Date: May 21 2024

To: **Robert McDonough, MD**
Executive Director of Clinical Policy Research & Development
Aetna
1000 Middle Street MC17
Middletown, CT 06457

Subject: Aetna Back Pain – Invasive Procedures coverage policy number 0016

Dear Dr. McDonough,

Thank you for responding to our letter regarding Aetna Back Pain—Invasive Procedures coverage policy number 0016. We are disappointed with Aetna's decision not to amend this policy. We have analyzed the evidence you presented and would like to present a counterargument.

Firstly, we would like to highlight that the clinical studies you reference (Buchbinder et al. [2009]; Clark et al. [2016]; Kallmes et al. [2009]; Firanescu et al. [2018]; Buchbinder et al. [2018]) only provide clinical data on the vertebroplasty procedure and do not provide any evidence on kyphoplasty or mechanical augmentation.

Next, would like to direct your attention to a large body of evidence which:

A) supports earlier interventional treatment for patients with VCFs who fall outside the restriction of *"minimum 6 weeks of optimal non-invasive therapy".*
&
B) supports interventional treatment for fractured vertebrae that fall outside the very restrictive criteria of *"at least 25 % height loss but is at least 1/3 of its original height".*

While it is, of course, acknowledged by the medical community that non-surgical management (NSM) remains a treatment option for VCFs, this approach is not always appropriate for numerous reasons, which is why we raise concerns regarding the 6-week treatment delay your policy currently forces on this cohort. Practitioners may make the clinical decision that NSM for 6 weeks is not appropriate for their individual patient for one or several reasons listed below:

- The patient may have an impaired healing response (e.g., Diabetes mellitus, Cushing's syndrome, etc.)
- The patient may have spinal deformity, which is not corrected with NSM. This kyphosis can impact mobility, predispose patients to falls (which is of particular concern in elderly patients), and has a cosmetic impact, affecting psychosocial wellbeing and self-esteem[1].
- The patient may be susceptible to the risks associated with prolonged bedrest/immobilisation, to name a few, venous thromboembolism, reduced cardiac reserve, orthostatic hypotension, muscle atrophy, contractures, degenerative joint disease, pressure sores, constipation and worsening of osteoporosis[2].
- The patient may not be suitable for 6 weeks of NSAIDs, e.g., those with a history of GI ulceration. This is especially a concern in the elderly, who are susceptible to NSAID-induced AKIs[3].
- The patient may not be a candidate for opioid therapy. This includes patients with a history of substance misuse and addiction, who if prescribed opioids generally develop tolerance

and dependence, requiring higher doses more frequently[4]. Opioids can be incredibly sedative which can prevent those with VCFs in the workforce from returning to many careers (e.g., driving, operating equipment etc.)[5]. Additionally, elderly patients are particularly at risk of adverse effects due to opioid use, including falls, respiratory depression, and agitation/behavioural disturbances[6].

- The patient may not be able to tolerate bracing. The use of thoracolumbar spine orthoses (TLSO) aims to maintain a relative extension locked position, limiting segmental motion and subsequently leading to fracture healing. However, several studies have shown that prolonged brace use may lead to diminished pulmonary capacity, skin breakdown, weakness of paraspinal musculature, and no significant difference in pain and functional outcomes between patients treated with or without a brace[7].

These are just some of the factors that a physician may need to consider before deciding whether their VCF patient is appropriate for 6 weeks of NSM, and we can see from these examples that the risks of prolonged NSM may outweigh the benefits of avoiding VA, especially when we considering the ultra-minimally invasive options there are currently available for VA.

The literature also supports our recommendation to remove this criterion. Several key studies support the use of VA for the early treatment of OVCFs with the key clinical benefits outlined below:

- VERTOS II trial [2012][8]: Fractures (mean onset 5.6 weeks) treated with surgical intervention had a significantly decreased VAS score when compared to NSM as early as 1 day post procedure and the result was sustained at 1 year. QoL questionnaires showed improved outcomes after VA compared to conservative treatment.
- VAPOUR trial [2016][9]: QoL outcomes improved at 6 months compared to control group when surgical intervention was performed within 3 weeks of fracture. Analysis of early surgical intervention (<3 weeks) shows clinically significant benefits exist, with reductions in pain scores.
- A randomized controlled trial from Yang, et al.[10] compared vertebroplasty versus conservative therapy in patients with vertebral fractures averaging 8.4 days and found that vertebroplasty produced faster and better pain relief and improved functional outcomes that were maintained at one year and had fewer complications.

