGINAL</b>	<ul style="list-style-type: none"> <li>• VAGINAL WALL</li> <li>• VULVAL</li> <li>• CERVICAL</li> </ul>		

Table C6.1: Location of genital warts (Photos courtesy of MSHC)

**TREATMENT AND MANAGEMENT**

**TREATMENT INDICATORS**

- Clinical diagnosis based on examination findings
- Clients preference for treatment

**TREATMENT**

- **Cryotherapy-Liquid Nitrogen and/or**
- **Imiquimod 5% cream or**
- **Podophyllotoxin 5% cream or paint**

- All treatments have significant failure and relapse rates.
- Treatment choice depends on the morphology, number, and distribution of warts.
- Treatment may involve discomfort and local skin reactions. Written information on management of treated area and potential treatment side effects is recommended.
- Soft non-keratinised warts often respond well to podophyllin, podophyllotoxin, and imiquimod<sup>8,9,10</sup>
- Keratinised warts are better treated with ablative methods such as cryotherapy<sup>8,11</sup>
- Imiquimod may also be suitable for both types.<sup>8,10</sup>
- Clients with a small number of low volume warts irrespective of type are best treated with ablative therapy from the outset.
- Podophyllotoxin 0.5% solution for 4 week cycles and imiquimod for up to 16 weeks are suitable for home treatment by clients.<sup>8</sup>
- Non treatment is an option at any site and may apply particularly to warts in the vaginal and anal canal.<sup>3,5</sup>

## MANAGEMENT

- The choice of therapy is based on the number, size, site and morphology of the warts, as well as patient preference, treatment cost, convenience, adverse effects and provider experience<sup>4,5,6</sup>
- Recording of lesions on genital maps at each visit is useful, providing a visual record of approximate number, distribution, and response to treatment

## IMIQUIMOD

- Imiquimod is an immune response modifier available as a 5% cream. It induces a cytokine response when applied to skin infected with human papilloma virus.<sup>8,12</sup>
- It is suitable for use on all external anogenital warts,
- It is not recommended for use in pregnancy, lactation or internally.
- Use in uncircumcised men has been shown to be safe
- The cream is applied to lesions three times weekly (at night) and washed off 6-10 hours later for up to 16 weeks.
- Response to treatment may be delayed for some weeks.
- Clients should be over 18 years
- Should not be used with co-existing dermatosis or candidiasis
- Review client every 4 weeks to assess progress
- Clinical trials have shown response rates comparable with other chemical agents, but an encouragingly low relapse rate

## CRYOTHERAPY

- Liquid nitrogen is used to freeze cell membranes. On application intra circular ice forms in cells during freezing and is thought to damage intracellular mitochondria and endoplasmic reticulum.<sup>5,8</sup> The slow thawing of infected cells post treatment is associated with re-crystallisation of ice and this approach is known to be more effective than rapid thawing. An immune response to the wart virus develops in patients whose warts have been treated with several cryotherapy treatments.<sup>6,8,9</sup> Destruction of the tissue does not effect a cure unless the virus is also eradicated, so immunological response is important to viral clearance.<sup>9,10</sup> Using a liquid nitrogen spray or a cryoprobe results in cytolysis at the dermal epidermal junction resulting in necrosis.
- Treatment should be applied until a "halo" of freezing has been established a few millimeters round the treated lesion.
- A freeze, thaw, freeze technique should be used (x3 freezes per treatment)
- Cryoglobulinaemia is the only contraindication
- Cryotherapy is suitable for most warts

SIDE EFFECTS	COMPLICATIONS ASSOCIATED WITH LIQUID NITROGEN TREATMENT
Pain and Inflammation	A simple analgesia such as paracetamol is recommended if pain persists. Salt baths may provide symptom relief
Blistering	Water blisters or occasionally haemorrhagic blisters may develop within a day or two.
Pigmentary Changes	Hypopigmentation of the area treated can occur, more common in darkly pigmented clients. Hyperpigmentation can also occur. Both generally only last for a few months, but can be longer lasting.

