NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

Review of Clinical Guideline (CG75) – Metastatic spinal cord compression: diagnosis and management of adults at risk of and with metastatic spinal cord compression

Background information

Guideline issue date: 2008

4 year review: 2012

National Collaborating Centre: Cancer

Review recommendation

- The guideline should not be updated at this time.

- The guideline should cross refer to the new Technology Appraisal: Bone metastases from solid tumours – Denosumab (expected date of issue: September 2012) that was previously not mentioned in the guideline.

Factors influencing the decision

Literature search

1. Through an assessment of abstracts from a high-level randomised control trial (RCT) search, new evidence was identified relating to the following clinical areas within the guideline:
    - Treatment of spinal metastases and metastatic spinal cord compression:

    - Treatments for painful spinal metastases (bisphosphonates, radiotherapy, vertebroplasty and kyphoplasty)
    - Care of the threatened spinal cord in patients with metastatic spinal cord compression
    - Case selection for definitive treatment of metastatic spinal cord compression
    - Surgery for the definitive treatment of metastatic spinal cord compression
- Supportive care and rehabilitation

2. No new evidence was identified in these areas which would invalidate the current guideline recommendations.

3. However, the guideline will need to cross refer to a new technology appraisal that is expected to publish in September 2012: Bone metastases from solid tumours - Denosumab.

4. From initial intelligence gathering, qualitative feedback from other NICE departments, the views expressed by the Guideline Development Group, as well as the high-level RCT search, an additional focused literature search was conducted for the following clinical area:
    - Surgery for the definitive treatment of metastatic spinal cord compression (minimally invasive spinal fixation)

5. The identified new literature included small numbers of patients and did not include comparator groups. As such, this new evidence may not be significant enough to warrant updating the guideline at this point. This area will be examined again in the next review of the guideline.

6. Eight clinical trials (publication dates unknown) were identified focusing on bisphosphonates in treating painful spinal metastases; radiotherapy for treatment of metastatic spinal cord compression and surgical treatment of metastatic spinal cord compression. However, at this time

it is unclear whether the ongoing clinical trials will have any impact on the guideline recommendations in the future.

Guideline Development Group and National Collaborating Centre perspective

7. A questionnaire was distributed to GDG members and the National Collaborating Centre to consult them on the need for an update of the guideline. Seven responses were received with some respondents highlighting the publication of audits indicating experience of altered practice following publication of the guideline. One respondent suggested that minimally invasive spinal fixation is gaining popularity and may be useful in patients with metastatic spinal cord compression. This feedback contributed towards the development of the clinical question for the focused search.

8. The majority of respondents felt that there is insufficient variation in current practice and minimal new evidence to warrant an update of the current guideline.

Implementation and post publication feedback

9. In total 15 enquiries were received from post-publication feedback, most of which were routine.

10. Feedback from the NICE implementation team indicated that there has been an increase in the number of decompression of thoracic spinal cord procedures conducted in secondary care in England between 2003/04 and 2010/11.

11. No new evidence was identified through post publication enquiries or implementation feedback that would indicate a need to update the guideline.

Relationship to other NICE guidance

12. NICE guidance related to CG75 can be viewed in Appendix 1.

Summary of Stakeholder Feedback

Review proposal put to consultees:
The guideline should not be updated at this time.
The guideline will be reviewed again according to current processes.

13. In total ten stakeholders commented on the review proposal recommendation during the two week consultation period. The table of stakeholder comments can be viewed in Appendix 2.

14. Five stakeholders agreed and five stakeholders disagreed with the review proposal.

15. Stakeholders that disagreed with the review proposal commented that:
    - The guideline does not provide recommendations on pain management. However, the guideline provides recommendations on analgesia for treatment of painful spinal metastases and rehabilitation and supportive care services. Through the review of the guideline no evidence was found in these areas that would invalidate current recommendations and it was concluded that these topics do not need to be updated at this time.
    - Treatment with corticosteroids should start while metastatic spinal cord compression is being confirmed or refuted. However, during the development of the guideline the GDG carefully considered the use of steroids in the management of spinal cord compression. They identified very little evidence except that patients given steroids pre-operatively have better outcome than those that do not. Beyond this evidence the GDG concluded that there is a great deal of opinion and personal practice but nothing which the GDG could reach an evidence based conclusion or consensus on. The GDG

also concluded that a critical step in diagnosing and effectively treating spinal cord compression is urgent MRI which should be done as soon as possible according to clinical need without temporizing by steroids. If MRI is done immediately and a sound radiological diagnosis reached then steroids are recommended.