Additionally, your response from November 2023 included the following comment, “Our policy reflects the view that conservative management be tried prior to consideration invasive procedures, given the potential for surgical complications.”. While there are surgical complications, when they are measure there are far less complications with vertebral augmentation than with conservative or non-surgical management. In addition to the conclusion of the randomized control trial by Yang, et. al.[10] mentioned directly above, a recent study by Liu et. al. that evaluated the clinical effectiveness and complication rates of kyphoplasty compared to conservative care and found that not only was kyphoplasty statistically significantly better at improving patients’ symptoms it was found to have significantly less complications at 1.72% as compared to NSM with complications found in 15.52% of the patients ($p < 0.05$)[11]. When measured in this study the complication rate of conservative care was nine times higher than the surgical complication rate[11].

Furthermore, Anselmetti et al. conducted a study using the RAND/UCLA Appropriateness Method (RAM) to assess the appropriateness of different treatment options for osteoporotic VCFs was assessed[12]. The aim of this study was to establish criteria for individually tailored treatment choice in patients with osteoporotic VCFs, by combining the evidence from clinical studies with the judgment of a multidisciplinary team of experts. The authors reported that the appropriateness of BKP was

considered highest for patients with a fracture of less than 6 weeks, highlighting the importance of treating early to correct segmental kyphosis[12]. Besides just pain relief, restoring the vertebral shape may be a treatment goal, and the opportunity to correct segmental kyphosis decreases with time.

Moreover, work conducted by Hirsch et al. aimed to develop a comprehensive clinical care pathway (CCP, see Figure 1) for VCFs[13]. A multispecialty expert panel (orthopedic and neurosurgeons, interventional radiologists and pain specialists) assessed the importance of signs and symptoms for the suspicion of VCF, the relevance of 5 diagnostic procedures, the appropriateness of vertebral augmentation versus nonsurgical management for 576 clinical scenarios, and the adequacy of 6 aspects of follow-up care [13]. The panel identified 10 signs and symptoms believed to be relatively specific for VFF. Vertebral augmentation was considered appropriate in patients with positive findings on advanced imaging and in whom symptoms had worsened and in patients with 2 to 4 unfavorable conditions (e.g., progression of height loss and severe impact on functioning). Supporting our argument, time since fracture was considered less relevant for treatment choice [13].