Table C.6:2 Side effects of cryotherapy <sup>4,6,8,10</sup>

### PODOPHYLLOTOXIN

Podophyllotoxin, a purified extract of podophyllin in the form of a 0.5% solution or 0.15% cream, is suitable for home treatment <sup>8,9,12</sup>

- Treatment cycles consist of twice daily application for 3 days, followed by 4 days rest for 4 cycles. <sup>8,11</sup>
- The cream may be easier for many patients to apply, especially at the anus.
- The client should discontinue treatment if significant side effects occur.
- Podophyllin is a non-standardized cytotoxic compound. <sup>8,12</sup>
- Podophyllin should not be used for vaginal or cervical warts or areas effected by dermatitis
- Application should be limited to 10 cm<sup>2</sup> or 0.5 ml for external warts, and less than 2 cm<sup>2</sup> for vaginal warts
- Podophyllin has caused side effects if applied in excess such as ulceration and erythema. Increased systemic absorption is likely if used internally.
- The potential oncogenic and teratogenic effects indicate it should be avoided on the cervix and in the anal canal, and in pregnancy

### COMBINATION THERAPY

- Applying Podophyllin in conjunction with cryotherapy is a common practice

### SPECIAL CONSIDERATIONS

#### INTRAVAGINAL

- Cryotherapy is not recommended due to the risk of fissures <sup>11</sup>
- Regular review and referral may be required

#### URETHRAL MEATUS

- If the base of lesions are seen, treat with cryotherapy, podophyllotoxin or imiquimod. <sup>10</sup>
- Lesions deeper in the urethra should be referred to a Urologist for surgical ablation

#### INTRA-ANAL

- Treatment options include cryotherapy with visualisation under proctoscope

#### PREGNANCY

- Treatment aims to minimise the number of lesions present at delivery to reduce the neonatal exposure to virus
- Avoid podophyllin, podophyllotoxin, because of possible teratogenic effects.
- Imiquimod is not approved for use in pregnancy. <sup>12</sup>

- Potential problems for new borns include the development of laryngeal papillomatosis anogenital warts <sup>2</sup>
- Very rarely a caesarean section is indicated because of blockage of the vaginal outlet with warts or the presence of gross cervical warts <sup>2</sup>

### **IMMUNOSUPPRESSED**

- Clients with impaired cell mediated immunity for example, renal transplant patients or human immunodeficiency virus (HIV) infection, are likely to have poor treatment responses, increased relapse rates, and cervical and or anal dysplasia. <sup>8</sup>
- Careful follow up is required in all these clients

