

# Title of the article: Treatment options for Oral Potentially Malignant Disorder (OPMDs)

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**Abstract:** *Oral Cancer is a deadly infection, causing serious mortality and morbidity globally. Almost all oral cancerous lesions are derived from Oral potentially malignant disorder (OPMD). Among overall 60 to 70% of the Indian patients were introduced for therapy just in the advanced stage of oral malignant growth prompting a high death rate. The absence of public awareness about the screening and treatment during the premalignant stage along with the lack of knowledge for early detection by medical and health care providers are the main reason for this diagnostic delay and treatment initiation. This article aims to give different treatment options for Oral Potentially Malignant Disorder (OPMD) to prevent the progression of OPMD into malignancy.*

**Keywords:** *Oral potentially malignant disorder (OPMD), treatment of OPMD, leukoplakias, Erythroplakia, Oral submucous Fibrosis, Chronic candidiasis, actinic cheilitis, Discoid lupus erythematosus, syphilitic glossitis and oral lichen planus*

## 1. Introduction

Oral cancer is the 11th most common cancer in the world and the top 3rd most common malignancy in India. Oral malignancy is among the most common malignancies worldwide and frequency rates are higher in men than women. There are expected 657,000 new cases of oral cancer every year, and nearly 330,000 deaths. Oral squamous cell carcinoma (OSCC) is a very common oral and maxillofacial malignancy and is usually preceded by OPMDs. The early detection and diagnosis of OPMDs allow dentists to monitor and treat oral cancer at an initial stage and improve the survival rate and reduce the mortality rate of the patients.

Various treatment options such as pharmacological management, laser therapy, and surgical management of each OPMDs are discussed in this article.

**Oral potentially Malignant Disorder (OPMDs)<sup>1</sup>**

**What is an oral potentially malignant disorder?**

The World Health Organization (WHO) suggested the utilization of the term oral “potentially malignant disorders” (PMDs) rather than precancerous lesions/disorders.

In 2005 WHO defined OPMDs as “clinical presentations that carry a risk of cancer development in the oral cavity, whether in a clinical definable precursor lesion or clinically normal oral mucosa”.

1. Leukoplakia
2. Erythroleukoplakia
3. Erythroplakia
4. Oral submucous Fibrosis
5. Dyskeratosis congenita
6. smokeless tobacco keratosis
7. Palatal lesion associated with reverse smoking
8. Chronic candidiasis
9. lichen planus
10. Discoid lupus erythematosus
11. syphilitic glossitis
12. Actinic Cheilitis (lip only)

Oral potentially malignant disorder	Etiologic factors	Main clinical features	Common sites in oral cavity	Malignant potential
1. Leukoplakia	Alcohol, tobacco, smoking, betel nut chewing, human papillomavirus	White plaque	Seen in mucosal surface such as alveolar mucosa, buccal and labial mucosa	medium <30%
2. Erythroleukoplakia	Alcohol, tobacco, smoking, betel nut chewing, human papillomavirus	Red and white plaque	Seen in mucosal surface of oral cavity	medium <30%

	avirus			
3. Erythroplakia	Alcohol, tobacco, smoking, betel nut chewing,	Flat red plaque	Buccal vestibule, tongue, floor of the mouth and soft palate	High>60%
4.Oral submucous Fibrosis (OSMF)	Areca Nut and betel nut chewing	White plaque and immobile mucosa	Buccal mucosa, any part of the oral cavity and also pharynx	medium <30%
5. Dyskeratosis congenita	genetic	White plaque	Buccal mucosa, tongue, gingiva and palate	High>60%
6. smokeless tobacco keratosis	Chewing tobacco, dry and moist snuff	White or grey plaque	Buccal or labial vestibule of mandible	low<10%
7. Palatal lesion associated with reverse smoking	Smoking and tobacco	White or speckled plaque	Palate and tongue	low<10%
8. Chronic	Heavy	White	Cheek,	medium

candidiasis	smoking	leathery plaque	lip and tongue	<30%
9. lichen planus	idiopathic	White plaque and erosion	Tongue, gingiva, bilateral buccal mucosa	low<10%
10. Discoid lupus erythematosus	idiopathic	White plaque and erosion	Buccal mucosa, labial mucosa and vermilion border	low<10%
11. syphilitic glossitis	Third stage in syphilis infection	White plaque	Tongue, buccal mucosa, tonsils, lips and oropharynx	medium <30%
12. Actinic Cheilitis (lip only)	sunlight	White plaque and erosion	Lower lip	medium <30%