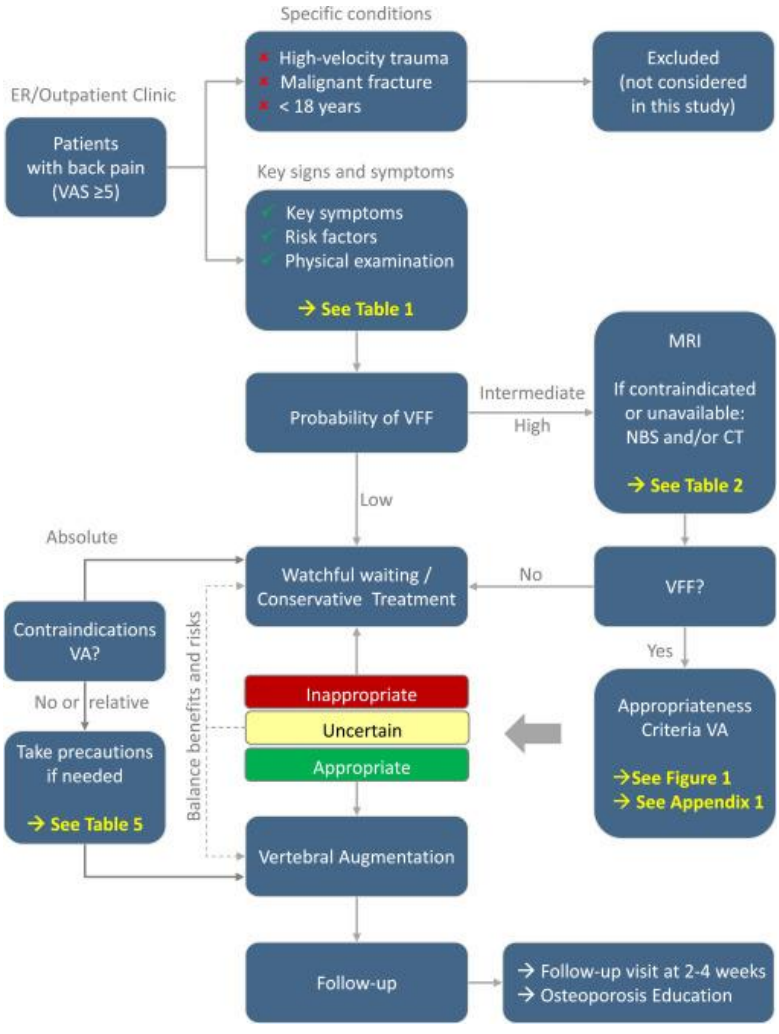

Fig. 1: CCP for the management of VCF. VAS, visual analogue scale; VFF, vertebral fragility fracture; MRI, magnetic resonance imaging; NBS, nuclear bone scan; CT, computed tomography; VA, vertebral augmentation [11].

In summary, there is a large body of evidence which supports earlier interventional treatment for patients with VCFs. Based on our review of the current body of literature, we ask that Aetna reconsider their decision to keep the requirement to provide 6 weeks of NSM.

Next, we would like to take this opportunity to ask Aetna to consider removal of the following restriction, *"not been extensively destroyed and is at least 1/3 of its original height".* Vertebra plana, also known as a pancake vertebra, is the term given when a vertebral body has lost almost its entire height anteriorly and posteriorly, representing a very advanced VCF. There are numerous studies conducted which suggest that it is safe and effective to treat these fractures with VA:

- Becker et al. [2008][16]: Researchers retrospectively reviewed and compared the efficacy of balloon kyphoplasty for vertebra plana. Restoration of the vertebral height was superior in patients with advanced vertebral collapse than with 'normal' osteoporotic fractures.
- Joyce et al. [2021][15]: In this review of 6 patients with vertebra plana osteoporotic compression fractures that had different size titanium expandable implants, it is clear that it is technically feasible to place these implants, even the larger 4.2 and 5.0 mm size, without any additional technical issues or risks compared to less severely collapsed vertebral fractures.
- Joyce et al. [2022][16]: This is a retrospective study that evaluated surgical versus non-surgical treatment of 100 patients followed for up to 6 years diagnosed with severe osteoporotic vertebral compression fractures (VCF). Fractures were classified by percent collapse of vertebral body height as "high-degree fractures" (HDF) (>50%) or vertebra plana (>70%). A total of 310 patients with VCF were reviewed, identifying 110 severe fractures in 100 patients. This large series, with follow-up up to 6 years, demonstrated that the more severe fractures respond well to different percutaneous cement augmentation procedures with reduction of pain without increased complications in a comparison to conservatively treated patients.

A number needed to treat (NNT) analysis of more than 2 million patients with VCFs revealed that just 15 patients need to be treated to save 1 life at 1 year[17]. This has an obvious clinically significant impact and given that all augmentation clinical trials are underpowered to detect a mortality benefit, this large dataset analysis reveals that vertebral augmentation provides a significant mortality benefit over nonsurgical management with a low NNT. To put this number into practical terms, in a study of patients taking aspirin for 1 year to prevent a first heart attack or stroke, a cardiovascular event was prevented for 1 person in a patient population of 1667, compared with 1 in 3000 for stroke[18].

We sincerely hope you analyse this evidence and reconsider your position on coverage policy number 0016. Additionally, it cannot be ignored that six medical specialty societies, comprised of physicians who regularly utilize and/or perform percutaneous vertebral augmentation procedures, support this request.

If you have any questions or comments related to this request. Please contact Ashley Maleki, Senior Manager of Health Policy and Economics at the Society of Interventional Radiology, at amaleki@sirweb.org.

Sincerely,

American College of Radiology (ACR)
American Society of Neuroradiology (ASNR)
American Society of Spine Radiology (ASSR)
International Pain and Spine Intervention Society (IPSIS)

References:

1. Koelé MC, Willems HC, Swart KMA, van Dijk SC, Lips P, de Groot LCPGM, van der Cammen TJM, Zillikens MC, van Schoor NM, van der Velde N. The association between hyperkyphosis and fall incidence among community-dwelling older adults. Osteoporos Int. 2022 Feb;33(2):403-411.
2. Dittmer DK, Teasell R. Complications of immobilization and bed rest. Part 1: Musculoskeletal and cardiovascular complications. Can Fam Physician. 1993 Jun;39:1428-32, 1435-7. PMID: 8324411; PMCID: PMC2379624.
3. Nash DM, Markle-Reid M, Brimble KS, McArthur E, Roshanov PS, Fink JC, Weir MA, Garg AX. Nonsteroidal anti-inflammatory drug use and risk of acute kidney injury and hyperkalemia in older adults: a population-based study. Nephrol Dial Transplant. 2019 Jul 1;34(7):1145-1154.
4. Deyo RA, Von Korff M, Duhrkoop D. Opioids for low back pain. BMJ. 2015 Jan 5;350:g6380.
5. Cameron-Burr KT, Conicella A, Neavyn MJ. Opioid Use and Driving Performance. J Med Toxicol. 2021 Jul;17(3):289-308.
6. Dufort A, Samaan Z. Problematic Opioid Use Among Older Adults: Epidemiology, Adverse Outcomes and Treatment Considerations. Drugs Aging. 2021 Dec;38(12):1043-1053.
7. Agabegi, Steven S. MD; Asghar, Ferhan A. MD; Herkowitz, Harry N. MD. Spinal Orthoses. American Academy of Orthopaedic Surgeon 18(11):p 657-667, November 2010.
8. Klazen CA, Lohle PN, de Vries J, Jansen FH, Tielbeek AV, Blonk MC, Venmans A, van Rooij WJ, Schoemaker MC, Juttmann JR, Lo TH, Verhaar HJ, van der Graaf Y, van Everdingen KJ, Muller AF, Elgersma OE, Halkema DR, Fransen H, Janssens X, Buskens E, Mali WP. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. Lancet. 2010 Sep 25;376(9746):1085-92.
9. Diamond T, Clark W, Bird P, Gonski P, Barnes E, Gebski V. Early vertebroplasty within 3 weeks of fracture for acute painful vertebral osteoporotic fractures: subgroup analysis of the VAPOUR trial and review of the literature. Eur Spine J. 2020 Jul;29(7):1606-1613.
10. Yang EZ, Xu JG, Huang GZ, Xiao WZ, Liu XK, Zeng BF, Lian XF. Percutaneous Vertebroplasty Versus Conservative Treatment in Aged Patients With Acute Osteoporotic Vertebral Compression Fractures: A Prospective Randomized Controlled Clinical Study. Spine (Phila Pa 1976). 2016 Apr;41(8):653-60. doi: 10.1097/BRS.0000000000001298. PMID: 26630417.
11. Liu Q, Cao J Kong JJ. Clinical effect of balloon kyphoplasty in elderly patients with multiple osteoporotic vertebral fracture. *Niger J Clin Pract* 2019; 22:289-92.
12. Anselmetti GC, Bernard J, Blattert T, Court C, Fagan D, Fransen H, Fransen P, Sabharwal T, Schils F, Schupfner R, Siddiqi MA, Stoevelaar H, Kasperk C. Criteria for the appropriate treatment of osteoporotic vertebral compression fractures. Pain Physician. 2013 Sep-Oct;16(5):E519-30.
13. Hirsch JA, Beall DP, Chambers MR, Andreshak TG, Brook AL, Bruel BM, Deen HG, Gerszten PC, Kreiner DS, Sansur CA, Tutton SM, van der Meer P, Stoevelaar HJ. Management of vertebral fragility fractures: a clinical care pathway developed by a multispecialty panel using the RAND/UCLA Appropriateness Method. Spine J. 2018 Nov;18(11):2152-2161. doi: 10.1016/j.spinee.2018.07.025. Epub 2018 Aug 7. PMID: 30096377.
14. Becker S, Tuschel A, Chavanne A, Meissner J, Ogon M. Balloon kyphoplasty for vertebra plana with or without osteonecrosis. J Orthop Surg (Hong Kong). 2008 Apr;16(1):14-9.
15. Joyce DM, Granville M, Jacobson RE. Re-expansion and Stabilization of Vertebra Plana Fractures Using Bilateral SpineJack® Implants. Cureus. 2021 Mar 11;13(3):e13839.
16. Joyce DM, Granville M, Berti A, Jacobson RE. Vertebral Augmentation Compared to Conservative Treatment of Vertebra Plana and High-Degree Osteoporotic Vertebral Fractures: A Review of 110 Fractures in 100 Patients. Cureus. 2022 Feb 8;14(2):e22006.
17. Hirsch JA, Chandra RV, Carter NS, Beall D, Frohbergh M, Ong K. Number Needed to Treat with Vertebral Augmentation to Save a Life. AJNR Am J Neuroradiol. 2020 Jan;41(1):178-182.
18. Antithrombotic Trialists Collaboration. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet* 2009;373:1849–60.