Anti-discrimination and equalities considerations

16. No evidence was identified to indicate that the guideline scope does not comply with anti-discrimination and equalities legislation. The original scope is inclusive of adults with metastatic spinal disease at risk of developing metastatic spinal cord compression, adults with suspected and diagnosed spinal cord and nerve root compression due to metastatic malignant disease and adults with primary malignant tumours (for example, lung cancer, mesothelioma or plasmacytoma) and direct infiltration that threatens spinal cord function.

Conclusion

17. Through the process, new literature was identified focusing on the use of minimally invasive surgical techniques for metastatic spinal cord compression. However, as the identified trials were small with no comparator groups, this new evidence may not be significant enough to warrant updating the guideline at this point.

18. One ongoing related Technology Appraisal was also identified: Bone metastases from solid tumours – Denosumab (expected date of issue: September 2012). Therefore, there needs to be consideration of cross-referral to this Technology Appraisal when it is published.

19. No additional areas were identified which would indicate a significant change in clinical practice. There are no factors described above which would invalidate or change the direction of current guideline recommendations. The Metastatic Spinal Cord Compression guideline should not be updated at this time.

Relationship to quality standards

20. This topic is part of the library of NICE Quality Standard NHS healthcare topics.

21. This topic is not currently related to a published quality standard or a quality standard in development.

Mark Baker – Centre Director
Louise Millward – Associate Director
Emma McFarlane – Technical Analyst

Centre for Clinical Practice
10 July 2012

Appendix 1

The following NICE guidance is related to CG75:

Guidance	Review date
IPG12: Percutaneous vertebroplasty, 2003.	Review date: TBC.
CG7: The use of pressure relieving devices for the prevention of pressure ulcers in primary and secondary care, 2003.	Review decision date: May 2011. The guideline is currently being updated and will be amalgamated with the update of CG29 Pressure ulcers: the management of pressure ulcers in primary and secondary care, under a single scoping process.
CG29: The management of pressure ulcers in primary and secondary care, 2005.	Review decision date: May 2011. Following the review decision, this guideline is currently being updated.
NICE cancer service guidance: Improving supportive and palliative care for adults with cancer, 2004.	Review date: TBC.
CG23: Management of depression in primary and secondary care, 2004.	This guidance has been replaced by CG90 Depression in adults (update), 2009 which is currently under review (expected review decision date: October 2012).
IPG166: Balloon kyphoplasty for vertebral compression fractures, 2006.	Review date: N/A.
CG46: Venous thromboembolism	This guidance has been replaced by

(surgical), 2007.	CG92: Venous thromboembolism – reducing the risk, 2010. Next review date: January 2013.
CG49: The management of faecal incontinence in adults, 2007.	Next review date: June 2013.
CG58: Prostate cancer: diagnosis and treatment, 2008.	Review decision date: July 2011. Following the review decision, an update of this guideline is currently in the process of being scheduled into the work programme. Expected publication date: December 2013.
Related NICE guidance in progress	
Technology Appraisal: Bone metastases from solid tumours - Denosumab.	Expected publication date: September 2012.

Appendix 2

National Institute for Health and Clinical Excellence

Metastatic spinal cord compression
Guideline Review Consultation Comments Table
6 – 20 June 2012

Stakeholder	Agree with proposal not to update?	Comments	Comments on areas excluded from original scope	Comments on equality issues	Responses
Yorkshire Cancer Network	Yes	No issues with review	Nil	Nil	Thank you for your comment.
St James' University Hospitals NHS Trust	Yes	No issues with review	Nil	Nil	Thank you for your comment.
The British Association of Spinal Surgeons (BASS)	Yes	The new developments either reinforce or are not sufficiently certain to warrant changes to the guidelines at this time.	Relevant areas have been assessed.	Not relevant	Thank you for your comment.
The British Association of Spinal Surgeons (BASS)		Thank you I have studied this document and see no obvious problems with surgical component			Thank you for your comment.
British Pain Society	No	Pain is a significant symptom in these patients and the main reason why mobilisation is restricted if there is no loss of motor power. There has been mention of various options for MSCC, but pain management in these patients is not discussed. Much as medications like bisphosphonates and interventions	There is not much importance given to the role Pain and Palliative Care services play in managing these patients. Patients are to have the full benefit of specialist pain services and also the full		Thank you for your comments. The guideline provides recommendations on analgesia for treatment of painful spinal metastases and rehabilitation and supportive care services. Through the review of the guideline no evidence was found

