MUSCLE SPASTICITY

CHI Formulary Development Project

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM- October 2023

To the CHI Original Muscle Spasticity Clinical Guidance- Issued April 2020

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Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

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Abbreviations

AAN	American Academy of Neurology
aboBoNT-A	AbobotulinumtoxinA
ACOG	American College of Obstetricians and Gynecologists
AE	Adverse Event
BoNT	Botulinum Neurotoxin
CD	Cervical Dystonia
CHI	Council of Health Insurance
CM	Chronic Migraine
CMD	Complex Motor Disorders
CP	Cerebral Palsy
CPG	Clinical Practice Guideline
EMA	European Medicines Agency
FDA	Food and Drug Administration
GDG	Guideline Development Group
GMFCS	Gross Motor Function Classification System
GPP	Good Practice Point
IDF	CHI Drug Formulary
incoBoNT-A	Incobotulinumtoxina
ITB	Intrathecal Baclofen
NHSGGC	National Health Service Greater Glasgow and Clyde
Onabont-A	Onabotulinumtoxina
PRM	Physical and Rehabilitation Medicine
PSS	Post-Stroke Spasticity
Rimabont-B	Rimabotulinumtoxinb
SCI	Spinal Cord Injuries
SFAR	French Society of Anesthesia and Intensive Care
SFDA	Saudi Food and Drug Authority
TZD	Tizanidine

Executive Summary

Spasticity is prolonged muscle tightness resulting from damage to the brain, spinal cord, or motor nerves, commonly seen in neurological conditions like cerebral palsy, multiple sclerosis, stroke, and traumatic brain or spinal cord injuries[1]. This condition arises due to disruptions in the communication between muscles and the brain, conveyed through nerves and the spinal cord[1]. Cerebral palsy-related spasticity stems from brain damage affecting muscle tone and movement control, often becoming more apparent as children with the condition mature[1]. In multiple sclerosis, leg and hip muscles can exhibit flexor or extensor spasticity, locking them in bent or straight positions[1]. After traumatic brain injuries, spinal cord injuries, or strokes, muscle tightness may occur in different body areas, potentially improving as the brain heals, although managing it can be complex due to disruptions in communication signals between the brain and muscles[1].

At a global level, muscle spasticity impacts more than 12 million individuals globally, with around 80 percent of people diagnosed with cerebral palsy and 80 percent of those suffering from multiple sclerosis experiencing its effects[1].

There is a lack of extensive research regarding the occurrence of cerebral palsy (CP) across Saudi Arabia's various regions and cities. However, a study conducted in 2006, focused on a single tertiary hospital in Riyadh, found a relatively high prevalence of CP, specifically 4.1 cases per 10,000 individuals[2]. On the other hand, the general occurrence of multiple sclerosis was documented as 40.40 per 100,000 in the entire population and 61.95 per 100,000 among Saudi nationals[3].

CHI issued Muscle Spasticity clinical guidelines after thorough review of renowned international and national clinical guidelines in April 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI Muscle Spasticity clinical guidance and seeks to offer guidance for the effective management of Muscle Spasticity. It provides an **update on the Muscle Spasticity Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update were summarized, being **the issuance updated versions of previously reviewed guidelines** namely the Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache (2016). Moreover, **new guidelines are added to the report** such as the French clinical guidelines for peripheral motor nerve blocks in a PRM setting (2019), the NHSGGC Spasticity management guideline, the

Spinal Cord Injury Guidelines Department of Physical Medicine and Rehabilitation/ Trauma Rehabilitation Resources Program (2019), and the NICE Multiple sclerosis in adults: management (2022)[4].

After carefully examining clinical guidelines and reviewing the SFDA drug list, lidocaine and ropivacaine are to be added to the CHI formulary, and Daxxify (daxibotulinumtoxinA-lanm) injection is a new drug approved by the FDA for the treatment of cervical dystonia in adults.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in Muscle Spasticity therapeutic management.

Below is a table summarizing the major changes based on the different Muscle Spasticity guidelines used to issue this report:

Table 1. General Recommendations for the Management of Muscle Spasticity

Management of Muscle Spasticity		
General Recommendations	**Level of Evidence/ Grade of Recommendation**	**Reference**
Consider oral baclofen for spasticity-related discomfort, muscle spasms, or functional impairment.	N/A	NICE Spasticity in under 19s, 2012[5]
Consider oral Diazepam at bedtime when dealing with spasticity that results in discomfort, muscle spasms, or functional disability. If the initial response falls short of expectations, adjustments can be made by either increasing the dosage or incorporating a daytime dose.	N/A	NICE Spasticity in under 19s, 2012[5]
In instances where a single-drug trial of oral diazepam or baclofen for four to six weeks yields unsatisfactory results, exploring a combination treatment involving both drugs may be beneficial.	N/A	NICE Spasticity in under 19s, 2012[5]
Consider botulinum toxin type A treatment in children and young people in whom focal spasticity of the upper limb is impeding fine	N/A	NICE Spasticity in

motor function, compromising care and hygiene, causing pain, impeding tolerance of other treatments, such as orthoses, and causing cosmetic concerns to the child or young person.		under 19s, 2012[5]
Do not offer botulinum toxin type A treatment if the child or young person has severe muscle weakness had a previous adverse reaction or allergy to botulinum toxin type A is receiving aminoglycoside treatment.	N/A	NICE Spasticity in under 19s, 2012[5]
Consider treatment with continuous pump-administered intrathecal baclofen in children and young people with spasticity if, despite the use of non-invasive treatments, spasticity or dystonia are causing difficulties with any of the following: pain or muscle spasms, posture or function, or self-care.	N/A	NICE Spasticity in under 19s, 2012[5]
Botulinum toxin type A (BoNT-A) is a safe and effective treatment for upper and lower limb spasticity, resulting in both passive and active functional gains.	N/A	Spasticity in adults, Royal college of physicians, 2018[6]
The agents currently licensed in the UK for treating spasticity are baclofen, tizanidine, dantrolene and diazepam. Off-label, gabapentin is also recommended as first or second line treatment for spasticity in UK National Guidelines for Multiple Sclerosis.	N/A	Spasticity in adults, Royal college of physicians, 2018[6]
Blepharospasm: Consider using OnaBoNT-A and incoBoNT-A injections as treatment options	Level B	AAN, 2016[7]
Cervical Dystonia: Offer AboBoNT-A and rimaBoNT-B as primary treatment options.	Level A	AAN, 2016[7]
For patients with upper limb spasticity, provide aboBoNT-A, incoBoNT-A, and onaBoNT-A as treatment choices	Level A	AAN, 2016[7]
When treating lower limb spasticity in adults, offer onaBoNT-A and aboBoNT-A as options.	Level A	AAN, 2016[7]

Consider using OnaBoNT-A as a treatment option before TZD for managing upper extremity spasticity.	Level B	AAN, 2016[7]
For localized/segmental spasticity in the upper and lower extremities of children with CP that warrants treatment, BoNT-A should be offered as an effective and generally safe treatment.	Level A	Spasticity in children and adolescents with CP, AAN, 2010[8]
Dantrolene is rarely used in clinical practice to reduce spasticity in children with CP.	N/A	Spasticity in children and adolescents with CP, AAN, 2010[8]
Antispastic oral medications (baclofen, tizanidine, dantrolene, and benzodiazepines) can effectively reduce post-stroke spasticity (PSS), but their use is limited by many adverse effects.	N/A	PSS Management, AHA, 2012[9]
For physical and rehabilitation medicine (PRM) motor nerve blocks, it is advisable to use lidocaine due to its lower toxicity (local or general). Ropivacaine can be used if a prolonged effect is desired.	N/A	French guidelines, 2019[10]
First-line options include Baclofen or Diazepam. Initiate treatment at a low dose and gradually increase to achieve the optimal therapeutic effect.	N/A	Spasticity Management, NHSGGC[11]

At the end of the report, a key recommendation synthesis section is added highlighting the latest updates in **Muscle Spasticity clinical and therapeutic management**.

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Muscle Spasticity report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This part contains the updated versions of the guidelines mentioned in the April 2020 CHI Muscle Spasticity Report and the corresponding recommendations:

Table 2. Clinical Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated Versions**
Section 1.1 National Institute for Health & Care excellence (**NICE**) guidelines-Spasticity in under 19s: management (**2012**)[5]	N/A*
Section 1.2 Spasticity in adults: management using botulinum toxin-**Royal College of Physicians** (**2018**)[6]	N/A*
Section 1.3 **AAN** Practice Guideline Update Summary: Botulinum Neurotoxin for the Treatment of blepharospasm, Cervical Dystonia (CD), Adult Spasticity, and headache (**2008**)	Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache (**2016**)[7]
Section 1.4 Assessment: Botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the **American Academy of Neurology** (**2008**)[12]	N/A*
Section 1.5 The American Academy of Neurology (**AAN**) guideline for	Reaffirmed in 2022.

pharmacological treatment of spasticity in children and adolescents with cerebral palsy (CP) (**2010**)[8]	
Section 1.6 Poststroke Spasticity Management (PSS)- American Heart Association (**AHA**) (**2012**)[9]	N/A*

*: No updated versions available

1.1.1 National Institute for Health & Care excellence (NICE) Guidelines - Spasticity in Under 19s: Management (2012)

*Please refer to **Section 1.1** of CHI Muscle Spasticity Report.*

There are no new updates. The recommendations of this guideline remain unchanged[5].

