Purchasing Guidance: Considered Judgement Form

This form is a checklist of issues that may be considered by the Purchasing Guidance Advisory Group when making purchasing recommendations

Meeting Date:	**30 August 2017**
Topic:	**The effectiveness of injection of botulinum neurotoxin to the lower back as a form of interventional pain management**

Purpose

This purchasing guidance (considered judgement) document accompanies a systematic review commissioned by ACC Research from the International Centre for Allied Health Evidence (ICAHE), University of South Australia.

The objective of this review is to update and summarise the evidence regarding:

- Efficacy of botulinum neurotoxin injections into the lower back in relieving pain and/or improving functional outcomes in patients with pain; and
- Safety of botulinum neurotoxin injections into the lower back

Botox injection for low back pain was not covered by the original IPM guidance released in 2005 because, at that time, no relevant research studies that met the IPM inclusion criteria were identified. In 2009 ACC commissioned Adelaide Health Technology Assessment (AHTA) to review the evidence for botox injections for chronic back pain and a further update of the IPM guidance was completed by ACC in 2011. The purchasing decision following those reviews was:

> Do not purchase botox injection for the routine treatment of low back pain.
>
> However, in rare circumstances where conventional treatment has failed, it may be considered on a case-by-case basis:
>
> - following a comprehensive pain assessment in consultation with a Senior Medical Advisor.
> - as part of a multidisciplinary rehabilitation and self-management plan.
>
> Appropriate outcome data must be collected. Providers must submit an end-of-care report to CSD to include appropriate clinical and functional outcome data.

The current review updates the evidence base with studies published since 2011.

Background

Botulinum neurotoxin acts to relieve lower back pain by temporarily relaxing overactive muscles which may be the source of the pain. It is also thought to act on pain by disrupting the neurotransmitters responsible for central and peripheral sensitisation, inflammation, and pain sensation (Sim, 2011; Patil et al, 2016). The interest in botulinum neurotoxin injections for the treatment of chronic pain is partly related to its relatively long duration of action compared with conventional therapies and its potential to provide pain relief to those that have failed to respond to first-line treatments (Chen 2012).

Botulinum neurotoxin is available in two serotypes, Type A (BoNT-A) and Type B (BoNT–B). BoNT-A is the most frequently used form and there are several preparations commercially available, each with unique

pharmacological profiles, side effects, and indications for use (Baizabal-Carvallo, Jankovic et al. 2011). Commercially available preparations include onabotulinumtoxinA (Botox®), incobotulinumtoxinA (Xeomin®), and abobotulinumtoxinA (Dysport®) (Patil, Willett et al. 2016). RimabotulinumtoxinB (Myobloc®) is a commercially available BoNT-B preparation and has been used to treat neurological, cosmetic, autonomic, and pain disorders (Baizabal-Carvallo, Jankovic et al. 2011). Medsafe datasheets are available for Botox®, Dysport® and Xeomin®.

For low back pain, BoNT is typically injected into the paraspinal extensor muscles at five levels (L1, L2, L3, L4, and L5), either unilaterally or bilaterally depending on the site of pain (Machado, Kumar et al. 2016). Alternatively, in cases of myofascial back pain, injection can be made into trigger points lateral to the lumbar spine (Müller-Schwefe and Überall 2011). Electromyographic imaging can be used to provide guidance in targeting deeper non-palpable muscles, allowing placement of injectate at the greatest point of muscle activity (Klein and Mantell 1998).

1. Effectiveness, Volume of Evidence, Applicability / Generalisability and Consistency / Clinical impact

Comment here on the extent to which the service/product/ procedure achieves the desired outcomes. Specific reference needs to be made to safety. Report number needed to treat and harm where possible, any issues concerning the quantity of evidence and its methodological quality and the extent to which the evidence is directly applicable or generalisable to the New Zealand population, and the degree of consistency demonstrated by the available evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence. Comment on the clinical impact e.g. size of population, magnitude of effect, relative benefit over other management options, resource implications, balance of risk and benefit.

Volume and quality of evidence:

The current systematic review updated evidence published between 2011 and 2017 and identified two systematic reviews and three additional randomised controlled trials which met inclusion criteria.