		like vertebroplasty may help with the pain, the use of neuropathic agents and pain interventional procedures are also to be considered in alleviating the pain and symptoms in these patients.	complement of supportive care provided by palliative care services at the time of diagnosis, if patient has not already established contact during their cancer journey. Once the "active" management of these conditions are over, the rehabilitation process benefits from continuing input from the pain and palliative care services, both in the hospital and in the community.		that would invalidate current recommendations in these areas and it was concluded that these topics do not need to be updated at this time.
Association for Palliative Medicine of Great Britain and Ireland	No		*We surveyed our membership and while supporting that no major revisions were required there were suggestions for three minor revisions.*		Thank you for your comment.
Association for Palliative Medicine of Great Britain and Ireland	No		*Corticosteroids 1.5.2.6 Unless contraindicated (including a significant suspicion of lymphoma) offer all patients with MSCC a loading dose of at least 16 mg of dexamethasone as soon as possible after assessment, followed by a short course of 16 mg*		Thank you for your comments. During the development of the guideline the GDG carefully considered the use of steroids in the management of spinal cord compression. They identified very little evidence except that patients given steroids pre-operatively have better outcome than those that do not (this is not dose dependant – the same

			dexamethasone daily while treatment is being planned. This can be read to suggest steroids should be delayed till actually "with MSCC" i.e. once proven by MRI, when I am sure the intent is for those potentially "with MSCC" i.e. suspected "after assessment" meaning that treatment should start while MSCC is being confirmed or refuted. I suspect the literature is not helpful in this regard, but we would start steroids pending MRI in view of the perceived acute benefit. I suspect most colleagues would do so too. It could be clearer if the phrasing was "*offer all patients suspected with MSCC...*"		results are seen with 16 and 100mg). Beyond this evidence the GDG concluded that in relation to steroid use there is a great deal of opinion and personal practice but nothing which the GDG could reach an evidence based conclusion or consensus on. The GDG also concluded that a critical step in diagnosing and effectively treating spinal cord compression is urgent MRI which should be done as soon as possible according to clinical need without temporizing by steroids. If MRI is done immediately and a sound radiological diagnosis reached then steroids are recommended. Through the review of the guideline no new literature relating to corticosteroids for treatment of MSCC was identified. This area will be examined again in the next review of the guideline.
Association for Palliative Medicine of Great Britain and Ireland	No		One of our members wrote "As a consultant in Specialist Palliative Care and as Specialist in Neuropathic pain management, I have a very special interest in		Thank you for your comments. During the development of the guideline the GDG carefully considered the use of steroids in the management of spinal cord compression. They identified

			this important topic. I wish to add that detection of or at least the clinical suspicion of 'epidural compression or impending spinal cord/Cauda-Equina compression' deserves a special mention. The key clinical features are as follows: Escalating spinal pain in a patient known to have spinal metastases; pain made worse by any attempted movement or straining/coughing etcetera; 'girdle distribution' pain [from the Dorsal spine] or 'sciatic distribution' pain [from the Lumbo-Sacral spine] in addition to the above; 'point tenderness' in the area of the spinal pain; normal neurological function. Once above is detected, immediate use of high dose Dexamethasone 8mg BD [with a PPI] can easily avert the development of overt spinal cord/ Cauda-		very little evidence except that patients given steroids pre-operatively have better outcome than those that do not (this is not dose dependant – the same results are seen with 16 and 100mg). Beyond this evidence the GDG concluded that there is a great deal of opinion and personal practice but nothing which the GDG could reach an evidence based conclusion or consensus on. The GDG also concluded that a critical step in diagnosing and effectively treating spinal cord compression is urgent MRI which should be done as soon as possible according to clinical need without temporizing by steroids. If MRI is done immediately and a sound radiological diagnosis reached then steroids are recommended. Through the review of the guideline no new literature relating to corticosteroids was identified. This area will be examined again in the next review of the guideline.

			Equina compression and pave the way for a safe radiotherapy regime if subsequently proven on an MRI of the spine."		
Association for Palliative Medicine of Great Britain and Ireland	No		"*Every secondary or tertiary care centre should have an identified lead healthcare professional for MSCC (who is usually, but not necessarily, medical) whose responsibilities include...."* This function is better performed by a team including a medical and a nursing members and so may better be phrased (as per the co-ordinator function) "professionals"		Thank you for your comments. Through our review of the guideline we did not identify any literature relating to service configuration. This area will be examined again in the next review of the guideline.
RCN	Yes	The Royal College of Nursing agree that the guideline should not be updated at this time as new evidence does not support any changes to current guideline.	Nil	Nil	Thank you for your comment.
RCN		We agree that the guideline should cross refer to the new Technology Appraisal: Denosumab for the treatment of bone metastases from solid tumours and multiple myeloma			Thank you for your comment.