1.1.2 Spasticity in Adults: Management Using Botulinum Toxin - Royal College of Physicians (2018)

*Please refer to **Section 1.2** of CHI Muscle Spasticity Report.*

There are no new updates. The recommendations of this guideline remain unchanged[6].

1.1.3 Practice Guideline Update Summary: Botulinum Neurotoxin for the Treatment of Blepharospasm, Cervical Dystonia, Adult Spasticity, and Headache (2016)

*Please refer to **Section 1.3** of CHI Muscle Spasticity Report.*

The American Academy of Neurology (AAN) issued an update on the practice guideline for the use of botulinum neurotoxin in several indications, including adult spasticity[7]. Evidence levels and grades of recommendations are outlined below:

Table 3. Grading Scheme for Recommendations

Grading Scheme for Recommendations	
Level A for effectiveness	Signifies intervention should be offered
Level B for effectiveness	Signifies intervention should be considered
Level C for effectiveness	Signifies intervention may be considered

Level U	Signifies insufficient evidence to support or refute effectiveness of intervention
Level A for ineffectiveness	Signifies intervention should not be offered
Level B for ineffectiveness	Signifies intervention should not be considered

The following recommendations are provided by the American Academy of Neurology (AAN) Guidelines on the use of Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache[7]:

- Botulinum neurotoxin (BoNT) is commercially available in 2 serotypes, A and B. There are 4 US Food and Drug Administration approved preparations of BoNT: onabotulinumtoxinA (onaBoNT-A), abobotulinumtoxinA (aboBoNT-A), incobotulinumtoxinA (incoBoNT-A), and rimabotulinumtoxinB (rimaBoNT-B), shown in the table below:

Table 4. Botulinum Neurotoxins and Their FDA-Approved Indications (Adapted from the AAN 2016 Guidelines)

BoNT Preparation	Brand Name (Manufacturer)	FDA-Approved Indications (Relevant to this Guideline)
OnabotulinumtoxinA	Botox (Allergan, Inc., Irvine, CA)	Blepharospasm, CD, upper extremity spasticity, lower extremity spasticity, CM
AbobotulinumtoxinA	Dysport (Ipsen Ltd., Paris, France	CD, upper extremity spasticity
IncobotulinumtoxinA	Xeomin (Merz Pharmaceuticals, Frankfurt, Germany)	Blepharospasm, CD, upper extremity spasticity
RimabotulinumtoxinB	Myobloc Neurobloc (US WorldMeds/Solstice Neurosciences, Louisville, KY)	CD
Abbreviations: BoNT = botulinum neurotoxin; CD = cervical dystonia; CM = chronic migraine; FDA = Food and Drug Administration.		

- Blepharospasm: Consider using OnaBoNT-A and incoBoNT-A injections as treatment options (Level B), and you may also contemplate using aboBoNT-A (Level C) for managing blepharospasm.
- Cervical Dystonia: Offer AboBoNT-A and rimaBoNT-B as primary treatment options (Level A) and consider OnaBoNT-A and incoBoNT-A (Level B) for addressing cervical dystonia.
- Focal Manifestations of Adult Upper Limb Spasticity: For patients with upper limb spasticity, provide aboBoNT-A, incoBoNT-A, and onaBoNT-A as treatment choices (Level A), and consider rimaBoNT-B (Level B).
- Focal Manifestations of Adult Lower Limb Spasticity: When treating lower limb spasticity in adults, offer onaBoNT-A and aboBoNT-A as options (Level A). There is insufficient evidence to determine the efficacy of incoBoNT-A or rimaBoNT-B for this condition.
- Adult Upper Extremity Spasticity: Consider using OnaBoNT-A as a treatment option before TZD for managing upper extremity spasticity (Level B). Also consider both high-volume, low-potency injections of onaBoNT-A and endplate targeting of onaBoNT-A into proximal upper extremity muscles to enhance tone reduction in spasticity (Level B).
- The recommendations are summarized in the figure below:

Table 5. Evidence-Based Conclusions and Recommendations for the Efficacy of Various Botulinum Neurotoxin Formulations by Indication (Adapted from the AAN 2016 Guidelines)

Indication	Level A effective	Level B probably effective	Level C possibly effective	Level U insufficient evidence	Level A ineffective	Level B ineffective
Blepharo-spasm		Onabotulinumtoxin A, incobotulinumtoxin A	Abobotulinumtoxin A	Rimabotulinumtoxi nB		
Cervical Dystonia	Abobotulinumtoxin A, rimabotulinumtoxin B	Onabotulinumtoxin A, incobotulinumtoxin A				
Upper Limb Spasticity*	Abobotulinumtoxin A, onabotulinumtoxin A**, incobotulinumtoxin A	Rimabotulinumtoxi nB				
Lower limb spasticity	Onabotulinumtoxin A, abobotulinumtoxin A			Incobotulinumtoxin A, rimabotulinumtoxin B		

Chronic migraine	Onabotulinumtoxin A***					
Episodic migraine					Onabotulinumtoxin A	
Tension-type headache						Onabotulinumtoxin A

Level A recommendation for effectiveness signifies intervention should be offered.

Level B recommendation for effectiveness signifies intervention should be considered.

Level C recommendation for effectiveness signifies intervention may be considered.

Level U recommendation signifies insufficient evidence to support or refute effectiveness of intervention.

Level A recommendation for ineffectiveness signifies intervention should not be offered.

Level B recommendation for ineffectiveness signifies intervention should not be considered.

* Evidence demonstrates efficacy in reducing spasticity but is inadequate to determine improvement in active function associated with limb spasticity.

** Probably superior to tizanidine and exercise alone for reducing spasticity.

*** Established as effective for decreasing the number and severity of headaches; probably effective in improvement of health-related quality of life.

1.1.4 Assessment: Botulinum Neurotoxin for the Treatment of Movement Disorders (An Evidence-Based Review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (2008)

*Please refer to **Section 1.4** of CHI Muscle Spasticity Report.*

There are no new updates. The recommendations of this guideline remain unchanged [12].

1.1.5 The American Academy of Neurology (AAN) Guideline for Pharmacological Treatment of Spasticity in Children and Adolescents with Cerebral Palsy (CP) (2010)

*Please refer to **Section 1.5** of CHI Muscle Spasticity Report.*

There are no new updates. The recommendations of this guideline remain unchanged, as they were reaffirmed in 2022[8].

1.1.6 Poststroke Spasticity Management (PSS) - American Heart Association (AHA) (2012)

*Please refer to **Section 1.6** of CHI Muscle Spasticity Report.*

There are no new updates. The recommendations of this guideline remain unchanged[9].

1.2 New Guidelines

This part includes the added guidelines to the previous CHI Muscle Spasticity report, along with their recommendations.

Table 6. List of Additional Guidelines

Additional Guidelines
French Clinical Guidelines for Peripheral Motor Nerve Blocks in a PRM Setting (2019)[10]
Spasticity Management Guideline - NHSGGC[11]
Spinal Cord Injury Guidelines Department of Physical Medicine and Rehabilitation/ Trauma Rehabilitation Resources Program (2019)[13]
NICE Multiple Sclerosis in Adults: Management (2022)[4]

1.2.1 French Clinical Guidelines for Peripheral Motor Nerve Blocks in a PRM Setting (2019)

Evidence levels and recommendation grades are not outlined.

The following recommendations are provided by the French Clinical Guidelines on peripheral motor nerve blocks)[10]:

- Motor blocks may be employed for patients with neurological impairments, involuntary muscle spasticity, or hyperactivity to determine the appropriate therapeutic approach.
- There is no comprehensive list of targets for motor nerve blocks.
- There is no evidence in the literature to discourage the use of specific motor nerve blocks (in theory, all motor or mixed nerves could be subject to a motor block).
- Priority should be given to selective blocks (distal motor branch) as they allow for more precise clinical analysis, lower doses of local anesthetic, and outcomes closer to those achieved with sustainable therapies (phenolization, neurotomy, botulinum toxin injection).

- **Products and Contraindications**
    - Choice and Dosage of Anesthetic Agent
        - For PRM motor nerve blocks, it is advisable to use lidocaine due to its lower toxicity (local or general). Ropivacaine can be used if a prolonged effect is desired.
        - Adrenalized forms of anesthetics (that contain epinephrine (also known as adrenaline) as an additive) are not suitable for PRM motor nerve blocks.
        - The use of other anesthetic agents is not recommended.
        - Recommended doses: It is advisable to use the lowest possible doses.
        - Depending on professional consensus, the following precautions may be suggested:
        - Level 1 precautions:
            - For lidocaine doses (up to 2 mg/kg): check for contraindications, have an emergency kit nearby, no pre-anesthetic consultation is needed, and an anesthetist is not required.
            - For doses of ropivacaine (up to 1.5 mg/kg, with a maximum of 100 mg): same as above but with a preliminary intravenous line.
        - Level 2 precautions for higher doses (> 2 mg/kg Lidocaine; > 1.5 mg/kg or > 100 mg ropivacaine), it is recommended to follow the precautions published by the French Society of Anesthesia and Intensive Care (SFAR) (including intravenous line, monitoring, emergency kit, immediate availability of an anesthetist resuscitator).
    - Minimum Time Interval Between Two Blocks: The time gap between two successive injections (up to the maximum dose) should not be less than the half-life of the specific agent, which is 60 minutes for lidocaine and 180 minutes for ropivacaine.
    - Procedure for Patients on Anticoagulant and Anti-aggregating (Antiplatelet Drug) Therapy
        - Continuing anti-aggregating agents during a block is not contraindicated but should be evaluated on a case-by-case basis, considering the specific agent (aspirin vs. others), the patient's condition, and the type of block.

