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Department of
**Health, Social Services
and Public Safety**

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AN ROINN

**Sláinte, Seirbhísí Sóisialta
agus Sábháilteachta Poiblí**

MÁNNYSTRIE O

**Poustie, Resydènter Heisin
an Fowk Siccar**

Best Practice Guidance

Subject:
Osteonecrosis associated with Bisphosphonate usage

For action by:

Chief Executive, HSC Board
Dental Directors, HSC Board
Pharmaceutical Directors, HSC Board
Director of Primary Care, HSC Board
Chief Executive, Public Health Agency
Director of Public Health, Public Health Agency
Chief Executive, HSC Trusts for cascade to:

- Medical Directors
- Community Dental Service staff
- CSCG Leads

General Medical Practitioners
General Dental Practitioners
Community Pharmacists

For Info:

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Dr Owen Barr, Head of School of Nursing, UU
Professor Paul McCarron, Head of School of Pharmacy, UU
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Summary of Contents:

The purpose of this Circular is to highlight the risk of Osteonecrosis associated with Bisphosphonate usage.

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Related documents

Osteonecrosis associated with Bisphosphonate usage – Letter issued from Chief Dental Officer & Chief Pharmaceutical Officer on 21/12/2006

Superseded documents

N/A

Status of Contents:

Best Practice Guidance

SQSD material can be accessed on:

<http://www.dhsspsni.gov.uk/index/phealth/sqs.htm>

Working for a Healthier People

Chief Medical Officer Group



INVESTOR IN PEOPLE

Dear colleagues

RE: OSTEONECROSIS ASSOCIATED WITH BISPHOSPHONATE USAGE: ADVICE FOR HEALTH CARE PROFESSIONALS.

The content of the attached circular at Appendices 1 to 3 has been reviewed by relevant professional colleagues in the Department and approved for regional dissemination.

The risk of osteonecrosis of the jaw associated with the use of bisphosphonate therapy has been widely reported in recent years in medical and dental literature. The problem of osteonecrosis associated with bisphosphonate therapy is not fully understood and is an evolving issue. The precise relationship between bisphosphonates, osteonecrosis and dental care will require further research.

The Department's current position is to follow the advice of the Medicines and Healthcare products Regulatory Agency (MHRA) which states:

- Dental examination, with appropriate preventive dentistry, should be considered before bisphosphonate treatment in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, and poor oral hygiene)
- During bisphosphonate treatment, patients with concomitant risk factors should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw during bisphosphonate treatment, dental surgery may exacerbate the condition
- Whether discontinuation of bisphosphonate treatment in patients who need dental procedures reduces the risk of osteonecrosis of the jaw is not known. Clinical judgment should guide the management of every patient on the basis of an individual benefit-risk assessment.

The Department was asked by medical and dental colleagues in the HSC to provide more detailed guidance to support clinicians in their management of patients on bisphosphonate therapy.

There are currently no consensus guidelines available from a recognized body in the UK to refer to other than the high level advice from the MHRA. In the absence of such guidance, the Department convened a group comprising dental, medical and pharmaceutical professionals to consider the issue further. The background to the development of the guidance can be found in Appendix 3. The British Dental Association (BDA) and British Medical Association (BMA) along with Departmental medical, dental and pharmaceutical professionals were represented on this group.

This group has developed this guidance to assist medical, dental and other healthcare professionals in the management of patients undergoing bisphosphonate therapy. This guidance is based on expert opinion as there is currently insufficient information available for evidence based guidelines to be issued. Health care professionals should therefore view the guidance in this context and as with any guidance, final clinical opinion will be based on the assessed needs of the individual patient. Should more robust guidance emerge from a recognised body then the attached guidance will be revised.

I would ask you to bring this to the attention of relevant practitioners and key health and social care staff within your organisation. They should consider the best practice for their setting and take appropriate steps to minimise the risk to patients undergoing bisphosphonate therapy.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Jim Livingstone', written in a cursive style.