## **PUBLIC HEALTH CONSIDERATIONS - FOLLOW UP AND REVIEW**

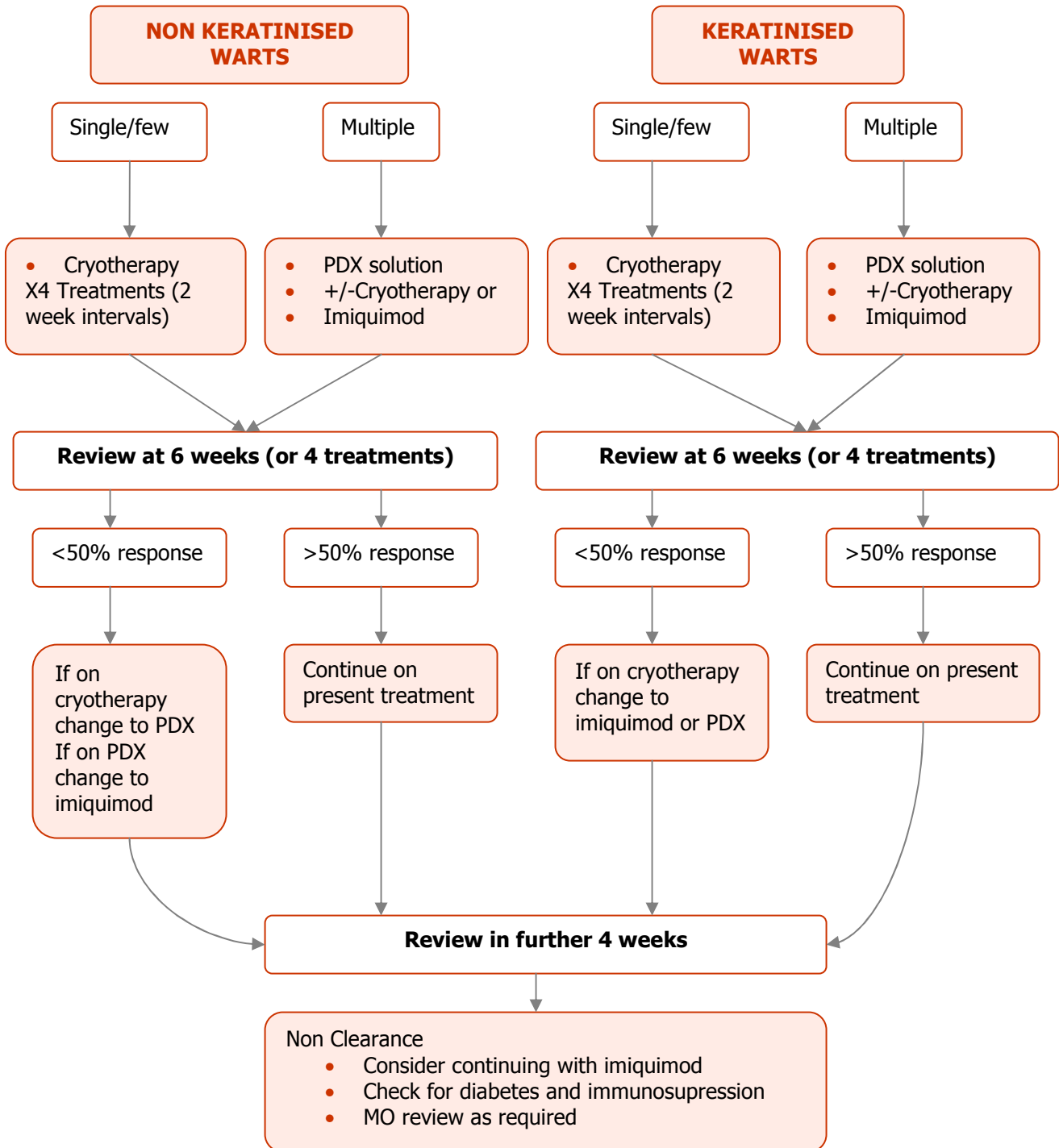
### **SEXUAL PARTNERS**

Current sexual partner(s) may benefit from assessment as they may have undetected genital warts, undetected other sexually transmitted infections, or need information and advice about disease process in their partner <sup>8</sup>

### **FOLLOW UP AND REVIEW**

- Review clients at the end of treatment cycles to monitor response and assess the need for changes in therapy. <sup>10</sup>
- Clients whose original lesions have responded well to treatment but new lesions are evolving, can continue with current regimen. <sup>10</sup>
- Change is indicated if the client is not tolerating the current treatment, or if there is under 50% response rate to current treatment. <sup>10</sup>
- Relapses should be treated as appropriate to the lesion types. <sup>9</sup>
- Tracing of previous sexual partners is not recommended. <sup>11</sup>

## CLINICAL ALGORITHM



**MEDICATION FORMULARY <sup>12</sup>**

DRUG	INDICATIONS	ROUTE	DOSE	FREQUENCY	THERAPEUTIC CLASS/ Poisons Schedule	CONTRAINDICATIONS/ INTERACTIONS	PRECAUTIONS/ ADVERSE EFFECTS
<b>Imiquimod 5%</b>	Genital warts	topical	250mg per sachet  apply 1/3 of sachet	3 times at night weekly for 4-16 weeks	Immunomodifier (B1) S4	Pregnancy, lactation hypersensitivity	Occlusive dressings Excessive use, inflammatory skin conditions, UV light, prolonged use Remove cream before sexual contact
						Nil known	Local skin reactions, erythema, oedema, erosion, excoriation, itching, pigmentation changes
<b>Podophyllotoxin .05%</b>	Genital warts	topical	3.5mL	7 day cycle 2 applications per day for 3 days, 4 days no treatment; 4 week treatment	Wart remover S4	Pregnancy, lactation, Hypersensitivity, Use in children,	Damage to good skin Skin affected by dermatosis
						Nil known	Irritation to normal skin, erythema, pain, superficial ulceration, erosion, burning

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