        - For patients on anticoagulant therapy:
            - Avoid the risk of discontinuing an effective anticoagulant treatment (e.g., antivitamin K, direct oral coagulants, or heparins) for a non-vital procedure.
            - Consider the risk of hematoma and potential complications, such as compartment syndrome, associated with the hematoma.
            - Differentiate between low-risk blocks (single, superficial puncture, etc.) and high-risk blocks (deep, multiple injections, etc.) to avoid performing the latter if effective anticoagulation is present.
            - For low-risk blocks performed under antivitamin K (AVK) treatment, the block can proceed when the international normalized ratio (INR) is < 3, with an emphasis on the use of ultrasound detection techniques.

- **Medical Supervision and Patient Care During and After the Procedure; How to Respond to Incidents?**
    - General Precautions in All Cases:
        - Ensure the presence of a physician during the procedure and a nurse for post-block monitoring, with the physician remaining nearby.
        - Maintain accessibility to a procedure for addressing toxicity effects.
        - Administer the injection slowly with regular checks for the absence of blood reflux during aspiration.
        - Keep verbal communication with the patient.
        - Monitor early signs of neurotoxicity and cardiotoxicity.
        - Monitor the patient for 30 minutes after lidocaine injection and 60 minutes after ropivacaine injection.
        - No contraindications to getting up and performing functional tests.
        - Look for complications (especially hematoma) during the procedure.
    - Depending on the Level of Precautions (See Recommendation 2):

        - Level 1: Verify contraindications; perform the procedure in a suitable room with oxygen mask availability; no pre-anesthetic consultation, no need for an anesthetist; no intravenous line or monitoring required; emergency trolley nearby; Intralipid1 20% available.
        - Level 2: Apply recommendations published by the SFAR, regardless of the operator.
- Injection and Tracking Equipment
    - An anatomical tracking technique should be supplemented with another tracking technique; anatomical tracking alone is insufficient.
    - Identification can be achieved through electrostimulation and/or ultrasound. There is no demonstrated superiority of one over the other, but they have different advantages and disadvantages, sometimes making them complementary. The technique should be selected based on the operator's experience.
    - Recommendations for the tracking mode for nerve blocks can be extrapolated for chemical neurolysis.
- Preparing the Patient and Possible Analgesia
    - The patient should be informed about the procedure and possible discomfort.
    - The patient's input into the choice of premedication should be actively sought.
    - Anxiolytic premedication may be beneficial, with increased monitoring of toxicity warning signs in such cases.
    - Non-pharmacological techniques (e.g., conversational hypnosis, music therapy, dermal stimulation) can be useful complementary methods.
    - Analgesic prevention can be offered before the motor nerve block. Options include the application of a local skin anesthetic agent (e.g., EMLA type) or an equimolar gas mixture of oxygen and nitrous oxide (EMONO).
- Efficacy Control
    - The design of the motor nerve block should begin with assumptions about the factors contributing to discomfort, with specific questions to be answered.
    - Consider the time required for the motor nerve block to take effect (depends on the drug used) and verify the effectiveness of the nerve

block, if possible (e.g., abolition of spasticity, presence of sensory disorders for mixed nerves, etc.).

- Evaluation encompasses:
  - Analytical evaluation to analyze the mechanisms of the neuro-motor disorders contributing to the observed difficulties.
  - Situation evaluation to assess the effect of the motor nerve block in the situations causing patient-reported discomfort, as well as the patient's subjective feelings.
  - Utilization of validated tools adapted to the patient's issues.
- Evaluation data should be documented in the medical record, and conclusions should be drawn, including therapeutic proposals whenever possible.

- Patient Information (Form and Content)
  - Patient information is mandatory before performing a diagnostic motor nerve block. It should be provided verbally, but it is advisable to use written support. Oral consent is necessary and sufficient.
  - In the case of a minor patient, the consent of at least one legal representative is required. In the case of a protected adult, consent from the legal representative is not routinely required. The principle of personal autonomy applies unless explicitly stated by the guardianship judge. However, the legal representative should always receive information to assist the protected person in their decision.
  - Records of patient information provision (including any difficulties encountered) and consent collection should be maintained in the medical records.
  - Objectives of the block should be defined in advance in consultation with the patient.
- Training of Practicing Physicians
  - Performing motor nerve blocks requires training in their specific indications, potential risks, and knowledge of these recommendations.
  - Identification techniques require training with a learning curve and a prerequisite of anatomical knowledge.
  - This training should be provided through an initial and ongoing PRM (Physical and Rehabilitation Medicine) training program.

1.2.2 NHSGGC Spasticity Management Guideline

The National Health Service of Greater Glasgow and Clyde (NHSGGC) published a guideline for the management of spasticity in children[11]. Evidence levels and grades of recommendations were not defined.

The main recommendations are summarized below.

- Objectives of managing spasticity:
    - To assist in maintaining proper posture.
    - To enhance ease of caregiving.
    - To alleviate pain associated with spasticity.
    - To improve the quality of sleep.
    - To enhance motor function.
    - To prevent or slow the development of contractures and joint deformities.
- Stage 1:
    - 24-Hour Postural Management
        - Consider the use of upper and/or lower limb orthotic devices for addressing reduced joint ranges, such as ankle-foot orthoses, wrist-hand orthoses for resting, and thumb abduction splints.
        - Evaluate the suitability of employing a standing frame, seating system, and sleep system for non-ambulant children with Gross Motor Function Classification System (GMFCS) IV-V or an equivalent level of mobility.
        - Consider providing a Postural Management Passport to parents, caregivers, and the child or young person's nursery or school.
    - Active Therapy Program
        - Customize physical therapy to meet the specific needs of the child or young person and target individual goals, such as improving motor function, enabling participation in daily activities, and preventing pain or contractures.
        - Utilize progressive muscle strengthening techniques to enhance function.
        - Consider bimanual or constraint therapy for cases of hemiplegia.
    - Medical Treatment

        - Consider medical intervention to address pain, muscle spasms, posture management, ease of caregiving, and motor function improvement.
        - First-line options include Baclofen or Diazepam. Initiate treatment at a low dose and gradually increase to achieve the optimal therapeutic effect.
        - In cases of inadequate response, reevaluate the effectiveness of other stage 1 interventions and explore potential sources of discomfort. Refer to Pediatric Complex Motor Disorders service if lack of response to stage 1 treatments.

- Stage 2:
    - Referral to Pediatric Neurology Complex Motor Disorders (CMD) Service
        - Indications for referral include an inadequate response to stage 1 treatments and the need to identify the most suitable treatment options. Consider referral for children with diagnostic uncertainty or those experiencing dystonia or dyskinesia.
    - Referral to Pediatric CMD Botulinum Toxin Service
        - Indications for referral encompass focal dynamic spasticity and/or dystonia that impacts function, caregiving, joint range of motion, causes pain, or reduces orthotic tolerance. Contemplate referring to the CMD Upper Limb Clinic for significant thumb, wrist, or elbow spasticity. Children eligible for botulinum toxin treatment may require an adapted therapy program or orthotic review after treatment.
    - Referral to Pediatric Orthopedic Service
        - Indications for referral comprise reduced joint ranges, increasing difficulties with orthotics, seating, or the use of standing or walking aids, the presence of scoliosis, and foot deformities. A hip migration index exceeding 40% on pelvic x-ray is also an indicator. Treatment options may include botulinum toxin therapy, serial casting, or surgical intervention. Consider the use of Gait Analysis to assess ambulant children with significant gait abnormalities to inform their management. Children with clinically significant scoliosis will be referred to the National Pediatric Spinal Service.

- Stage 3:
    - Intrathecal Baclofen (ITB)
        - Refer to the CMD service for evaluation of ITB in cases of significant generalized spasticity and/or dystonia in children with GMFCS IV or V who have an inadequate response or intolerance to oral medications.
    - Selective Dorsal Rhizotomy
        - Indications include children typically aged 5 to 10 years with bilateral lower limb spasticity resulting from periventricular leukomalacia (PVL).

1.2.3 Spinal Cord Injury Guidelines Department of Physical Medicine and Rehabilitation/Trauma Rehabilitation Resources Program (2019)

The Department of Physical Medicine and Rehabilitation/Trauma Rehabilitation Resources Program at the University of Arkansas for Medical Sciences (UAMS) published in 2019 clinical guidelines on the management of spinal cord injury[13]. Evidence levels and grades of recommendations are not outlined.

- Medical management/treatment goals: The primary objective is to minimize the positive signs of spasticity while avoiding worsening of the negative signs.
- Non-pharmacological treatments:
    - Implement a regular exercise routine that incorporates daily range of motion exercises with a focus on muscle stretching (lasting 1-2 hours): Short-term physical therapy to educate the patient and caregiver. Long-term self-stretching program to maintain joint and muscle range and reduce spasticity.
    - Consider casting and splinting to preserve muscle and tendon length, with serial casting if tendons have shortened.
    - Explore externally applied repetitive cycling.
    - Evaluate hippotherapy to decrease lower limb spasticity through rhythmic movements associated with horseback riding to regulate muscle tone.
    - Explore electrical stimulation applied to the spinal cord.
    - Consider physical modalities, such as tendon pressure application, cold and warmth therapy, vibration, bandaging, massage, low-power laser treatment, and acupuncture.