The two systematic reviews included one high quality Cochrane systematic review (Waseem et al, 2011) and one low quality review (Jabbari and Machado, 2011). The low quality review was rated lower because of concerns regarding the comprehensiveness of the search, limitations in the reporting of the methods used in the review, and minimal reporting of the characteristics of included studies. The Cochrane review evaluated the effectiveness of injection with BoNT-A for low back pain and sciatica and included three randomised controlled trials.

Three additional RCTs not included in either of the systematic reviews also met inclusion criteria. One was a high quality study examining dose-related effects of botox injection (Müller-Schwefe and Überall 2011), albeit limited by a lack of patient or investigator blinding. One was of adequate quality owing to insufficient details regarding the process of treatment allocation and concealment (Jazayeri et al, 2011), and one considered to be of low quality given poor reporting of study methodology and patient characteristics (Machado et al, 2016).

One case series and one case study which met inclusion criteria were used to evaluate the safety of botox injections for low back pain.

Effectiveness (pain relief and/or improved function)

Botulinum toxin-A compared with placebo injection

The Cochrane review (Waseem et al, 2011) identified two RCTs which compared BoNT-A with a placebo injection for the treatment of chronic low back pain. Combined results suggested that there was low quality evidence in the short term (at three and eight weeks post-treatment), and very low quality in the intermediate term (up until 12 weeks post-treatment), that BoNT-A injections reduced pain intensity better than placebo/saline injections in participants with chronic low back pain. There was low quality evidence that BoNT-A injections improved function better than placebo/saline injections in the intermediate term. Due to the high risk of bias in one of the included studies (Fishman et al, 2002), the authors offered a tentative conclusion that BoNT-A is possibly effective for the management of refractory back pain.

The other systematic review (Jabbari and Machado, 2011) identified one RCT and one case series, with low quality evidence that BoNT-A decreased pain better than placebo injection at 3 weeks and 2 months post-treatment for patients with chronic low back pain.

Two RCTs, one rated of adequate quality (Jazayeri et al, 2011) and one low quality (Machado et al, 2016), compared the effectiveness of abobotulinum toxin A (Dysport®) against placebo/saline injection in patients with chronic low back pain. Both provided injection across five lumbosacral paraspinal muscles and examined outcomes of pain and function. Jazayeri et al (2011) reported that a 200 unit dose of BoNT-A unilaterally (the minimal effective dose) resulted in significantly greater improvements in pain and disability scores compared with placebo at four and eight weeks post-treatment. They concluded that BoNT-A is effective at improving pain and function associated with chronic low back pain.

Machado et al (2016) found that a 500/1000 unit dose of BoNT (uni- or bi-laterally) resulted in a significant reduction in pain compared with placebo at four weeks, but not at six weeks. BoNT was also associated with a significant improvement in function (measured by the Oswestry Disability Questionnaire) compared with placebo at six weeks. The authors concluded that BoNT-A was considered effective at improving pain up to 6 weeks and function at six weeks following treatment.

Miller-Schwefe and Uberall (2011) investigated the effectiveness of different doses of BoNT-A for myofascial lower back pain. Pain and functional outcomes improved for all treatment groups, with no difference according to dose.

Botulinum toxin-A compared with corticosteroid injection

The Cochrane review (Waseem et al, 2011) included one RCT (Fishman, Anderson et al. 2002) which compared injection of 300 units of BoNT-A with injection of 20mg triamcinolone with anaesthetic in 87 patients with piriformis syndrome. BoNT-A was found to be significantly better at reducing pain that corticosteroid injection; however, given the high risk of bias attached to this study, Waseem et al concluded that there was very low quality evidence that BoNT-A injections were better than corticosteroid injections for reducing pain intensity or improving function in chronic LBP in the short term.

Botulinum toxin-A compared with acupuncture

The Cochrane review (Waseem et al, 2011) included one RCT (Liu et al, 2008) which compared BoNT-A with acupuncture for 25 patients with third lumbar transverse process syndrome. The BoNT-A group demonstrated greater improvement in pain and function than the acupuncture group at eight weeks post-treatment. However, the study was considered to be low quality with a high risk of bias.