### Leukoplakia

#### Treatment modalities

Behaviour Modification	<ul style="list-style-type: none"> <li>• Quit habits like tobacco, alcohol, and smoking</li> <li>• A good diet and oral hygiene are encouraged.</li> </ul>
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Pharmacological treatment	<ul style="list-style-type: none"> <li>• Beta-carotene- oral doses of 90mg/day, for three cycles of 3 months each can be used.<sup>2</sup></li> <li>• Lycopene: Dosage- 4to 8 mg/day.<sup>3</sup></li> </ul>
Vitamins	<ul style="list-style-type: none"> <li>• L-Ascorbic Acid (vitamin C)- daily intake for ascorbic acid ranges between 100–120 mg/per day for adults.</li> <li>• <math>\alpha</math>-Tocopherol (Vitamin E)- The recommended daily limit rates are 10 mg/day for adult men and 8 mg/day for adults.<sup>4</sup></li> <li>• Retinoic Acid (Vitamin A)- systemic vitamin A 200,000IU/week</li> <li>• Fenretinide (4-HPR) or N-(4-hydroxyphenyl) retinamide- Systemic use with 200 mg/day for 3 months.</li> </ul>
Antineoplastic agent	<ul style="list-style-type: none"> <li>• Bleomycin- Topical doses of 0.5%/day for 15 days or 1%/day for 14 days.</li> <li>• 5-fluorouracil (5-FU) mainly used for chemotherapy of head and neck cancer which induces the apoptotic death of any cancer cells.</li> </ul>
Non-invasive techniques	Photodynamic therapy, CO2 lasers, Nd: YAG lasers, and diode lasers
Surgical Treatment	Surgical excision (scalpel) and cryosurgery for good cure rates.

### Erythroleukoplakia

#### Treatment modalities

Group 1: low risk of malignant lesion shows mild dysplasia with a thickness of less than 200 mm.	Regular patient follow-up. use of retinoids, vitamins A, C, E, ketorolac,
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	<p>celecoxib, green tea, fenretinide, lycopene and</p> <p>topical or oral retinoids {e.g: 13-Cis-Retinoic Acid (1.5 to 2mg/kg body weight for 3 months)}<sup>5</sup>.</p> <p>non-invasive techniques, such as cryotherapy and carbon dioxide laser therapy show better results at this stage</p>
<p>Group 2: high-risk of malignant transformation.</p> <p>Leukoplakias with mild dysplasia located in high-risk areas measuring more than 200 Mm shows moderate or severe dysplasia;</p>	<p>In this group, the excision of the entire thickness of the mucosa is recommended.</p> <p>Surgical treatment is indicated for entire lesion removal, cryosurgery, and laser therapy.</p> <p>Advice to patients to stop the habits of smoking and alcohol consumption and Regular check-up of these patients is essential for every 3, 6, and then 12 months, both in treated and untreated patients.</p>

**Erythroplakia:**

Treatment modalities

Surgery	Surgical excision of lesion with high malignant potential and long term follow up is necessary after surgery.
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**Oral submucous fibrosis**

Treatment modalities

Minerals and vitamins	Vitamin A, B complex, C, D and E, iron, copper, calcium, zinc, magnesium, selenium and others.
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Turmeric	Alcohol extracts of turmeric <sup>3</sup> (3g), turmeric oil(600mg), turmeric oleoresin (600 mg) daily for 3 months.
Milk	45g of milk powder twice daily usually for 3 months. <sup>6</sup>
Lycopene	8mg twice daily for 2 months. <sup>7</sup>
Pentoxifylline	400mg thrice daily for 7 months. <sup>8</sup>
Steroids	submucosal injections twice a week in multiple sites for 3 months and topical for 3 months. <sup>9</sup>
Interferon gamma	Intralesional injection (0.01 - 10.0 U/mL) 3 times a day for 6 months. <sup>9</sup>
Chymotrypsin, hyaluronidase and dexamethasone	Chymotrypsin (5000 IU), Hyaluronidase (1500 IU) and dexamethasone(4mg) twice weekly submucosal injections for 10 weeks. <sup>9</sup>
Hyalase+ dexamethasone	1500 IU of hyaluronidase and dexamethasone 4mg (7 weeks) <sup>10</sup>
Placental extracts	Inj. Placentrex 2ml once a week <sup>11</sup>
Non-invasive treatment	ErCr: YSGG laser is used for fibrotomy.
Surgery	In advanced stage radial neck dissection is indicated.