    - Evaluate magnetic stimulation over the thoracic spinal cord.
- Medications (Note: Selective serotonin reuptake inhibitors [SSRIs] like Prozac, Lexapro, Celexa, etc., may exacerbate spasticity):
    - Baclofen (Lioresal®): Initiates GABA-B receptor activation, leading to the inhibition of calcium conductance, reduced gamma-motor neuron activity, decreased drive to intrafusal muscle fibers, and reduced muscle spindle sensitivity.
        - Start with 5 mg three times a day; maximum dose is determined by side effects like drowsiness (Literature suggests up to 80 mg per day in divided doses, although significantly higher doses are tolerated and effective). Usually taken four times a day.
        - Average therapeutic half-life is 3.5 hours but ranges from 2 to 6 hours.
        - Gradual discontinuation is necessary to avoid hallucinations, seizures, and confusion.
    - Tizanidine (Zanaflex®): An imidazoline derivative that binds to alpha2 receptor sites both spinally and supraspinally, enhancing presynaptic inhibitory modulation of spinal reflexes.
        - Maximum dose is 36 mg per day.
        - Side effects include drowsiness, dry mouth, hypotension, and rarely hallucinations.
        - Liver functions should be monitored at least annually.
        - Be cautious of drug interactions with ciprofloxacin, an antibiotic that inhibits hepatic metabolism, potentially increasing tizanidine levels and the risk of hypotension and bradycardia.
    - Gabapentin (Neurontin®): An adjunctive treatment for epileptic seizure disorders, structurally related to GABA, and used off-label for spasticity, spastic hypertonia, and central pain syndromes in spinal cord injuries (SCI).
        - The maximum dose is 3600 mg, divided into three or four daily doses.
        - More effective for neuropathic pain than spasticity.
        - Common side effects include dizziness and drowsiness.
    - Dantrolene (Dantrium®): Reduces calcium flux across the sarcoplasmic reticulum of skeletal muscle, uncoupling motor nerve excitation and muscle contraction.

        - Maximum dose is 400 mg, divided into three- and four-times daily doses.
        - Peak blood concentration occurs within 3 to 6 hours.
        - Side effects include liver toxicity (1%), drowsiness, nausea, diarrhea, and dizziness.
    - Diazepam (Valium®): A long-acting benzodiazepine that enhances GABAA receptor currents, reducing polysynaptic reflexes and offering muscle relaxant, sedative, and antispasticity effects.
        - Maximum dose is 60 mg per day in divided doses.
        - Side effects include intellectual impairment, decreased motor coordination, potential psychological addiction, and abuse.
- Muscle Relaxants: Centrally acting muscle relaxants, typically not recommended for treating spasticity, include:
    - Cyclobenzaprine (Flexeril®) - Maximum daily dosage of 30 mg. Typically taken in a 10 mg dose at night. It may also offer pain relief due to its similar molecular structure to amitriptyline, a tricyclic antidepressant.
    - Carisoprodol (Soma®) - Has potential for addiction and is classified as a Schedule IV medication. The average dose is 350 mg taken four times a day. Its active metabolite is meprobamate, which affects various central nervous system sites, leading to anxiety reduction and sedation.
- Cyproheptadine (Periactin®): An antagonist at 5-HT2, histamine H1, L-calcium channels, and muscarinic cholinergic receptors, used off-label for spasticity secondary to SCI:
    - Initiate at 2-4 mg orally every 8 hours, not exceeding 24 mg per day.
    - Side effects include drowsiness, dizziness, nausea, diarrhea, and increased appetite. Advanced age may increase the risk of anticholinergic effects and toxicity, such as confusion, dry mouth, constipation, and others.
- Injections
    - Botulinum toxins:
        - Neurotoxins derived from Clostridium botulinum act as potent neuromuscular blockers when injected into motor point areas.
        - Available serotypes: A, B
        - Injection prevents acetylcholine release, leading to muscle inactivity.

        - Typically administered by a physician every three months to manage spastic muscles.
        - Adhesive taping and casting can enhance botulinum toxin effects.
        - Rare side effects include allergic reactions and distant toxin spread causing swallowing and breathing difficulties, as well as antibody development.
    - Phenol or alcohol:
        - Phenol denatures nerve fiber proteins and acts as a reversible local anesthetic.
        - Alcohol dehydrates nerve tissue, causing sclerosis of nerve fibers and the myelin sheath.
        - Both agents can be injected at motor points identified by electrical stimulation or ultrasound, as well as directly onto nerves for motor point blocks and nerve blocks.
        - Potential complications include pain, dysesthesias lasting weeks to months, arrhythmias, variable duration and magnitude of effect, and incomplete reversibility.
- Restrictions:
    - Patients effectively managing their spasticity should be evaluated for any new medical conditions causing increased spasticity. Refer them to a local medical doctor for further assessment, considering secondary complications of spinal cord injury (e.g., DVT, fractures, gastric ulcers, heterotopic ossification, syringomyelia) if necessary.
    - Recognize that minimal to moderate spasticity may be beneficial for stability and functional tasks, such as standing, transfers, or bed entry.
- Major outcomes:
    - Well-managed spasticity that does not hinder function or safety.
    - Minimal side effects from the chosen management strategy.
    - Ability to use the treatment strategy for the long term without excessive risks, side effects, or costs.
- Prevention and Education:
    - Assess the patient's utilization of basic management techniques before considering medication dose increases or injections.

- Establish a stretching schedule for spastic muscle groups and promote routine stretching.
- Minimize sources of painful input to the spinal cord, including implementing a catheter schedule to prevent bladder distention, reducing the risk of bladder infection or stones, utilizing an effective bowel program to avoid bowel distention, avoiding tight-fitting shoes or clothing, ensuring proper wheelchair positioning.
- Use the smallest effective dose of spasticity medication.
- Be aware of changes in ambient temperature, as colder weather can increase spasticity and tone.
- Exercise caution when using Valium and Soma, considering their addictive potential and street value.

1.2.4 NICE Multiple Sclerosis in Adults: Management (2022)

The National Institute for Health and Care Excellence (NICE) published a clinical guidance on the management of multiple sclerosis (MS) in adults, in which treatment of spasticity is tackled[4]. Evidence levels and grades of recommendations are outlined in the table below:

Table 7. Grading Scheme of Recommendations

Level	Type of evidence	Grade	Evidence
1	Evidence obtained from a single randomized controlled trial or a meta-analysis of randomized controlled trials	**A**	At least 1 randomized controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence level 1) without extrapolation
2a	Evidence obtained from at least 1 well-designed controlled study without randomization	**B**	Well-conducted clinical studies but no randomized clinical trials on the topic of recommendation (evidence levels 2 or 3); or extrapolated from level 1 evidence
2b	Evidence obtained from at least 1 other well-designed quasi-experimental study	–	–
3	Evidence obtained from well-designed	–	–

	non-experimental descriptive studies, such as comparative studies, correlation studies and case studies		
4	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	**C**	Expert committee reports or opinions and/or clinical experiences of respected authorities (evidence level 4) or extrapolated from level 1 or 2 evidence. This grading indicates that directly applicable clinical studies of good quality are absent or not readily available
4	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	**GPP**	Recommended good practice based on the clinical experience of the guideline development group (GDG).

The main recommendations from the NICE 2022 guidelines are detailed below:

Spasticity

- Identify spasticity in individuals with MS if they exhibit any of the following:
    - Involuntary muscle movements (spasms)
    - Muscle stiffness
    - Pain and difficulty in performing certain activities due to restricted movements or positions
    - Changes in mobility or upper limb function.
- Evaluate individuals with MS who show signs of spasticity for factors that may exacerbate it, such as pressure ulcers, bladder and bowel dysfunction, infections, poor posture or positioning, and pain. Offer guidance and support to help individuals with MS, as well as their families and caregivers where applicable, in preventing and managing these factors.
- Engage in a discussion with the individual regarding the balance between the benefits and drawbacks of treating spasticity. Specifically, clarify that some individuals rely on their spasticity to maintain posture and the ability to stand, walk, or transfer, and that treatment with muscle relaxants could potentially have adverse effects on this.

- Consider oral baclofen as the primary drug treatment for addressing spasticity in individuals with MS who have specific treatment goals, such as improving mobility or alleviating pain and discomfort. Take into account any contraindications, coexisting conditions, and the individual's preferences.
- If oral baclofen is not well-tolerated or does not provide sufficient relief, contemplate gabapentin as a secondary option for managing spasticity in individuals with MS. For guidance on the safe prescription of gabapentin and management of withdrawal symptoms, refer to NICE's guideline on medicines associated with dependence or withdrawal symptoms.
- When utilizing oral baclofen or gabapentin for spasticity management in individuals with MS, educate them on the following:
    - Gradually increase the dosage in intervals of at least 1-2 weeks to optimize symptom relief or until reaching the maximum tolerated dose
    - Cease medication if no benefits are observed at the maximum tolerated dose (emphasize that abrupt discontinuation of baclofen can be harmful and may require specific precautions)
    - Schedule annual medication reviews once the optimal dose is established.
- Contemplate a combination of oral baclofen and gabapentin for individuals with MS if:
    - Individual medications do not yield sufficient relief, or side effects from individual medications hinder dose escalation.
- If spasticity significantly impairs mobility, posture, or function and initial treatments prove ineffective, refer the individual to a multidisciplinary team with experience in spasticity management for assessment and treatment planning.

