Guidelines for Prevention and Management of Oral Mucositis

*These guidelines apply to all SACT patients, as well as patients receiving radiotherapy to head, neck or oesophagus*

**Mucositis** is defined as the damage that occurs to the oral mucosa and gastrointestinal tract following chemotherapy or radiotherapy (especially radiotherapy to the head, neck or oesophagus), leaving the tissue exposed to infection.

**Stomatitis** refers to the diffuse inflammatory, ulcerative condition affecting the mucous membranes lining the mouth.

All SACT drugs have the potential to cause oral mucositis. Treatments most commonly associated with oral mucositis include:

- Anti-metabolites e.g. 5-FU, capecitabine, methotrexate
- Anthracyclines e.g. epirubicin, doxorubicin
- All lymphoma or leukaemia patients who have recently had treatment
- Tyrosine kinase inhibitors (such as sunitinib, pazopanib, afatinib) and everolimus
- Radiotherapy to the head and neck region

Oral mucositis typically occurs 7 to 14 days after chemotherapy or radiotherapy and may last for 2-3 weeks after the completion of treatment. It may result in pain, discomfort and difficulty eating.

It is important to take preventative measures against mucositis (see page 3) and to recognise and treat it promptly and effectively if it occurs.

Management involves mouth care, management of oral pain and consideration of nutritional support in severe cases.

**Assessment of patient**

Patients presenting with acute oncological problems, during and immediately after their treatment, should be assessed for the presence of oral mucositis.

- Clinical examination of oral mucosa – see page 3 for more details
- Functional status - ability to eat
- Bloods – FBC (check if neutropenic), U&Es, CRP

**Grading of Oral Mucositis (CTC criteria)**

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Examination</td>
<td>Erythema of the mucosa</td>
<td>Patchy ulcerations or pseudomembranes</td>
<td>Confluent ulcerations or pseudomembranes; bleeding with minor trauma</td>
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<tr>
<td>Functional/symptomatic</td>
<td>Asymptomatic or mild symptoms; normal diet; intervention not indicated</td>
<td>Moderate pain, not interfering with oral intake; modified diet indicated</td>
<td>Severe pain, interfering with oral intake and hydration</td>
</tr>
</tbody>
</table>

Reason for Update: steroid mouthwash added for everolimus; dose for Oramorph removed; Orabase removed; fluconazole dose reviewed; link to oral assessment tool added

Approved by Chair of Alliance Chemotherapy Group: Dr J De Vos

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Patients currently receiving radiotherapy or SACT (or within last 2-4 weeks) and with oral, pharyngeal or oesophageal mucositis

Encourage good oral hygiene and frequent mouth washing (see page 3)
Check to see if patient has any evidence of oral infection **

Grade 1 or 2 *

1st line
Diffam (benzydamine) mouthwash: 15ml up to every 1½ hours, to provide local pain relief for stomatitis. It may be diluted with a little water if stinging occurs.

2nd line options
The options below may be considered according to the affected area, clinical situation and patient preference:

Systemic options:
Co-codamol 30/500 dispersible tablets - 2 tablets up to QDS (remember to co-prescribe laxative as required)
Soluble Paracetamol 1g QDS

Topical options:
Mucaine equivalent* (antacid and oxetacaine) 10ml QDS, taken before meals to aid eating, in patients with oral or oesophageal ulceration
May be used alongside other pain relief options
Hydrocortisone 2.5mg buccal tablets
• one tablet to be allowed to dissolve slowly in the mouth in contact with the ulcer 4 times daily
• are considered useful in localised radiotherapy reactions, for patients with a single ulcerated area.
Lidocaine 2% gel* (e.g. Optilube) applied qds
Soluble aspirin 300mg
• An option for radiotherapy-induced mucositis, for patients who cannot tolerate Diffam but who wish to continue to try a topical option as well as systemic analgesia
• 1-2 tablets dissolved in a little water and used as a mouthwash up to QDS, and gargled if any oro-pharynx pain (may be swallowed unless any contra-indications e.g. risk of thrombocytopenia, history of peptic ulcers)
Bonjela (Choline salicylate dental gel) applied up to every 3 hours
Betamethasone 500mcg soluble tablets – for patients on everolimus
ONE tablet dissolved in 20ml water and rinsed round the mouth for at least 2 minutes, repeated twice daily (not to be swallowed)
*Due to its local anaesthetic effect, advise patients to take care to ensure that food/drinks are not too hot.