		(expected date of issue: June 2012), which was previously not mentioned in the guideline.			
GDG member		As previous Lead Clinician for this guideline I have taken the opportunity this review has provided to discuss at length with relevant colleagues whether there is sufficient new evidence, or problems with the previous guidance to suggest an update would be worthwhile or necessary. The overwhelming view is that the GL remains fit for purpose without review I have not therefore submitted more detailed comment. I would be happy to participate in review of comments if felt helpful. I anticipate that in a further four years time a review will prove necessary.			Thank you for your comment.
Ferring	No	Ferring Pharmaceutical supports the proposed update of the guidelines following considerable advances in the successful management of actual impending spinal cord compression in metastatic prostate cancer since 2008. In order for NICE to give guidance reflective of all evidence and	Ferring pharmaceuticals Ltd suggests that all modalities of treatment are reviewed including androgen deprivation therapy with a GnRH antagonist, such as degarelix, for patients with metastatic prostate cancer at risk of spinal	Ferring is aware that there is considerable variation within the UK regarding best practice in the management of metastatic prostate cancer,	Thank you for your comments. CG75 covers the diagnosis and management of adults at risk of and with metastatic spinal cord compression. Treatment and management of prostate cancer is outwith the scope of CG75 and is covered in CG58: Prostate cancer: diagnosis and

		changes in practice since 2008, the update will be welcomed by clinicians and patients alike to offer the best clinical outcome.	cord compression. In February 2009, degarelix was granted a licence by the EMEA for use adult male patients with advanced hormone dependent prostate cancer. EAU guidelines 2011 state *"The rapid and effective castration of LHRH antagonists plays an important role in patients with symptomatic metastatic disease (bone metastases, neurologic symptoms due to impending spinal cord compression, subvesical obstruction."* Thus since 2008, significant positive opinion from recognised bodies (EAU / SMC), clinical evidence and evidence of regional variation suggest that appraisal of degarelix by NICE is warranted in this indication. NICE is currently considering degarelix for technology appraisal following our submission for CG58 update, based	including inequality concerns with regard to regional variations in the access to degarelix (GnRH antagonist), which can be used in the acute setting to rapidly reduce testosterone and PSA without the risk of flare, which is commonly seen with agonists. It has been advocated for use by EAU (Guidelines 2011 / 2012), the London Cancer New Drugs Group (Workplan v5.0 2011) and IPNTS (April 2011). NECDAG has approved the use of degarelix in all patients	treatment, 2008 which is currently undergoing an update.

			the above.	with a PSA>20 . in addition, around 70 formularies in the UK are able to prescribe degarelix – restrictions vary but always include " at risk" patients(Ferring data on file 2012)	
Ferring	No	Ferring pharmaceuticals would also like to suggest that the most common primary tumours linked to SpCC should be listed separately within the guidelines as the management of spinal secondaries eg. breast cancer and prostate cancer may be very different, especially regarding medical therapies to complement surgery or radiotherapy. This may give clinicians additional clarity with regard to the optimum management of their patients.	Classification of management pathways specific to primary cancers were not addressed in 2008 and should be in 2012 to reflect current clinical practice and optimise patient safety and outcomes. This will also reflect the oncology environment moving towards tailored therapy.	The lack of classification and NICE endorsement means that clinicians and patients may not be able to gain access to medicines which could improve clinical outcomes. Degarelix is such a medicine. It is currently prescribed in the UK and often used in hormone sensitive prostate cancer	Thank you for your comments. This guideline scope covers the diagnosis and management of adults at risk of and with metastatic spinal cord compression and includes the following groups: • Adults with metastatic spinal disease at risk of developing metastatic spinal cord compression. • Adults with suspected and diagnosed spinal cord and nerve root compression due to metastatic malignant disease. • Adults with primary

