Medtronic
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NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Multiple Technology Appraisal (MTA)

Percutaneous vertebroplasty (PVP) and percutaneous balloon kyphoplasty (PERCUTANEOUS BALLOON KYPHOPLASTY (WITHOUT SENTING)) for the treatment of osteoporotic vertebral compression fractures (OVCFs)

Medtronic Response to NICE ACD (ID 308)

21 November 2012

Appraisal Committee Document	Medtronic's response
Key conclusions	
Percutaneous balloon kyphoplasty (without stenting) and Percutanteous vertebroplasty recommended ***only*** for OVCF people who: • have severe ongoing pain after a recent vertebral fracture (within 6 weeks) despite optimal pain management **and** • in whom the pain has been confirmed to be at the level of the fracture (by physical examination and imaging). 1.1. Page 3	Medtronic suggests to further clarify AC's recommendation by substituting "percutaneous balloon kyphoplasty" with "Percutaneous balloon kyphoplasty (without stenting)". This aims to ensure consistency with AC's recommendation in section 3.3 of the ACD, where the technology is featured as above and confirms which technology the body of evidence refers to. Therefore, Medtronic will refer to kyphoplasty as percutaneous balloon kyphoplasty (without stenting).
The technology "no specific claim of innovation	Percutaneous balloon kyphoplasty (without stenting) should not be considered as a variation of percutaneous vertebroplasty. It is best referred to as a relevant incremental innovation. The innovative step of using the balloon to induce spinal realignment with angular correction, coupled

was made” Page 44 Kyphoplasty (without stenting) is a variation of vertebroplasty 3.3. Page 5	with pain relief is specific to Percutaneous Balloon Kyphoplasty (without stenting). Furthermore, balloon cavity creation and crushed trabecular bone border coupled with low pressure cement injection minimises the risk of the cement leakage. This step is related to the “improvement in biomechanical factors after treatment” referred by the AG as a possibility for the mortality benefit. In fact, according to the *academic-in-confidence* evidence submitted along with comments to the AG report (Supplementary references, Edidin 2012 morbidity), a credible biological plausibility for the mortality benefit is emerging, consistent with hypothesis from clinical specialists heard by the committee. While Medtronic agrees there may still be unobserved, uncontrolled confounding, these relative differences in morbidity risks contribute to understanding the mortality risk differences, which are best explained by the surgical approach. In summary, Medtronic requests the technology description is corrected for the final appraisal document, to percutaneous balloon kyphoplasty (without stenting) and without stating this technology is a variation of vertebroplasty.
Kyphon Percutaneous Balloon Kyphoplasty (without stenting) kit (Medtronic) is available in the UK for kyphoplasty (…) 3.4 Page 5	Medtronic would like to clarify that Kyphon ActivOs cement is not part of the Kyphopak (single use sterile pack), but rather supplied as a separate component.
Adverse Reactions Adverse reactions from vertebroplasty and kyphoplasty	Medtronic would further reinforce that cement leakages of clinical relevance can be minimised by

relate primarily to cement leakage, particularly for vertebroplasty. The Committee concluded that cement leakage associated with vertebroplasty and kyphoplasty was manageable if a skilled clinician with specialised training in these procedures performs the operation. In addition, the balloon can rupture in kyphoplasty which can result in the retention of balloon fragments within the vertebral body. 3.7 Page 6 4.3.7 page 39	choosing higher viscous cements, creating a cavity and crushed trabecular bone border. With respect to the reference made to risk of balloon rupture (4.3.7), Medtronic would like to report a complaint ratio of .54% and an adverse event ratio of .011%, specific to their Kyphon Balloon (from our internal report system - March 2007 to November 2012).
Evidence for clinical effectiveness **Availability, nature and quality of evidence** The FREE study included less than 80% of randomised patients in its final analysis, had an imbalance in drop-outs by treatment arm, and reported	Concerning the largest RCT submitted as evidence of percutaneous balloon kyphoplasty (without stenting) compared to optimal pain management (FREE study), further explanation seems warranted as well as highlighting inaccuracies in the ACD : 78% follow-up at 12-months and 77% at 24-months is anticipated for this elderly patient population. Contrary to statement that outcomes were reported selectively, all primary and secondary

outcomes selectively. The Blasco, FREE and VERTOS II trials had substantial numbers of patients crossing over (changing treatment arms). 4.1.2 Page 7	outcomes per study protocol were reported in the following papers for publication: • "FREE 1 year results" (Wardlaw, Lancet 2009), • "FREE 2 year results" (Boonen, JBMR 2011) and • "FREE surgical" (van Meirhaeghe 2012, in peer-review process, submitted to AC by Medtronic along with comments to AG report, under "supplementary refs" as academic in confidence) Cross-over in FREE study was less than 10% and an intent to treat analysis was conducted leaving them in the control arm.
Mortality benefit Mortality data available from a large study based on US Medicare registry data that followed patients for up to 4 years indicated a statistically significant mortality benefit with narrow confidence intervals, with both vertebroplasty and kyphoplasty compared with optimal pain management. The Committee noted these results, which were substantiated by 5 year mortality data from the Medicare registry as well as mortality data from a smaller German study. 4.3.5 page 37	Further to the AG comment on the possibility that improvement in biomechanical factors after treatment improves survival, please refer to Medtronic's comment above, relating to section 3.3. of the ACD.

The Assessment Group stated that, apart from the possibility of uncontrolled confounding, these studies raise the possibility that improvement in biomechanical factors after treatment improves survival 4.1.21 Page 17 4.3.2 Page 35	