### **Dyskeratosis congenita**

#### Treatment modalities

Stem cell transplant	No targeted therapies for DC and patients usually die of BMF due to a deficient renewing capability of hematopoietic stem cells. Allogeneic hematopoietic stem cell transplantation is the only curative treatment for BMF.
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### **Smokeless tobacco keratosis**

#### Treatment modalities

Behaviour modification	Apart from stopping the habit, no other treatment is indicated. Long term follow-up is usually carried out.
Surgical treatment	Some recommend biopsy if the lesions persists more than 6 weeks after quitting smokeless tobacco use, or if the lesion undergoes a change in appearance (e.g. thickening, colour changes, ulceration, especially to speckled white and red or entirely red). Surgical excision is indicated in advanced stage.

### **Chronic candidiasis**

#### Treatment modalities

Behavioural modification	if the smoking habit is stopped the condition is reversible within a few weeks.
Pharmacological management	Antifungal therapy.

Non-invasive treatment method	Lasers therapy.
Surgical management	Surgery is indicated in case of non-responsive cases.

## Lichen planus

### Treatment modalities

Natural methods	lycopene, curcumin, alovera, green tea.
Pharmacological methods 1. Antifungal drugs	Clobetasol 0.025%, 0.05%, Miconazole 2%, Amphotericin B 0.1%, Tab Griseofulvin 500mg/day for 6 months. <sup>12</sup>
2. corticosteroids <sup>12</sup>	Topical (combined with adhesive base carboxymethyl cellulose, or used on custom trays, mouthwashes or sprays) Flucinoloneacetone 0.1% or 0.025% Disodium betamethasone phosphate 0.05% Clobetasol propionate 0.05% or 0.025% Fluticasone spray 0.01% Topical triamcinolonacetone 0.1%
Intralesional <sup>13</sup>	Triamcinolone acetone 0.2–0.5 mL Injection containing 40 mg/mL Morning dose of 40–80 mg, for 10 days Methyl Prednisolone initial higher dose of 1–1.5 mg/kg/day recommended.  Systemic Betamethasone 0.5 mg OD after breakfast on 2 consecutive days every 2 weeks for 10 weeks.
3. immunosuppressants <sup>13</sup>	Cyclosporine 50 mg/mL or 0.025% topical application, four times daily. Tacrolimus Cream or ointment twice daily for 1 week with no occlusive dressing. Primacrolimus 1% cream.
Other drugs	Thalidomide, Mycophenolate (used in cases resistant to topical steroids), Tretinoin Isotretinoin Fenretinide Etrinate, Dapsone, Griseofulvin, Hyaluronic acid.

Non-invasive method	PUVA, photodynamic therapy, laser therapy.

### Discoid lupus erythematosus

Treatment modalities

Topical calcineurin inhibitors	Topical retinoids Tocoretinate R-salbutamol
Systemic therapies <sup>14</sup>	Antimalarials Azathioprine Systemic retinoids Methotrexate Fumaric acid esters Mycophenolate mofetil Thalidomide, Lenalidomide Systemic corticosteroids Clofazimine
Alternative therapies	Laser Photodynamic therapy <sup>15</sup> Intravenous Immunoglobulin

### Syphilitic glossitis

Treatment modalities

Pharmacological management	Antibacterial therapy and regular follow up are indicated.
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### Actinic Cheilitis (lip only)

Treatment modalities

Topical treatment	Avoid sunlight exposure and use sunscreen lotion regularly and use full clothing pattern to cover the skin from over UV radiation exposure. <sup>16</sup>
Non-invasive technique	Vermilionectomy, electrodesiccation and curettage, chemo cautery, cryosurgery with liquid nitrogen, dermabrasion or topical application of medications such as retinoic acid is used in the management of Angular Cheilitis of lip. <sup>16</sup>

## 2. Conclusion

Most OPMDs and their related complications are preventable through early detection and treatment planning. Therefore, improvement of knowledge of OPMDs among physician and dentist may play a key role to treat in the early stage and prevent malignant transformation which helps in saving the patient's life.

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