Grade 3 *

ADMIT, RESUSCITATE
Discuss with consultant ASAP
Manage as for Grade 3

As for Grade 1 and 2, PLUS:
Immediate release opioids
e.g. oral morphine sulphate solution (Oramorph®) every 4 hours, if the patient can tolerate the oral route.
Otherwise, consider fentanyl patches (C/I if patient on aprepitant) or s/c syringe driver. Consult palliative care/pain team.
• remember to co-prescribe laxative and antiemetics as required

Gelclair oral gel (15ml sachets)
This is classified as a device, not a medicine, and is not included in local formularies. Its use is restricted to patients with Grade 3 / 4 mucositis.
It does not contain any active drug, and does not promote healing. However, it may provide symptomatic relief in some patients.
The contents of one sachet are rinsed around the mouth to form a protective layer over the sore areas, which may make it more comfortable to eat and drink. The manufacturers state that it may provide relief for up to 7 hours.
Discontinue if the patient does not report any benefit.
If bleeding from mouth, consider tranexamic acid 5% mouthwash, 10ml rinsed around the mouth qds, then spit out
Consider enteral feeding – refer for dietician review

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For patients on capecitabine or continuous 5FU, ensure they have their treatment interrupted for Grade 2 or above mucositis.

- Severe mucositis (and diarrhoea) early in the first treatment cycle can be the first presenting toxicity due to DPD deficiency\(^\#\), in which case potentially fatal neutropenia can quickly follow.
- \(^\#A\) genetic disorder in which there is significantly decreased activity of dihydropyrimidine dehydrogenase, an enzyme involved in the metabolism of active 5FU to inactive metabolites
- For further information specific to the regimen, including subsequent dose reductions, refer to the relevant chemotherapy or radiotherapy protocol.

** Anti-Infectives

- Susceptibility to mouth ulcers associated with Herpes simplex or Candida is increased with prolonged neutropenia and monocytopenia. Antiviral or antifungal prophylaxis may be required for highly myelosuppressive chemotherapy regimens (refer to specific protocols).
- If any signs of infection, take oral swabs
- Candida – fluconazole 100mg daily for 7 - 14 days
- Viral – consider topical aciclovir 5% for local infection in low risk patients. If highly immunocompromised, consider oral or IV aciclovir. If in doubt, discuss with Consultant.
- Patients who are neutropenic and have signs of infection should be treated according to local neutropenic sepsis guidelines.

Oral Assessment

An oral assessment should be carried out and recorded **once daily** for all haematology and oncology in-patients, according to a locally agreed assessment tool e.g. see Appendices 1 - 4 of the RSCH Mouth Care Policy; [http://trustnet2.royalsurrey.nhs.uk/Documents/PoliciesandProcedure/Mouth%20Care%20Policy%202017.pdf](http://trustnet2.royalsurrey.nhs.uk/Documents/PoliciesandProcedure/Mouth%20Care%20Policy%202017.pdf)

This requires visual inspection of the oral cavity using a torch, and tongue depressor if necessary, to examine the oral mucosa.

Nutrition, hydration and pain should all be managed according to a locally agreed care plan, and with reference to the oral pain management options listed above.

For out-patients, an oral assessment should be carried out at each out-patient chemotherapy appointment.

Prevention of Oral Mucositis - Maintaining Good Oral Hygiene

A Good Mouth Care leaflet, containing the following information, should be given to all patients before starting the relevant treatment:

1. **All patients** should be encouraged to clean teeth with toothpaste and a soft toothbrush or electric toothbrush after each meal, as well as at bedtime.
   Advise patients to replace their toothbrush regularly to minimise infection risk.

