

**NATIONAL INSTITUTE FOR HEALTH AND
CLINICAL EXCELLENCE**

Multiple Technology Appraisal (MTA)

**Percutaneous Vertebroplasty (PVP) and
Balloon Kyphoplasty (BKP) for the
treatment of Osteoporotic Vertebral
Compression Fractures (OVCFs)**

February 2012

Executive summary

Patients with osteoporotic vertebral fractures (OVCFs) who are treated with Balloon Kyphoplasty (BKP) have a reduced all-cause mortality compared with the comparators under consideration in this MTA, namely non invasive management (NSM) and percutaneous vertebroplasty (PVP). The adjusted life expectancy of patients with vertebral fractures is +115% for BKP vs NSM and +34% for BKP vs PVP.

The clinical and cost effective evidence for NSM illustrates limited improvement in quality of life, functional disability related to spinal deformity and mortality risk for OVCF patients. In contrast, the overall body of evidence for BKP consistently shows a significant benefit by improving mortality risk, function and Health-Related Quality of Life (HRQoL) in this patient group. This benefit is derived from BKP's mechanism of action, the reproducibility offered by its standardisation and deployment in treating eligible OVCF patients.

BKP may be regarded as a worthy investment of NHS resources for hospitalised OVCF patients. The greater challenge relates to adopting imaging techniques to allow more accurate and timely diagnosis of symptomatic OVCFs and, in turn, optimisation of their treatment pathway.

No head-to-head randomised controlled trials have been published comparing BKP to PVP on HRQoL. Placebo-controlled studies comparing PVP to a sham procedure (1;2) do not provide appropriate evidence for informing the absolute efficacy of BKP.

The UK approved name, brand name, marketing status and principal mechanism of action of the proposed technology.

Kyphon[®] Balloon Kyphoplasty (BKP) is the approved (brand) name for this technology and is currently promoted in the NHS.

BKP is a minimally invasive procedure designed for the reduction and fixation of pathological vertebral fractures.

The mechanism of action of Balloon Kyphoplasty is related to the established AO¹ Principles of Surgical Fracture Management:

- 1) Anatomical Reduction: by the use of Inflatable Bone Tamps (IBT) for optimal fracture reduction
- 2) Stable internal fixation: injection of bone cement into vertebral body creates a cast thus providing stabilisation
- 3) Preservation of blood supply: the procedure performed minimally invasively
- 4) Safe and early mobilisation: the controlled and predictable injection of cement, no muscle stripping or bone removal and rapid hardening of cement, allows BKP patients to be immediately load-bearing.

The procedure for the use of this technology involves the bilateral insertion of two balloons into the vertebral body. These are then slowly inflated until the normal height of the vertebral body is restored or the balloons reach their maximum volume. When each balloon is deflated and removed, the cavity is filled with bone cement. The creation of a cavity within the vertebral body

¹ Arbeitsgemeinschaft für Osteosynthesefragen (Association for the Study of Internal Fixation) Percutaneous Vertebroplasty (PVP) and Balloon Kyphoplasty (BKP) for the treatment of Osteoporotic Vertebral Compression Fractures (OVCFs)

allows for the insertion of a pre-known volume of more viscous cement at lower pressure, reducing the risk of cement extravasations.

The formulation(s), strength(s), pack size(s), maximum quantity(ies), anticipated frequency of any repeat courses of treatment and acquisition cost.

As this is a medical device technology, it comes in a sterile, standard pack for single use only; therefore formulation, strength, dosage etc. is not applicable (Supplementary Document 1).

The indication(s) and its restriction(s).

Inflatable Bone Tamps (IBT) – Indications for Use

Kyphon[®] Xpander[™] and Kyphon[®] Express[™] Inflatable Bone Tamps (IBT) are intended to be used as conventional bone tamps for the reduction of fractures and/or creation of a void in cancellous bone in the spine (including use during balloon kyphoplasty with Kyphon[®] HV-R[®] Bone Cement), hand, tibia, radius, and calcaneus.

Kyphon[®] HV-R[®] Bone Cement – Indications for Use

Kyphon[®] HV-R[®] Bone Cement is indicated for the treatment of pathological fractures of the vertebral body due to osteoporosis, cancer, or benign lesions using a balloon kyphoplasty procedure.

The recommended course of treatment.