Section 2.0 Drug Therapy in Muscle Spasticity

This section comprises four subsections: the first contains the drug information tables and HTA recommendations of the newly recommended drugs (Lidocaine and Ropivacaine), the second covers drug modifications, the third outlines the drugs that have been withdrawn from the market, and the fourth contains medications that have been approved by the FDA and/or EMA but are not yet SFDA-registered.

2.1 Additions

2.1.1 Lidocaine

Table 8. Drug Information Lidocaine

SCIENTIFIC NAME **Lidocaine**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	M62.8
Drug Class	Local Anesthetic
Drug Sub-class	
ATC Code	N01BB02
Pharmacological Class (ASHP)	72:00 - Local Anesthetics
DRUG INFORMATION	
Dosage Form	**Solution for injection**
Route of Administration	Infiltration
Dose (Adult) [DDD]*	The lowest possible dose
Maximum Daily Dose Adults*	Up to 2mg/kg[10]
Dose (pediatrics)	
Maximum Daily Dose Pediatrics*	
Adjustment	eGFR <30 mL/minute/1.73 m2: Administer lower maintenance infusion rate with close monitoring for renal toxicity.
Prescribing edits*	MD

AGE (Age Edit): N/A	
CU (Concurrent Use Edit): N/A	
G (Gender Edit): N/A	
MD (Physician Specialty Edit): to be administered under the supervision of a specialist.	
PA (Prior Authorization): N/A	
QL (Quantity Limit): N/A	
ST (Step Therapy): N/A	
EU (Emergency Use Only): N/A	
PE (Protocol Edit): N/A	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** headache, shivering, radiculopathy **Most serious:** bradycardia, circulatory shock, coronary artery vasospasm
Drug Interactions*	X Fexinidazole X Fusidic Acid (Systemic) X Saquinavir D BUPivacaine (Liposomal) Depends on Route
Special Population	Older Adult Considerations: Due to decreases in Phase I metabolism and possibly decrease in splanchnic perfusion with age, there may be a decreased clearance or increased half-life in the elderly and increased risk for CNS side effects and cardiac effects.
Pregnancy	Lidocaine and its metabolites cross the placenta and can be detected in the fetal circulation following maternal injection for anesthesia prior to delivery. Adverse reactions in the fetus/neonate may affect the CNS, heart, or peripheral vascular tone. Fetal heart monitoring is recommended by the manufacturer. Lidocaine injection is approved for obstetric analgesia (eg, prior to epidural or spinal anesthesia). Lidocaine administered by local infiltration is used

	to provide analgesia prior to episiotomy and during repair of obstetric lacerations. Administration by the perineal route may result in greater absorption than administration by the epidural route. Cumulative exposure from all routes of administration should be considered. The ACOG recommends that pregnant women should not be denied medically necessary surgery regardless of trimester. If the procedure is elective, it should be delayed until after delivery. Medications used for the treatment of cardiac arrest in pregnancy are the same as in the nonpregnant woman. Doses and indications should follow current Advanced Cardiovascular Life Support guidelines. Appropriate medications should not be withheld due to concerns of fetal teratogenicity.
Lactation	Lidocaine is present in breast milk. The relative infant dose (RID) of lidocaine is 4.9% when calculated using the highest breast milk concentration located and compared to a weight-adjusted maternal dose of 183 mg for epidural anesthesia. In general, breastfeeding is considered acceptable when the RID of a medication is <10%. The RID of lidocaine was calculated using a mean milk concentration of 0.86 mcg/mL, providing an estimated daily infant dose via breast milk of 129 mcg/kg/day. This milk concentration was obtained following maternal administration lidocaine via local regional anesthesia to 22 women undergoing cesarean delivery. Milk was sampled 2 hours after the injection. Breast milk concentrations of lidocaine decreased

	over 12 hours. Lidocaine metabolites have also been detected in breast milk. Lower concentrations of lidocaine have been reported in breast milk following dental procedures, infusion for arrhythmias, and liposuction. Oral bioavailability to the breastfeeding infant is expected to be low. Available guidelines consider lidocaine to be compatible with breastfeeding when used as an antiarrhythmic or local anesthetic. Cumulative exposure from all routes of administration should be considered.
Contraindications	Hypersensitivity to lidocaine or any component of the formulation; hypersensitivity to another local anesthetic of the amide type; Adam-Stokes syndrome; Wolff-Parkinson-White syndrome; severe degrees of SA, AV, or intraventricular heart block (except in patients with a functioning artificial pacemaker); premixed injection may contain corn-derived dextrose and its use is contraindicated in patients with allergy to corn or corn-related products. Canadian labeling: Additional contraindications (not in US labeling): Hypersensitivity to ester local anesthetics (paraben-containing solutions only); supraventricular arrhythmias; severe myocardial depression; antimicrobial preservative-containing solutions should not be used intra-or retro-ocularly or for epidural or spinal anesthesia or any route that would introduce solution into the cerebrospinal fluid or in doses ≥15 mL for other types of blockades.

Monitoring Requirements	Liver function tests, lidocaine concentrations, ECG; in patients requiring drug >24 hrs, blood level monitoring recommended; consult individual institutional policies and procedures
Precautions	Concerns related to adverse effects: - Intra-articular infusion related chondrolysis: Continuous intra-articular infusion of local anesthetics after arthroscopic or other surgical procedures is not an approved use; chondrolysis (primarily in the shoulder joint) has occurred following infusion, with some cases requiring arthroplasty or shoulder replacement. - Methemoglobinemia: Has been reported with local anesthetics; clinically significant methemoglobinemia requires immediate treatment along with discontinuation of the anesthetic and other oxidizing agents. Onset may be immediate or delayed (hours) after anesthetic exposure. Patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, exposure to oxidizing agents or their metabolites, or infants <6 months are more susceptible and should be closely monitored for signs and symptoms of methemoglobinemia (eg, cyanosis, headache, rapid pulse, shortness of breath, lightheadedness, fatigue). Disease-related concerns:

	• Hepatic dysfunction: Use extreme caution in patients with severe hepatic dysfunction; may have increased risk of lidocaine toxicity. • Pseudocholinesterase deficiency: Use caution in patients with pseudocholinesterase deficiency; may have increased risk of lidocaine toxicity Dosage form specific issues: • Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; the "gasping syndrome" consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse; some data suggests that benzoate displaces bilirubin from protein binding sites; avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling. • Injectable anesthetic: Follow appropriate administration techniques so as not to administer any intravascularly. Solutions containing antimicrobial preservatives should not be used for epidural or spinal anesthesia. Some solutions contain a bisulfite; avoid in patients who are allergic to bisulfite. Resuscitative equipment, medicine and oxygen should be available in case of emergency. Adjust the dose

	for elderly, pediatric, acutely ill, and debilitated patients. • Intravenous: Constant ECG monitoring is necessary during IV administration. Use cautiously in hepatic impairment, HF, marked hypoxia, severe respiratory depression, hypovolemia, history of malignant hyperthermia, or shock. Increased ventricular rate may be seen when administered to a patient with atrial fibrillation. Use is contraindicated in patients with Wolff-Parkinson-White syndrome and severe degrees of SA, AV, or intraventricular heart block (except in patients with a functioning artificial pacemaker). Correct electrolyte disturbances, especially hypokalemia or hypomagnesemia, prior to use and throughout therapy. Correct any underlying causes of ventricular arrhythmias. Monitor closely for signs and symptoms of CNS toxicity. The elderly may be prone to increased CNS and cardiovascular side effects. Reduce dose in hepatic dysfunction and CHF. Other warnings/precautions: • CAST trial: In the Cardiac Arrhythmia Suppression Trial (CAST), recent (>6 days but <2 years ago) myocardial infarction patients with asymptomatic, non-life-threatening ventricular arrhythmias did not benefit and may have been harmed by attempts to suppress the arrhythmia with flecainide or encainide. An increased mortality or nonfatal cardiac arrest rate (7.7%) was seen in the active treatment group compared with patients in the

	placebo group (3%). The applicability of the CAST results to other populations is unknown. Antiarrhythmic agents should be reserved for patients with life-threatening ventricular arrhythmias.
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of muscle spasticity treatment options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations are for Lidocaine.**

Table 9. HTA Recommendations Lidocaine

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Lidocaine	NICE	No recommendations for this indication.
	CADTH	No recommendations for this indication.
	HAS	No recommendations for this indication.
	IQWIG	No recommendations for this indication.
	PBAC	No recommendations for this indication

CONCLUSION STATEMENT- Lidocaine

There are no recommendations for the use of Lidocaine in this indication. It is typically recommended for PRM motor nerve blocks due to its lower toxicity (local or general).