2. All patients should also be encouraged to rinse the mouth thoroughly four times a day (see below for mouthwash options), after each meal and at bed-time, after brushing teeth.
3. Careful dental flossing once daily to reduce plaque should be encouraged. However, if the patient is at risk of thrombocytopenia, flossing should be avoided as this may irritate the gums, thereby causing excessive bleeding.

4. Dentures should be cleaned after each meal and soaked overnight in patient’s usual solution.

5. Lips may also be moistened with Vaseline or soft paraffin, or the patient’s own lip salve.

6. Adequate oral fluid intake and diet should be encouraged, although alcohol and tobacco should ideally be avoided. Advise patient that spicy foods may irritate the mouth, and care should be taken with rough or crunchy foods as they may damage the mucosal lining or gums.

7. For patients receiving chemotherapy, assuming time permits, ask them to have a dental check-up before chemotherapy starts. Routine annual dental appointments should also continue throughout treatment and follow-up. For patients receiving head and neck radiotherapy, a pre-treatment dental examination must be undertaken.

If any urgent dental work is required once chemotherapy has started, it is important that a blood test is performed within 48 hours of any dental treatment and their doctor consulted, so as to determine the need for a platelet transfusion pre-treatment or for any prophylactic antibiotic cover.

8. It is recommended that patients do not visit a dental hygienist whilst undergoing chemotherapy, so as to avoid unnecessary trauma to the gums.

9. Chemotherapy patients may be directed to the Macmillan leaflet “Mouthcare during Chemotherapy” [http://www.macmillan.org.uk/Cancerinformation/Livingwithandaftercancer/Symptomssideeffects/Mouthcare/Mouthcare.aspx](http://www.macmillan.org.uk/Cancerinformation/Livingwithandaftercancer/Symptomssideeffects/Mouthcare/Mouthcare.aspx). There is also a Macmillan leaflet “Dry Mouth” specifically for patients receiving radiotherapy to the head, neck or mouth. [http://www.macmillan.org.uk/Cancerinformation/Livingwithandaftercancer/Symptomssideeffects/Mouthcare/Radiotherapy.aspx](http://www.macmillan.org.uk/Cancerinformation/Livingwithandaftercancer/Symptomssideeffects/Mouthcare/Radiotherapy.aspx)

**Choice of Mouthwash – as part of good oral hygiene routine**

1. Despite numerous trials, there is no mouthwash that has been proven to be superior to any other in chemotherapy patients. Frequency of mouthwashing is considered the most important factor, although the optimum frequency has not been defined.

2. For the above reason, local expert opinion is that water should be the standard solution used to rinse the mouth. It is important to encourage vigorous rinsing using a ballooning and sucking motion of the cheeks for at least 30 seconds, as it is this action that removes loose debris from the teeth.

3. If preferred, normal saline mouthwashes may be used instead. Ready-made saline is available from Pharmacy as 1 litre plastic bottles of Sodium Chloride 0.9% for Irrigation. This is well tolerated, economical and may also help with healing if stomatitis does occur.

Alternatively, patients can be advised to make their own salt solution by adding a little salt (¼ to ½ a teaspoon) to a cup of warm water.
4. There is no clinical benefit in using a commercial mouthwash instead of water. However, if the patient prefers to use one, recommend that they choose an alcohol-free product. (Examples include Dentyl, Colgate Plax, Oral B Alcohol Free)

5. **For patients on everolimus:** there is data to support the use of a steroid mouthwash, to reduce the incidence of everolimus-associated mucositis. There is no commercial product, but it has been agreed locally to use Betamethasone 500mcg soluble tablets; one tablet dissolved in 20ml water and rinsed round the mouth for at least 2 minutes, repeated twice daily (not to be swallowed).

6. **For patients receiving radiotherapy to head and neck:** Benzydamine (Difflam) mouthwash has been shown to be useful for both prevention and treatment of mucositis in this patient group, and so is recommended as the mouthwash of choice. Chlorhexidine mouthwash is not recommended for this group of patients.

References:

1 Rubenstein, EB et al; Cancer 2004; 100 (9 suppl): 2026 – 2046

2 Keefe, DM et al; Cancer 2007; 109: 820 – 831

Lalla, R et al; Cancer 2014; 1453 – 1461