The recommended course of treatment is as presented in the product brochure (Supplementary Document 1). This brochure illustrates a Kyphopak comprising two Kyphon[®] Xpander[™] IBTs and associated accessories. These are the components of the standardised procedure for which the evidence here presented was developed.

The main comparator(s).

Non-invasive management (NSM) or percutaneous vertebroplasty (PVP).

Key clinical evidence

In the absence of published head-to-head RCTs, key RCT clinical evidence comes from an indirect comparison between two separate RCTs ; namely FREE (4) and VERTOS II (5). These are the trials that are used to provide clinical evidence for the cost effectiveness modelling. The rationale behind the use of these two trials is a combination of the following observations:

- 1) FREE and VERTOS II represent the largest trials undertaken to assess the clinical effectiveness of BKP and PVP respectively.
- 2) Despite potentially relevant discrepancies in the two patientpopulations (cf. section 6.2.4), these trials still represent the most comparable osteoporotic patient populations studied.
- 3) The overall study quality.

In addition a total of 18 comparative non-RCT studies were retrieved for the systematic review. Finally, a retrospective US mortality study (Edidin (6)) reviewed the U.S. Medicare dataset (2005-2008) for the mortality risk of patientswith VCFs undergoing NSM, BKP or PVP with the aim of determining any association between surgical treatment or non-surgical treatment and survivorship.

Main results from FREE RCT evidence from 24 month follow up (4):

- 1) BKP treated patients have shown a significant gain over non-operated patients in physical function (SF-36 PCS 3.24 points, 1.47–5.01; $p<0.05$) and health-related quality of life (EQ-5D 0.12 points, 0.06-0.18; $p<0.05$), disability (RMDQ -3.01points, 4.14–1.89; $p<0.05$), and pain (VAS -1.49 points, 1.88-1.10; $p<0.05$) over 24 months.
- 2) Furthermore, BKP did not increase the risk of additional vertebral fractures compared to NSM (3.4% difference, 16.5-9.9; $p=0.68$). In year 2 of follow-up, the overall frequency of patients with AEs and serious AEs (SAEs) was similar between treatment groups.

Main results from relevant non-RCT evidence

- 1) BKP patients have a reduced all-cause mortality compared to both NSM and PVP (6). Of the 858,978 Medicare VCF patients analysed, those who received surgery (n=182,946) were 37% less likely to die than those who were managed non-surgically (n=676,032) at 4 years. Life expectancy of VCF patients was estimated using a parametric Weibull survival model, with an adjusted life expectancy of +115% for BKP vs NSM and +34% for BKP vs PVP (9)
- 2) Systematic reviews and meta-analysis (7) show that kyphotic correction is more easily attainable with BKP than any other treatment option, however probably because review of disease background has not been performed its importance has been disregarded (8).

Economic evaluation

BKP has shown to be a cost-effective option in hospitalised OVCF in the UK when compared both to NSM and PVP.

Additional considerations regarding clinical and cost effectiveness

MTA methods are best applied to pharmacological treatments where large RCTs can be conducted, where pharmacokinetic studies inform patients' group profiling and subgroup analysis as well as generate hypothesis for the interpretation of clinical data. These are critical building blocks for the understanding and demonstration of incremental effectiveness. These basic research steps are more often absent in the development of medical devices and surgical procedures especially for the non-active spinal implants . At least 2 HTA reports have highlighted the lack of evidence on disability related to kyphotic deformity. Notably, the lack of data correlating spinal deformity with clinical and patient reported outcomes has been referred to, even if epidemiological studies have been continuously showing this. It is extremely onerous and difficult to conduct population-based studies on the impact of biomechanical variations. This is why Medtronic considers current best available evidence to be the available RCTs with active comparators along with higher-quality real-world data.

Medtronic has devoted considerable resources to the basic understanding of the patient experience with vertebral fractures and spinal deformity. This effort has so far translated into the Outcome Measure Strategy for Kyphosis and Patient-Reported Outcome Measure dimensional analysis with data from the FREE study; the first qualitative study confirming the impact of kyphosis on patients with OVCFs is clinically relevant. Considering the clinical burden of OVCFs and the body of evidence on effectiveness and cost effectiveness for BKP, despite current evidence gaps identified, BKP should be made available to OVCF patients that have been shown to benefit from the intervention.