Safety and Risk

Volume and quality of evidence:

Both of the two included systematic reviews provided data on adverse events within included primary studies. From three RCTs (N=123), Waseem et al (Waseem, Boulias et al. 2011) found no reports of adverse events other than injection site pain immediately following BoNT injection. Jabbari and Machado (Jabbari and Machado 2011) reported three cases of flu-like symptoms resolving in 2-5 days in one case series study involving 75 patients treated with BoNT.

Two additional RCTs, one case series and one case study were also included in the safety/adverse effects outcomes of the review. The two RCTs reported nothing more than localised pain at the injection site. The case series reported influenza-like symptoms, one case of injection site pain and two cases of injection site reaction.

2. Cost

Where possible and reported in the published research literature any economic analysis of the new treatment is considered. Where possible the following will be considered; total costs of the new intervention and number of claimants likely to be affected are considered, along with comparison with the cost of current treatments or interventions, actuarial assessment of the impact of the intervention on scheme liability (including direct and indirect impact e.g. other services and access), expected "accrued benefit" in terms of quality of life, longer life or speedier return to the workforce, implications of cost to the wider health sector.

The cost per procedure for botox injection for low back pain is $1399 (excluding GST).

3. Equity

The extent to which the intervention reduces disparities in health status; in particular equity of access and health outcome.

No equity issues found

4.Consistency with the intent of the AC Act

Purchasing decisions made by ACC must be consistent with and reflect consideration of factors described in the AC Act, Schedule 1, clause 2(1 and 2) and these decisions must be defensible against this statutory requirement in respect of individual claimants.

5.Possible purchasing options

The options are:

1. Purchase,

2. Don't purchase, or

3 . Purchase on a case by case basis on the decision of the Corporate Medical Advisor (or equivalent).

6.Evidence statements

Summarise the advisory group's synthesis of evidence relating to this service, product or procedure, taking the above factors into account, and indicate the evidence level that applies.

The evidence base has increased in volume but not quality since the most recent IPM update of the use of botox to treat lower back pain. A high quality Cochrane systematic review (Waseem et al, 2011) identified only 3 RCTs which met inclusion criteria and two of the studies were considered to have a high risk of bias.

The authors concluded that there was low quality evidence that injections of BoNT-A decrease pain intensity and improve function better than saline injections in patients with chronic low back pain.

Two additional RCTs reported further low quality evidence that injections with BoNT-A result in short term (4 – 8 weeks) improvements in pain and disability outcomes. There was a lack of long-term follow-up across all the included studies in the review.

Reported adverse events were mild. For studies that reported adverse events the most commonly reported were localised pain at the injection site and flu-like symptoms for 2-5 days following treatment.

Recommendations from the ICAHE review:

Evidence of effectiveness against placebo

Injection of BoNT-A to the lumbosacral paraspinal muscles or trigger points is effective in the treatment of chronic low back pain in the short-term (2-3 months post-treatment) when compared to placebo (Level A Recommendation)

Evidence of effectiveness by dose

Increased dose of BoNT beyond the minimal effective dose does not result in improved pain relief or functional status for those with chronic low back pain in the short-term (up until 3 months) (Level C Recommendation)

Evidence of effectiveness against alternative treatments

There is currently insufficient evidence that injection of BoNT-A is more effective than acupuncture or corticosteroid injection in the relief of chronic low back pain in the short-term (2-3 months post-treatment) (Level B Recommendation)

7. Recommendation

Taking the evidence into account, PGAG advises that ACC adopts the following purchasing recommendation:

- Do not purchase botox injections for the routine treatment of low back pain.
- Purchase of a single cycle of treatment may be considered as a 3rd line intervention for chronic low back pain when other treatments have failed:
    - To enable participation in a multidisciplinary rehabilitation programme with a clear rehabilitation plan and clearly identified treatment goals.
    - Following a comprehensive pain assessment in consultation with medical advice.
    - Providers must submit an end-of-care report to CSD including appropriate clinical and functional outcome data.

These recommendations were ratified by the Clinical Governance Committee in September 2017.

PGAG Discussion

Current evidence still supports the 2011 recommendation of 'do not purchase' for routine treatment. However, PGAG considers botox injections do have a role as a one-off treatment to enable participation in multidisciplinary rehabilitation where other options have failed. PGAG therefore recommends clarifying the criteria for case-by-case purchase.