2.1.2 Ropivacaine

Table 10. Drug Information Ropivacaine

SCIENTIFIC NAME Ropivacaine	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes

EMA	Yes
MHRA	Yes
PMDA	No
Indication (ICD-10)	M62.8
Drug Class	Local Anesthetic
Drug Sub-class	
ATC Code	N01BB09
Pharmacological Class (ASHP)	N/A
DRUG INFORMATION	
Dosage Form	**Solution for infusion**
Route of Administration	Infiltration
Dose (Adult) [DDD]*	
Maximum Daily Dose Adults*	Up to 1.5mg/kg max 100mg[10]
Dose (pediatrics)	
Maximum Daily Dose Pediatrics*	
Adjustment	**Altered Kidney Function:** There are no dosage adjustments provided in the manufacturer's labeling. However, ropivacaine and its metabolites are renally excreted, and the risk of toxic reactions may be greater. **Hepatic Impairment**: There are no dosage adjustments provided in the manufacturer's labeling. Use with caution; ropivacaine undergoes hepatic metabolism and patients may be at a greater risk for developing toxic drug levels.
Prescribing edits*	MD
AGE (Age Edit): NA	
CU (Concurrent Use Edit): NA.	
G (Gender Edit): N/A	
MD (Physician Specialty Edit): to be administered under the supervision of a specialist.	
PA (Prior Authorization): N/A	
QL (Quantity Limit): N/A	
ST (Step Therapy): N/A	

EU (Emergency Use Only): N/A	
PE (Protocol Edit): N/A	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** bradycardia, nausea, hypotension, back pain, vomiting. **Most serious**: chest pain, tachycardia, acute myocardial infarction, atrial fibrillation, syncope
Drug Interactions*	X Bromperidol X BUPivacaine (Liposomal) D Amifostine D Obinutuzumab
Special Population	• Acutely ill patients: Use with caution in acutely ill; may be at greater risk for toxicity. • Debilitated patients: Use with caution in debilitated patient; may be at greater risk for toxicity. • Older adult: Use with caution in the elderly: may be at greater risk for toxicity. Cardiovascular adverse events (bradycardia, hypotension) may be age-related (more common in patients >61 years of age).
Pregnancy	Ropivacaine may potentially cause varying degrees of maternal, fetal, and neonatal toxicity involving the CNS, peripheral vascular tone, and cardiac function depending on dose and administration technique. Ropivacaine is approved for use in obstetric analgesia/anesthesia.
Lactation	Ropivacaine is present in breast milk. According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother; however, local

	anesthetics are considered compatible with breastfeeding.
Contraindications	Hypersensitivity to ropivacaine, amide-type local anesthetics (eg, bupivacaine, mepivacaine, lidocaine), or any component of the formulation. Canadian labeling: Additional contraindications (not in US labeling): Intravenous regional anesthesia (Bier block); obstetric paracervical block anesthesia
Monitoring Requirements	Heart rate, blood pressure, ECG monitoring (if used with antiarrhythmics)
Precautions	Concerns related to adverse effects: • CNS toxicity: Careful and constant monitoring of the patient's state of consciousness should be done following each local anesthetic injection; at such times, restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression, or drowsiness may be early warning signs of CNS toxicity. Treatment is primarily symptomatic and supportive. • Intra-articular infusion related chondrolysis: Continuous intra-articular infusion of local anesthetics after arthroscopic or other surgical procedures is not an approved use; chondrolysis (primarily in the shoulder joint) has occurred following infusion, with some cases requiring arthroplasty or shoulder replacement. • Methemoglobinemia: Has been reported with local anesthetics; clinically significant methemoglobinemia requires immediate treatment along with discontinuation of the anesthetic and

	other oxidizing agents. Onset may be immediate or delayed (hours) after anesthetic exposure. Patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, exposure to oxidizing agents or their metabolites, or infants <6 months of age are more susceptible and should be closely monitored for signs and symptoms of methemoglobinemia (eg, cyanosis, headache, rapid pulse, shortness of breath, lightheadedness, fatigue). • Respiratory arrest: Local anesthetics have been associated with rare occurrences of sudden respiratory arrest. • Seizures: Convulsions due to systemic toxicity leading to cardiac arrest have also been reported, presumably following unintentional intravascular injection. Disease-related concerns: • Cardiovascular disease: Use with caution in patients with hypotension, hypovolemia, heart block, or cardiovascular disease; may be at greater risk for toxicity. • Hepatic impairment: Use with caution in patients with hepatic impairment; may be at greater risk for toxicity. • Neurological disorders: Use with caution in patients with neurological disorders; may be at greater risk for toxicity. • Porphyria: Use with caution in patients with acute porphyria; consider use of alternative agents.

	• Psychiatric disorders: Use with caution in patients with psychiatric disorders; may be at greater risk for toxicity. • Renal impairment: Use with caution in patients with severe renal impairment; may be at greater risk for toxicity. Other warnings/precautions: • Administration: Intravascular injections should be avoided; aspiration should be performed prior to administration; the needle must be repositioned until no return of blood can be elicited by aspiration; however, absence of blood in the syringe does not guarantee that intravascular injection has been avoided. • Trained personnel: Clinicians using local anesthetic agents should be well trained in diagnosis and management of emergencies that may arise from the use of these agents. Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use.
Black Box Warning	N/A
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of muscle spasticity treatment options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations are for Ropivacaine.**

Table 11. HTA Recommendation Ropivacaine

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Ropivacaine	NICE	No results retrieved.

	CADTH	No recommendations for this indication.
	HAS	No recommendations for this indication.
	IQWIG	No recommendations for this indication.
	PBAC	No results retrieved.

CONCLUSION STATEMENT- Ropivacaine

There are no HTA recommendations for the use of Ropivacaine. It is typically used for PRM motor nerve blocks if a prolonged effect is desired.

2.2 Modifications

There are no modifications from the previous CHI Muscle Spasticity Report.

2.3 Delisting

All medications are SFDA registered (SFDA Drug List, June 2023). *Please refer to* ***Drug Therapy in Muscle Spasticity - Section 2*** *of CHI Muscle Spasticity original clinical guidance.*

2.4 Other Drugs

Dantrolene

FDA-approved 1974 for the treatment of spasticity associated with upper motor neuron disorders (eg, spinal cord injury, stroke, cerebral palsy, or multiple sclerosis).

Cyproheptadine

An antagonist at 5-HT2, histamine H1, L-calcium channels, and muscarinic cholinergic receptors, used off-label for spasticity secondary to SCI.

Rimabotulinumtoxin B

FDA-approved December 2000 for the treatment of cervical dystonia. FDA approval was based on two phase III studies with 186 subjects. The initial dose varies based on prior botulinum toxin injection history. Subsequent dosing is individualized by patient response and should be administered by experienced physicians. Clinical trials showed no significant difference between 5,000 and 10,000 Units, with some pain reduction but also increased symptoms reported.

Daxxify (daxibotulinumtoxinA-lanm)

FDA-approved August 2023 for the treatment of cervical dystonia in adult patients: Daxxify is administered via intramuscular injection with a recommended dosage ranging from 125 Units to 250 Units, divided among affected muscles. Its FDA approval was based on Phase 3 clinical trials involving 382 patients and 1,240 treatments over an 88-week period, demonstrating effectiveness and safety in both 125U and 250U dosage groups, with a median duration of effect of 24.0 and 20.3 weeks, respectively. In the ASPEN OLS study, symptom improvement persisted with successive Daxxify treatments at doses up to 300U, while adverse events, including difficulty swallowing (dysphagia), remained low.

Section 3.0 Key Recommendations Synthesis

- Consider oral baclofen for spasticity-related discomfort, muscle spasms, or functional impairment. Treatment typically commences with a low dosage, followed by a gradual increase over approximately four weeks to attain the optimal therapeutic effect. (NICE Spasticity in under 19s, 2012)
- Consider oral Diazepam when dealing with spasticity that results in discomfort, muscle spasms, or functional disability. If the initial response falls short of expectations, adjustments can be made by either increasing the dosage or incorporating a daytime dose. When discontinuing oral diazepam, it is advisable to taper the dose gradually to prevent withdrawal symptoms, especially if it has been taken for an extended period. (NICE Spasticity in under 19s, 2012)
- Diazepam should be considered as a short-term antispasticity treatment in children with CP (Level B, AAN, 2010)[8]
- In instances where a single-drug trial of oral diazepam or baclofen for four to six weeks yields unsatisfactory results, exploring a combination treatment involving both drugs may be beneficial. Additionally, if there is an indication to transition from oral diazepam to long-term baclofen treatment, such a transition should be considered. (NICE Spasticity in under 19s, 2012)
- Consider botulinum toxin type A treatment in children and young people in whom focal spasticity of the upper limb is impeding fine motor function, compromising care and hygiene, causing pain, impeding tolerance of other treatments, such as orthoses, and causing cosmetic concerns to the child or young person. Do not offer botulinum toxin type A treatment if the child or young person has severe muscle weakness had a previous adverse reaction or allergy to botulinum toxin type A is receiving aminoglycoside treatment. (NICE Spasticity in under 19s, 2012)
- Consider treatment with continuous pump-administered intrathecal baclofen in children and young people with spasticity if, despite the use of non-invasive treatments, spasticity or dystonia are causing difficulties with any of the following: pain or muscle spasms, posture or function, or self-care (or ease of care by parents or carers) It is also considered in patients with paraparesis. Patients should have a good response to intrathecal baclofen first before inserting the pump (NICE Spasticity in under 19s, 2012)
- Botulinum toxin type A (BoNT-A) is a safe and effective treatment for upper and lower limb spasticity, resulting in both passive and active functional gains (Spasticity in adults, Royal college of physicians, 2018)