Dr J F Livingstone
Director, Safety, Quality & Standards

ADVICE ON MANAGEMENT OF BONE OSTEONECROSIS (BON)

1. Advice to **Prescribers** for management of patients prior to prescription of bisphosphonates
2. Advice to **Prescribers** for management of patients who are currently on bisphosphonate therapy
3. Advice to **Dentists** for management of patients prior to prescription of bisphosphonates
4. Advice to **Dentists** for management of patients who are currently on bisphosphonate therapy

1. Advice to Prescribers for management of patients prior to prescription of bisphosphonates

Advice	Comments
Assess risk of BON and advise patient.	Concomitant risk factors include: <ul style="list-style-type: none"> • Local; poor oral hygiene, periodontal disease, dental caries, smoking • Systemic; cancer, chemotherapy, corticosteroids.
If concerned about a patient's oral health, advise patient to seek dental assessment and any remedial dental care.	Ideally a dental assessment should be sought prior to the commencement of IV bisphosphonate therapy. If not possible, aim for dental assessment and completion of invasive dental treatment within 6 months of commencing IV therapy. For patients on oral bisphosphonates, dental assessment and remedial dental care as soon as reasonably practicable.
Emphasise the need to practise good oral hygiene procedures, dietary advice and attend for regular dental check-ups.	Brush twice daily with a fluoride toothpaste and with interdental cleaning as appropriate. Reduce the frequency of sugary snacks and drinks. Patient to seek advice from a dental professional on the most suitable oral hygiene regimen. Smoking cessation advice to be provided if appropriate.

2. Advice to Prescribers for management of Patients who are currently on bisphosphonate therapy

Advice	Comments
Advise regular dental attendance and reinforce good oral hygiene procedures and dietary advice. There is no evidence to support the effectiveness of 'drug holidays' for patients who require invasive dental procedures nor that there is a safe time period after bisphosphonate treatment when the risk of BON reduces.	Brush twice daily with a fluoride toothpaste and with inter-dental cleaning as appropriate. Patient to seek advice from a dental professional on the most suitable oral hygiene regimen. Reduce the frequency of sugary snacks and drinks. Smoking cessation advice to be provided if appropriate.
Refer to oral surgery specialist in secondary care where BON is suspected.	Signs of BON include; exposed, necrotic bone in maxilla or mandible that has persisted for more than 8 weeks and where there has been no history of radiation therapy to the jaws. Patients may be asymptomatic or may exhibit pain due to secondary infection.

3. Advice to Dentists for management of patients prior to prescription of bisphosphonates

Advice	Comments
<p>Full oral examination and medical history to include questions on bisphosphonate therapy.</p>	<p>When taking medical history ensure that patient is asked about any IV bisphosphonate medication as well as concomitant risk factors which include:</p> <ul style="list-style-type: none"> • Local; poor oral hygiene, periodontal disease, dental caries, smoking • Systemic; cancer, chemotherapy, corticosteroids, <p>As well as obvious dental problems such as caries, unsalvageable teeth and periodontal disease, patients with dentures should be checked for any potential areas of mucosal trauma. Ideally assessment should be done before IV bisphosphonate therapy commences, but where not possible assessment should be done in parallel with commencement of therapy or within 6 months of commencement for IV patients. For patients on oral bisphosphonates routine dental check ups and treatment should be completed as soon as is reasonably practicable.</p>
<p>Emphasise importance of preventive care and complete all necessary treatment; eliminate potential sites of infection.</p>	<p>Ideally complete all invasive procedures and treat oral infections and periodontal disease before drug therapy commences. Unsalvageable teeth should be removed. Dentures should be adjusted as required. If treatment cannot be completed before drug therapy, then it may be carried out in parallel with the commencement of drug therapy and within 6 months of commencement for IV patients. For patients on oral bisphosphonates, treatment should be completed as soon as is reasonably practicable.</p>
<p>Be familiar with the generic and proprietary names of the commonly prescribed bisphosphonate medicines in the UK.</p>	<p>See Appendix 2.</p>