				patients at risk of SpCC.	malignant tumours (for example, lung cancer, mesothelioma or plasmacytoma) and direct infiltration that threatens spinal cord function. Treatment and management of specific cancers are outwith the scope of this guideline.
Ferring	No	Ferring pharmaceuticals believes that regional or hospital protocols in the diagnosis and management of metastatic prostate cancer are hugely variable but have also superseded the guidelines of 2008.	Ferring believes the management of SpCC in prostate cancer should be captured and clarified within new guidelines. In addition, imaging (MRI / targeted CT) and additional biochemistry, such as alkaline phosphatase, should be evaluated for guidance with regard to all patients with metastatic prostate cancer present. Improved management of this advanced stage of disease could lead to avoidance of actual SpCC and earlier appropriate management. Supportive evidence for degarelix suggest that	Several centres of excellence recognise the need for additional investigations in at risk patients, however due to costs or availability of scanning / biochemistry, there in inequality in terms of regional variations in the level of service for patients.	Thank you for your comment. CG75 covers the diagnosis and management of adults at risk of and with metastatic spinal cord compression. Treatment and management of prostate cancer is outwith the scope of CG75 and is covered in CG58: Prostate cancer: diagnosis and treatment, 2008 which is currently undergoing an update.

			decreases in alkaline phosphatase levels are maintained for longer compared to leuprorelin (a useful predictor of advancing bony disease) *Schroder et al BJUI 2010).*		
Ferring	No	Ferring pharmaceuticals would support a revision of the current guidelines to reflect current practice that spinal cord compression is not treated in a mutually exclusive manner. Consideration should be given to medicines such as degarelix, which complement radiotherapy, surgery or bisphosphonates and new agents such as denosumab, which we note is undergoing a technology assessment.	As before, we support the inclusion of other treatment modalities such as androgen deprivation therapy with a GnRH antagonist, such as degarelix,. In February 2009, degarelix was granted a licence by the EMEA for use adult male patients with advanced hormone dependent prostate cancer. The clinical effectiveness in rapidly reducing testosterone (and PSA) vs agonist (leuprorelin) was demonstrated in a phase III clinical trial in which >95% of patients on degarelix achieved castrate levels of testosterone within 3 days. *Klotz L et al. BJU Int 2008*	Ferring is aware that there is considerable variation within the UK regarding best practice in the management of metastatic prostate cancer, including inequality concerns with regard to regional variations in the access to degarelix (GnRH antagonist), which can be used in the acute setting to rapidly reduce testosterone and PSA without the risk of flare, which is	Thank you for your comment. CG75 covers the diagnosis and management of adults at risk of and with metastatic spinal cord compression. Treatment and management of prostate cancer is outwith the scope of CG75 and is covered in CG58: Prostate cancer: diagnosis and treatment, 2008 which is currently undergoing an update. In terms of denosumab, the guideline will cross-refer to this Technology Appraisal when it is published.

			This is unique to degarelix, and in patients at risk of, or with actual spinal cord compression, removing the tumour driver is essential to reduce the risk of further decline. In addition to this, there is no risk of tumour "flare" as seen with agonist therapy, which may worsen the SpCC, The use of Degarelix also avoids the need for antiandrogen cover to avoid the testosterone surge associated with LHRH agonists, which is particularly relevant for bed bound patients as some antiandrogens increase the risk of VTE. Thus there is a safety profile advantage to using degarelix in this patient population. *Bicalutamide Summary of Product Characteristics. Luton: AstraZeneca UK Ltd. (2008).* *Cyprostat Summary of Product Characteristics. Newbury: Bayer plc. (2011).*	commonly seen with agonists. As an example, LCNDG approved degarelix for use in September 2011 as follows :"*Advanced prostate cancer for subgroup with areas of critical metastases including those with established or incipient spinal cord compression are or at risk of urinary retention using standard LHRH & those where there is need to avoid prothrombotic risk of steroidal anti-androgens".*	

			Safety data does not suggest an increased risk of DVT when using degarelix, nor does it interact with warfarin. *Firmagon SPC West Drayton. Ferring (2011*)		
Ferring	No				Noted.
British Society of Rehabilitation Medicine	No	Benefit for rehabilitation extends to carers and family. This includes education as well as counselling.	nil	nil	Thank you for your comment. Through the review of the guideline no literature was identified relating to education, counselling or communication and information resources for patients, carers, family members and healthcare professionals. This area will be examined in the next review of the guideline.
British Society of Rehabilitation Medicine		Section on rehabilitation is far too brief - benefits of rehabilitation in this group extend far beyond pain and continence, to mobility (ambulant or acquiring wheelchair skills), sexual issues, employment, and skin care.			Thank you for your comment. Through the review of the guideline one study was identified relating to supportive care and rehabilitation however, this study did not invalidate current recommendations. This area will be examined in the next review of the guideline.
Royal College of Physicians (RCP)		The RCP wishes to endorse the submission of the British Society of Rehabilitation Medicine.			Thank you for your comment.