Spasticity: Intrathecal Baclofen

- Treatment option for those who do not respond to, or do not tolerate, oral medication (ie, baclofen, tizanidine, gabapentin, benzodiazepines, dantrolene)
- Programmable, subcutaneously implanted device with reservoir
- Catheter delivers low dose to spinal cord, <1% of oral dose
- Long-term retrospective chart review of 106 patients
  - Significant improvements in mean Ashworth, Penn, and VAS pain, stiffness, and discomfort scores
  - Improvements maintained for up to 20 years
  - Most patients withdrew from oral antispasmodic medication
  - Most common complication: catheter malfunction (17%)
  - One death due to catheter placement – postoperative pulmonary embolus

- Effective alternative to oral medication in many patients
- Availability varies among regions and countries

VAS, visual analogue scale.

Sammaraiee Y et al. *Mult Scler Relat Disord*. 2019;27:95-100.

Spasticity: Botulinum toxin A

- FDA approval for spasticity (based on studies in patients with stroke)[1]
  - Injections in elbow, wrists, fingers, thumbs, and/or ankles
- Few RCTs in MS population[2,3]
- Clinical observations of benefits in patients with MS
  - In a long-term study, 89% of patients continued treatment over 4-year period, indicating high level of efficacy and tolerance[4]
  - A meta-analysis of clinical studies found botulinum toxin A to have greater efficacy with fewer safety risks relative to other spasticity treatments[3]

RCT, randomized controlled trial.

1. Botox (onabotulinumtoxinA). Prescribing information. Allergan USA, Inc; 2022. 2. Dressler D et al. *J Neurol*. 2017;264:112-120;
3. Fu X et al. *Clin Rehabil.* 2018;32:713-721; 4. Novarella F et al. *Toxins (Basel)*. 2022;14:774.

Spasticity: Nabiximols

Nabiximols: Cannabis-Based Oromucosal Spray
Blend of THC and CBD, plus other cannabinoid and non-cannabinoid components[1]
Clinical trial results are mixed; indicate improvement in patient-reported spasticity and pain, but not objective or clinician-determined measures[2,3]
First approved in UK in 2010 for MS spasticity; currently approved in 29 countries[4]
No FDA approval
Recent Phase 3, placebo-controlled clinical trials: RELEASE MSS1, MSS3, MSS5
• **MSS1**: **Completed**. **No significant difference** for change in LLMT-6 from baseline (clinician-reported metric); 3 weeks; 68 enrolled[1,4]
• **MSS3**: **Terminated.** Primary endpoint is change from baseline in average daily spasm count; 12 weeks; 238 enrolled[1]
• **MSS5**: **Terminated**. Primary endpoint was change in LLMT-6 from baseline, 3 weeks; 56 enrolled[1]

CBD, cannabidiol; LLMT-6, Lower Limb Muscle Tone-6 (average of 6 Modified Ashworth Scale transformed scores); THC, Δ9-tetrahydrocannabinol.

1. ClinicalTrials.gov. Accessed March 17, 2023; 2. Koppel BS et al. *Neurology*. 2014;82:1556-1563; 3. Rice J et al. *Curr Neurol Neurosci Rep*. 2018;18:50; 4. Jazz Pharmaceuticals. June 28, 2022; https://investor.jazzpharma.com/news-releases/news-release-details/jazz-pharmaceuticals-announces-top-line-results-phase-3-trial. Accessed March 17, 2023.