4. Advice to Dentists for management of patients who are currently on bisphosphonate therapy

Advice	Comments
<p>For patients on any bisphosphonate therapy, focus on preventive care and reinforce good oral hygiene regimen and dietary advice. Regular check ups and radiological review as appropriate. Avoid dento-aveolar surgery including extractions, implant placement, periapical surgery, complex restorative treatment and periodontal surgery in patients, on IV bisphosphonate therapy. Review dentures regularly if applicable.</p>	<p>Advise on twice daily toothbrushing with fluoride toothpaste and inter-dental cleaning as appropriate. For susceptible patients consider fluoride mouth rinse. Reduce the frequency of sugary snacks and drinks. Smoking cessation advice to be provided if necessary. For non-restorable teeth, decoronation and endodontic treatment of remaining roots is the preferred option.</p>
<p>For patients on IV bisphosphonates who require dental extractions or other invasive dental procedures, refer to oral surgery specialist in secondary care.</p>	<p>Advice of oral surgeons/oral maxillo-facial surgeons to be followed which may include antibiotic cover.</p>
<p>For patients on oral bisphosphonates who are asymptomatic and require extractions, then extractions can be carried out in most cases in primary care. The following regimen is advised:</p> <ul style="list-style-type: none"> • Chlorhexidine mouthwash before and after extractions • Atraumatic extraction technique • Careful post operative follow up until socket healed • Avoid significant bone removal • For patients who smoke, provide smoking cessation advice at least in the peri-operative phase. 	<p>Informed consent from patient. Consultant oral surgeons or oral-maxillo facial surgeons may be approached for advice before commencing treatment. If infection is present, systemic antibiotics may be required.</p>
<p>If BON suspected, refer to oral surgery specialist in secondary care.</p>	<p>Signs of BON include exposed, necrotic bone in maxilla or mandible that has persisted for more than 8 weeks in a patient who was receiving or had been exposed to a bisphosphonate drug and where there has been no history of radiation therapy to the jaws. Patients may be asymptomatic or may exhibit pain due to secondary infection.</p>

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8. Bisphosphonates and osteonecrosis of the jaw (2006) Irish Medicines Board
9. Osteonecrosis of the jaws (2008) Power-point presentation by Dr John Marley, Consultant/Senior Lecturer in Oral Surgery, Queens University Belfast
10. Current Problems in Pharmacovigilance , Osteonecrosis of the jaw with bisphosphonates (May 2006) Volume 31. MHRA
11. Koshla et al. Bisphosphonate –Associated Osteonecrosis of the Jaw: Report of a Task Force of the American Society for Bone and Mineral Research (2007) Journal of Bone and Mineral Research. 22 (10) pp 1479-1491
12. Bisphosphonates Fact File, September 2008, British Dental Association

APPENDIX 2

Table 1 Bisphosphonates prescribed in the United Kingdom

Drug name	Trade name	Route of administration	Nitrogen containing*
Disodium etidronate	Didronel Didronel PMO (with calcium carbonate)	Oral	No
Tiludronic acid	Skelid	Oral	No
Sodium clodronate	Bonefos Loron	Oral / Parenteral	No
Disodium pamidronate	Aredia Dry Powder	Parenteral	Yes
Alendronic acid	Fosamax Fosamax Once Weekly Fosavance (with colecalciferol)	Oral	Yes
Risedronate sodium	Actonel Actonel Once a Week	Oral	Yes
Ibandronic acid	Bondronat Bonviva	Oral / Parenteral	Yes
Zoledronic acid	Aclasta (lower dose for osteoporosis & Pagets disease) Zometa (higher dose for malignant disease)	Parenteral	Yes

* Nitrogen containing preparations are more potent and are retained longer in skeletal tissue