- The agents currently licensed for treating spasticity in the UK are baclofen, tizanidine, dantrolene and diazepam. These are most useful for more widespread spasticity of modest severity, but their maximum effect may be limited by sedation, muscle weakness or occasional liver toxicity. (Spasticity in adults, Royal college of physicians, 2018)
- Off-label, gabapentin is also recommended as first or second line treatment for mild spasticity in UK National Guidelines for Multiple Sclerosis (Spasticity in adults, Royal college of physicians, 2018)
- Blepharospasm: Consider using OnaBoNT-A and incoBoNT-A injections as treatment options (Level B), and you may also contemplate using aboBoNT-A (Level C) for managing blepharospasm. (AAN, 2016)
- Cervical Dystonia: Offer AboBoNT-A and rimaBoNT-B as primary treatment options (Level A) and consider OnaBoNT-A and incoBoNT-A (Level B) for addressing cervical dystonia. (AAN, 2016)
- Focal Manifestations of Adult Upper Limb Spasticity: For patients with upper limb spasticity, provide aboBoNT-A, incoBoNT-A, and onaBoNT-A as treatment choices (Level A), and consider rimaBoNT-B (Level B). (AAN, 2016)
- Focal Manifestations of Adult Lower Limb Spasticity: When treating lower limb spasticity in adults, offer onaBoNT-A and aboBoNT-A as options (Level A). There is insufficient evidence to determine the efficacy of incoBoNT-A or rimaBoNT-B for this condition. (AAN, 2016)
- Adult Upper Extremity Spasticity: Consider using OnaBoNT-A as a treatment option before TZD for managing upper extremity spasticity (Level B). You should also consider both high-volume, low-potency injections of onaBoNT-A and endplate targeting of onaBoNT-A into proximal upper extremity muscles to enhance tone reduction in spasticity (Level B). (AAN, 2016)
- Botulinum neurotoxin should be offered as a treatment option for the treatment of cervical dystonia (Level A), may be offered for blepharospasm, focal upper extremity dystonia, adductor laryngeal dystonia, and upper extremity essential tremor (Level B), and may be considered for hemifacial spasm, focal lower limb dystonia, and motor tics (Level C). (Report of the Therapeutics and Technology Assessment Subcommittee of the AAN, 2008)
- For localized/segmental spasticity in the upper and lower extremities of children with CP that warrants treatment, BoNT-A should be offered as an effective and generally safe treatment (Level A†). (Spasticity in children and adolescents with CP, AAN, 2010)
- Dantrolene is rarely used in clinical practice to reduce spasticity in children with CP. This may be due to the lack of evidence in the literature to support its

efficacy and the general concern regarding its potential frequent and/or serious AEs. Although dantrolene has been associated with hepatotoxicity, none of the studies reviewed reported this AE in children, perhaps due to the small number of subjects included in these investigations (Spasticity in children and adolescents with CP, AAN, 2010)

- Antispastic oral medications (baclofen, tizanidine, dantrolene, and benzodiazepines) can effectively reduce PSS, but their use is limited by many adverse effects. Because of this, and because of the limited evidence of efficacy attributable to inadequate sample size and lack of quality-of-life measures, it is best to limit the use of these drugs in PSS (PSS Management, AHA, 2012)
- For PRM motor nerve blocks, it is advisable to use lidocaine due to its lower toxicity (local or general). Ropivacaine can be used if a prolonged effect is desired. (French guidelines, 2019)
- First-line options include Baclofen or Diazepam. Initiate treatment at a low dose and gradually increase to achieve the optimal therapeutic effect. (Spasticity Management, NHSGGC)
- Refer to the complex motor disorders (CMD) service for evaluation of intrathecal baclofen (ITB) in cases of significant generalized spasticity and/or dystonia in children with Gross Motor Function Classification System (GMFCS) IV or V who have an inadequate response or intolerance to oral medications. (Spasticity Management, NHSGGC)

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Muscle Spasticity report** and aims to provide recommendations to aid in the management of Muscle Spasticity. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Muscle Spasticity. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

Section 5.0 References

1. Spasticity. Accessed September 8, 2023. https://www.hopkinsmedicine.org/health/conditions-and-diseases/spasticity#:~:text=Spasticity%20is%20abnormal%20muscle%20tightness,Multiple%20sclerosis%20(MS)
2. Prevalence, Types, and Outcomes of Cerebral Palsy at a Tertiary Center in Jeddah, Saudi Arabia.
3. Rising prevalence of multiple sclerosis in Saudi Arabia, a descriptive study.
4. *Multiple Sclerosis in Adults: Management NICE Guideline*.; 2022. www.nice.org.uk/guidance/ng220
5. *Spasticity in under 19s: Management Clinical Guideline*.; 2012. www.nice.org.uk/guidance/cg145
6. Royal College of Physicians of London, British Society of Rehabilitation Medicine, Chartered Society of Physiotherapy (Great Britain), Association of Chartered Physiotherapists in Neurology, Royal College of Occupational Therapists. *Spasticity in Adults: Management Using Botulinum Toxin : National Guidelines 2018*.
7. Simpson DM, Hallett M, Ashman EJ, et al. *Practice Guideline Update Summary: Botulinum Neurotoxin for the Treatment of Blepharospasm, Cervical Dystonia, Adult Spasticity, and Headache*.; 2016.
8. Delgado MR, Hirtz FD, Aisen FM, et al. *Practice Parameter: Pharmacologic Treatment of Spasticity in Children and Adolescents with Cerebral Palsy (an Evidence-Based Review)*.; 2010. www.neurology.org
9. Francisco GE, McGuire JR. Poststroke spasticity management. *Stroke*. 2012;43(11):3132-3136. doi:10.1161/STROKEAHA.111.639831
10. Yelnik AP, Hentzen C, Cuvillon P, et al. French clinical guidelines for peripheral motor nerve blocks in a PRM setting. *Ann Phys Rehabil Med*. 2019;62(4):252-264. doi:10.1016/j.rehab.2019.06.001
11. Spasticity management guideline- NHSGGC. Accessed September 8, 2023. https://www.clinicalguidelines.scot.nhs.uk/nhsggc-guidelines/nhsggc-guidelines/neurology/spasticity-management-guideline/

12. Simpson DM, Blitzer A, Brashear A, et al. *Assessment: Botulinum Neurotoxin for the Treatment of Movement Disorders (an Evidence-Based Review)*.; 2008. www.neurology.org

13. Kiser T, Lindberg R. *Department of Physical Medicine and Rehabilitation/Trauma Rehabilitation Resources Program TELE-REHABILITATION GUIDELINE Medical Management of Spasticity in Spinal Cord Injury*.; 2019.

14. SFDA Drug List J. SFDA Drug List . Published 2023. Accessed June 20, 2023. https://www.sfda.gov.sa/en/drugs-list

Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses and sequence of therapy

II. Adult and Pediatric Quantity Limit?

This is either the adult or pediatric maximum amount of a drug that can be administered per day based on a maximum daily dose. If there is no clinical evidence supporting the quantity limit for that relevant indication, this column will be left as Blank.

III. What information is available in the notes?

"Notes" section provides details of the prescribing edits, extra important drug information and special warning and precautions.

IV. Drug interactions

- A: No known interaction
- B: No action needed
- C: Monitor therapy
- D: Consider therapy modification
- X: Avoid combination

V. Defined Daily Dose

The Defined Daily Dose (DDD) is to be set based on the WHO recommendations https://www.whocc.no/ddd/definition_and_general_considera/

VI. REMS

A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.

Appendix B. Muscle Spasticity Scope

Comparison of the 2020 and the 2023 Report

2020	Changes Performed	2023	Rationale
Section 1.0 Muscle Spasticity Clinical Guidelines			
National Institute for Health & Care excellence [NICE] guidelines- Spasticity in under 19s: management [2012][5]	**N/A**	**N/A**	
Spasticity in adults: management using botulinum toxin- Royal college of physicians [2018][6]	**N/A**	**N/A**	
AAN Practice Guideline Update Summary: Botulinum Neurotoxin for the Treatment of blepharospasm, Cervical Dystonia (CD), Adult Spasticity, and headache [2008]	**Updated**	**Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache 2016**[7]	**Insert table of recommendations by indication.** • Blepharospasm: Consider using OnaBoNT-A and incoBoNT-A injections as treatment options (Level B), and you may also contemplate using aboBoNT-A (Level C) for managing blepharospasm. • Cervical Dystonia: Offer AboBoNT-A and rimaBoNT-B as primary treatment options (Level A) and consider OnaBoNT-A and incoBoNT-A (Level B) for addressing cervical dystonia. • Focal Manifestations of Adult Upper Limb Spasticity: For patients with upper limb spasticity, provide aboBoNT-A, incoBoNT-A, and onaBoNT-A as

			treatment choices (Level A), and consider rimaBoNT-B (Level B). • Focal Manifestations of Adult Lower Limb Spasticity: When treating lower limb spasticity in adults, offer onaBoNT-A and aboBoNT-A as options (Level A). There is insufficient evidence to determine the efficacy of incoBoNT-A or rimaBoNT-B for this condition. • Adult Upper Extremity Spasticity: Consider using OnaBoNT-A as a treatment option before TZD for managing upper extremity spasticity (Level B). You should also consider both high-volume, low-potency injections of onaBoNT-A and endplate targeting of onaBoNT-A into proximal upper extremity muscles to enhance tone reduction in spasticity (Level B). **Medications not SFDA-registered:** • Rimabotulinumtoxin B
Assessment: Botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology [2008][12]	**N/A**	**N/A**	
The American Academy of Neurology (AAN) guideline for	**N/A**	**N/A**	

pharmacological treatment of spasticity in children and adolescents with cerebral palsy (CP) [2010][8]			
Poststroke Spasticity Management (PSS)- American Heart Association (AHA) [2012][9]	**N/A**	**N/A**	
	Missing	**French clinical guidelines for peripheral motor nerve blocks in a PRM setting- 2019**[10]	• Insert recommendations. **Newly Introduced Medications SFDA-registered**: • Lidocaine • Ropivacaine