**OSTEONECROSIS ASSOCIATED WITH BISPHOSPHONATE USAGE:
ADVICE FOR HEALTH CARE PROFESSIONALS**

Background

A letter was issued from the DHSSPS in December 2006 to Health and Social Services Boards (HSS Boards) alerting them to the risk of osteonecrosis associated with bisphosphonate usage and advising that remedial dental work should be carried out before commencing bisphosphonate therapy and that adequate oral hygiene procedures should be maintained during bisphosphonate therapy. This advice was cascaded from the Boards to the wider service. The letter was issued as a result of a serious adverse incident received from the WHSSB in November 2006 in relation to a significant number of cases of osteonecrosis which had developed following bisphosphonate usage.

Following on from this advice letter, the Department was contacted by medical colleagues and dental colleagues who are experiencing practical problems with implementing the advice mentioned above. The Department's current position is to follow the advice of the MHRA which states:

**Advice for Healthcare professionals (Drug Safety Update Vol 1, Issue 3
October 2007):**

- Dental examination, with appropriate preventive dentistry, should be considered before bisphosphonate treatment in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, and poor oral hygiene)
- During bisphosphonate treatment, patients with concomitant risk factors should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw during bisphosphonate treatment, dental surgery may exacerbate the condition

- Whether discontinuation of bisphosphonate treatment in patients who need dental procedures reduces the risk of osteonecrosis of the jaw is not known. Clinical judgment should guide the management of every patient on the basis of an individual benefit-risk assessment.

In order to address some of the practical problems encountered by clinicians with the current advice, in May 2008 the Department convened a group comprising dental, medical and pharmaceutical professionals to consider the issue further. The British Dental Association (BDA) and British Medical Association (BMA) were represented on this group.

Conclusions of the Group

- The problem of osteonecrosis associated with bisphosphonate therapy is not fully understood and is an evolving issue. The precise relationship between bisphosphonates, osteonecrosis and dental care will require further research.
- The current literature on the topic suggests that the likelihood of developing osteonecrosis associated with bisphosphonates is very low for patients on short term oral bisphosphonates, higher for patients on long term oral bisphosphonates and more so for those receiving intravenous bisphosphonates.
- The risk of developing osteonecrosis associated with bisphosphonates is much lower than the risk of developing bone fractures with their considerable morbidity and mortality should the bisphosphonate therapy be withheld, i.e. currently the benefit of bisphosphonates is considered to outweigh the risk associated with their use. However, the risks should be explained to patients before bisphosphonate therapy commences. Patients must also understand that they have a role in reducing the risk and take responsibility for this in respect of dental care.

- Bisphosphonates are incorporated into skeletal tissue without being degraded and persist in the skeletal tissue for many years. The risk of associated complications seems to increase with the increased time of bisphosphonate use for both oral and IV preparations. Thus the duration of effect of bisphosphonates extends well beyond the duration of treatment.
- Overall numbers of patients affected in Northern Ireland is low and consequently the response to the problem should be proportionate.
- **Prevention** of osteonecrosis is key. In this respect, elimination of co-morbidities (e.g. poor oral hygiene, oral infections, smoking) should ideally take place before, or shortly after bisphosphonate therapy begins and preventive oral care should be a priority for patients undergoing bisphosphonate therapy.
- There appears to be some confusion and concern amongst prescribers and dental practitioners in relation to the management of patients who are about to commence, or are currently receiving, bisphosphonate therapy. Management of these patients appears to vary across Northern Ireland. In view of this the group felt that some further advice would be helpful for health care professionals and patients.
- There is currently no consensus guideline on how to manage patients who are currently on, or have previously been, prescribed bisphosphonates. The group would endeavour to develop guidelines. Any guidelines or advice issued by the DHSSPS would lack an evidence base and would be based on expert opinion. However, in the absence of any evidence based guidelines expert opinion is the best option. Any guidance issued should be consistent with the MHRA advice and would be superseded should more robust guidance emerge from a recognised body.