	Missing	**Spasticity management guideline- NHSGGC**[11]	• Insert treatment recommendations.
			• Stage 1:
			  ○ 24-Hour Postural Management
			  ▪ Consider the use of upper and/or lower limb orthotic devices for addressing reduced joint ranges, such as ankle-foot orthoses, wrist-hand orthoses for resting, and thumb abduction splints.
			  ▪ Evaluate the suitability of employing a standing frame, seating system, and sleep system for non-ambulant children with GMFCS IV-V or an equivalent level of mobility.
			  ▪ Consider providing a Postural Management Passport to parents, caregivers, and the child or young person's nursery or school.

			○ Active Therapy Program ▪ Customize physical therapy to meet the specific needs of the child or young person and target individual goals, such as improving motor function, enabling participation in daily activities, and preventing pain or contractures. ▪ Utilize progressive muscle strengthening techniques to enhance function. ▪ Consider bimanual or constraint therapy for cases of hemiplegia. ○ Medical Treatment ▪ Consider medical intervention to address pain, muscle spasms, posture management, ease of caregiving, and motor function improvement. ▪ First-line options include Baclofen or Diazepam. Initiate treatment at a low dose and gradually increase to achieve the optimal therapeutic effect. ▪ In cases of inadequate response, reevaluate the effectiveness of other stage 1 interventions and explore potential sources of discomfort. • Stage 2: ○ Referral to Pediatric Neurology Complex Motor Disorders (CMD) Service ▪ Indications for referral include an inadequate response to stage 1 treatments and the need to identify the most suitable treatment options. Consider referral for children with diagnostic uncertainty or those experiencing dystonia or

			dyskinesia. ○ Referral to Pediatric CMD Botulinum Toxin Service ▪ Indications for referral encompass focal dynamic spasticity and/or dystonia that impacts function, caregiving, joint range of motion, causes pain, or reduces orthotic tolerance. Contemplate referring to the CMD Upper Limb Clinic for significant thumb, wrist, or elbow spasticity. Children eligible for botulinum toxin treatment may require an adapted therapy program or orthotic review after treatment. ○ Referral to Pediatric Orthopedic Service ▪ Indications for referral comprise reduced joint ranges, increasing difficulties with orthotics, seating, or the use of standing or walking aids, the presence of scoliosis, and foot deformities. A hip migration index exceeding 40% on pelvic x-ray is also an indicator. Treatment options may include botulinum toxin therapy, serial casting, or surgical intervention. Consider the use of Gait Analysis to assess ambulant children with significant gait abnormalities to inform their management. Children with clinically significant scoliosis will be referred to the National Pediatric Spinal Service. • Stage 3: ○ Intrathecal Baclofen (ITB) ▪ Refer to the CMD service for evaluation of ITB in cases of significant generalized spasticity and/or dystonia in children with GMFCS IV or V

			who have an inadequate response or intolerance to oral medications. o Selective Dorsal Rhizotomy ▪ Indications include children typically aged 5 to 10 years with bilateral lower limb spasticity resulting from periventricular leukomalacia (PVL).
	Missing	**SPINAL CORD INJURY GUIDELINES 2019 Department of Physical Medicine and Rehabilitation/ Trauma Rehabilitation Resources Program**[13]	• Insert recommendations on: • Non-pharmacological treatments: • Medications • Injections o Botulinum toxins o Phenol or alcohol • Restrictions • Prevention and Education recommendations Drugs not SFDA-registered: - Dantrolene - Cyproheptadine

Appendix C. MeSH Terms PubMed

The following is the result of the PubMed search conducted for guideline search:

Query	Filters	Search Details	Results
(((((Muscle Spasticity [MeSH Terms]) OR (Spasticity, Muscle[Title/Abstract])) OR (Spastic[Title/Abstract])) OR (Clasp-Knife Spasticity[Title/Abstract])) OR (Clasp Knife Spasticity[Title/Abstract])) OR (Spasticity, Clasp-Knife[Title/Abstract])	Guideline, in the last 5 years, English	("muscle spasticity"[MeSH Terms] OR "spasticity muscle"[Title/Abstract] OR "Spastic"[Title/Abstract] OR "clasp knife spasticity"[Title/Abstract] OR "clasp knife spasticity"[Title/Abstract] OR (("muscle spasticity"[MeSH Terms] OR ("Muscle"[All Fields] AND "Spasticity"[All Fields]) OR "muscle spasticity"[All Fields] OR "Spastic"[All Fields] OR "Spasticity"[All Fields] OR "spastics"[All Fields] OR "spasticities"[All Fields]) AND "Clasp-Knife"[Title/Abstract])) AND ((y_5[Filter]) AND (guideline[Filter]) AND (english[Filter]))	2

Appendix D. Treatment Algorithm

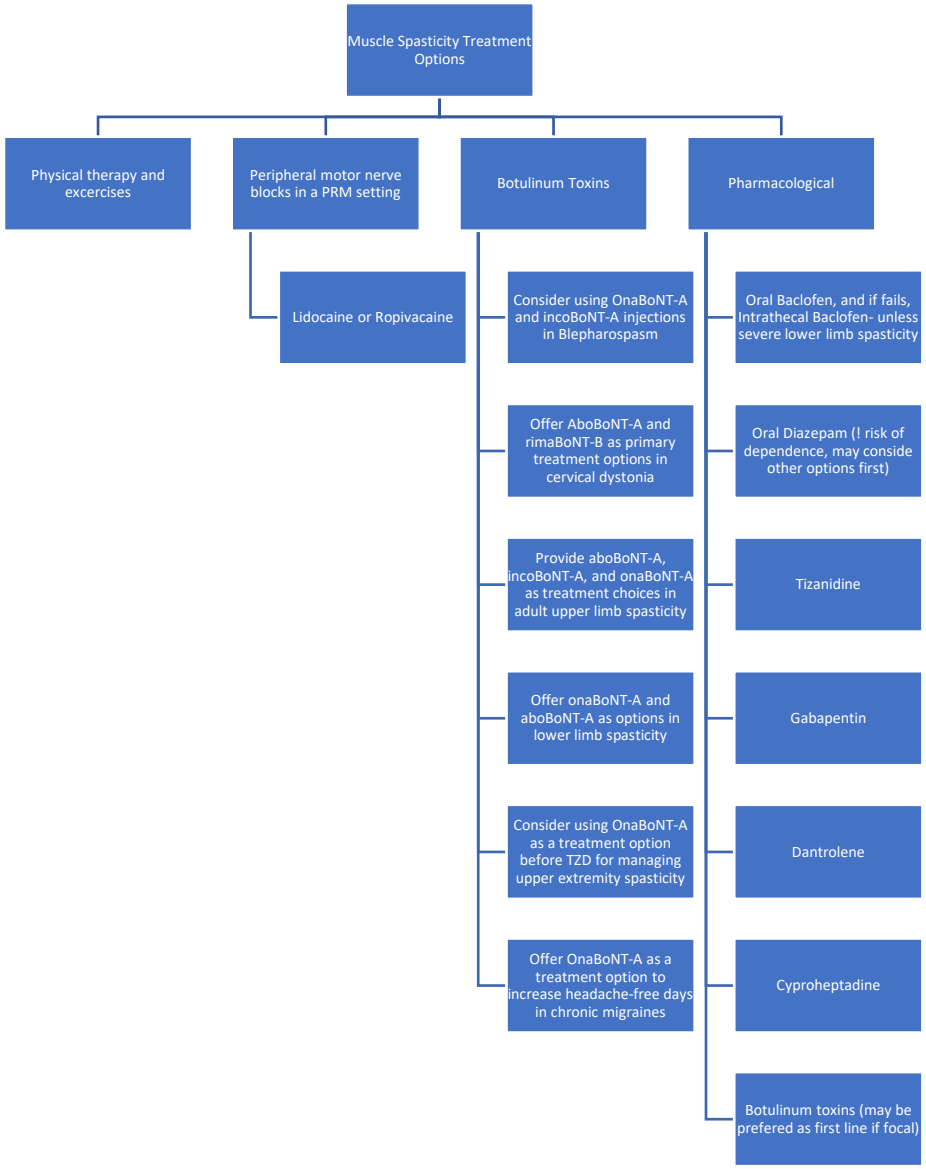

Figure 1. *Treatment Algorithm for the Management of Muscle Spasticity*