NHS
Northumberland, Tyne and Wear
NHS Foundation Trust

Pharmacological Therapy Policy Practice Guidance Note Prescribing Botulinum Toxin within NTW Neuro-rehabilitation Services - V02		
Date issued **Issue 1- May 18**	**Planned review** **May 2021**	**PPT-PGN-20** Part of NTW(C)38 – Pharmacological Therapy Policy
Author/Designation	**Teresa Barnes - Lead Clinical Pharmacist – North Locality**	
Responsible Officer / Designation	**Medical Director**	

Contents

Appendices attached to Policy

Document No:	Description
Appendix 1	Conversion Chart Dysport: Xeomin

This Practice Guidance Note (PGN) should be read in conjunction with:

- NTW(C)06 – Consent to Treatment and Examination Policy
- NTW(C)17 – Medicine Policy UHM- Practice Guidance Notes:
  - UHM-PGN-01 - General Principles on the Safe Custody and Storage of Medicines
  - UHM-PGN-02 - Principles of Prescribing and Transcribing
  - UHM-PGN-03 - Administration of Medicines

1. Introduction

1.1 Botulinum neurotoxin is a microbial protein that exits in seven serotypes (A to G). Type A and Type B are licensed for use in clinical practice. There is a small risk of becoming immune to one type – if this happens the other type can be tried. Since its introduction it has become an effective treatment for numerous movement disorders associated with increased muscle tone or muscle over activity. Botulinum toxins cause neuromuscular blockade by inhibiting the calcium-ion mediated release of acetylcholine at the motor nerve terminals, resulting in a diminished endplate potential and subsequent flaccid paralysis of the affected muscles. The paralysis persists until new nerve terminals form, usually within 2 to 4 months.

1.2 Its clinical effects are temporary as the toxin degrades and becomes inactive within the nerve terminal. The neuromuscular junction atrophies and then regenerates with re-sprouting. Muscle weakness resolves over three to four months.

2. Aim

2.1 This practice guidance note presents a standardised approach to the prescribing of Botulinum Toxin for the treatment of dystonia and spasticity within Northumberland, Tyne and Wear NHS Foundation Trust (the Trust/NTW) Neuro- rehabilitation Service.

3. Indications

3.1 Botulinum toxin offers reversible, therapeutic relief of:

- dystonia
- spasticity and related movement disorders
- hypersalivation
- hyperhidrosis

3.2 It may be used as an adjunct to other treatment techniques to:

- optimise the effects of splinting and casting to increase muscle length
- enhance motor/functional skills
- delay the need for/complement orthopaedic procedures

3.3 The toxin acts locally on the injected muscle to produce its therapeutic effects. The onset of action is delayed and the therapeutic effect takes 1-3 days to develop and reaches a peak after 2 weeks. The pharmacological effects of botulinum toxin type a last for 12-16 weeks.

4. Choice of Toxin and Dosage

4.1 Within NTW Neuro-rehabilitation service Xeomin is the first choice botulinum toxin A for all patients where clinically appropriate.

4.2 Dysport, Botox and NeuroBloc are all available on the North of Tyne Area Prescribing Committee Formulary as alternatives where Xeomin treatment has not had the required response. See information below – Table 1:

Table 1 – Botulinum Toxin products available within NTW

	Botulinum Type A - Xeomin	Botulinum Type A - Dysport	Botulinum Type A - Botox	Botulinum Type B - NeuroBloc
	100 units/vial	300 or 500 units/vial	100 or 200 units/vial	5000 units/ml
Complexing proteins	Low foreign protein content			
Human Albumin content	50U and 100U vials contain 1mg human serum albumin per vial	Each 500 unit vial of Dysport contains 125 mcg human serum albumin	All products contain human albumin specific details are shown where manufacturers have been able to provide this.	
Presentation	Powder for solution for injection			Solution for injection
Route	Generally IM injection			
Storage	Room temp.	2-8^{0}C		
Licensed indications (Adults)	blepharospasm cervical dystonia spasticity of the upper limb	blepharospasm hemifacial spasm spasmodic torticollis focal spasticity hyperhidrosis	blepharospasm hemifacial spasm cervical dystonia hyperhidrosis migraine bladder dysfunctions focal spasticity	cervical dystonia
	Due to the differing licensed indications of Botulinum Toxin products available in the UK, prescribers are advised to consult www.medicines.org.uk to confirm license status at the time of initial prescription.			
Dose range	The optimum dosage and number of injection sites in the treated muscle should be determined individually for each patient. Dose should be titrated according to the clinical response up to the recommended maximum for the product. See product literature for further details			
Maximum licensed dosage*	500 units	1500 units	300 units	10,000 units initially Nb. No maximum dose stated in SPC
If no response at follow up	Clinically verify the effect on the injected muscle Check injection technique and dosage – consider muscle isolation, too low dose, injection technique, fixed contracture, too weak antagonist or possible development of antibodies Review appropriateness of continuing Botulinum treatment Following clinical assessment, if no adverse reactions have occurred, an additional course should be considered using an appropriate method from below: • dose adjustment (this may take up to 3 courses or up to the maximum dose in the specific muscles) • EMG or ultrasound guidance (if available/clinically appropriate) • review of treatment interval If there is still no response check for immunity using an objective test			

*** This is the total maximum licensed dose in units per treatment session and will vary according to the muscle group involved**

4.3 Multiple Indications for Botulinum Toxin

4.3.1 When assessing a patient ahead of treatment with botulinum toxin a full history including medication usage should be undertaken. It is important to ascertain whether the patient is currently undergoing botulinum treatment for multiple indications when formulating a treatment plan.

4.3.2 There is currently limited data for cumulative toxin dosage when used for multiple indications – studies to date have concentrated on botulinum usage in single indications therefore manufacturer's advice regarding maximum dose should be followed for the selected product.

4.4 Switching products

4.4.1 Botulinum toxin doses are not interchangeable from one product to another and potency per unit varies between products. Therefore if the brand of toxin is changed, it can take a while to establish the right dosage of the new product and this can result in some short-term disruption in treatment effectiveness.

4.4.2 When switching products the following ratios can be used as guidance to establish an appropriate dosage:

- Dysport to Xeomin conversion ratio is 4:1 – see conversion table in Appendix 1
- Dysport to Botox is 4:1
- Xeomin to Botox is 1:1

4.5 Antibody formation

4.5.1 Too frequent dosing of botulinum toxin may result in antibody formation which may lead to treatment resistance. Clinically, neutralising antibodies might be suspected by a substantial deterioration in response to therapy and/or the need for consistent use of increased doses.

4.5.2 Clinicians are advised to check for immunity using an appropriate objective test. If the test is positive (no visible effect of the injection), the patient may try a period (from 6 months to 2 years) without toxin. Sometimes, this causes the immunity to disappear – but unfortunately in other cases the immunity can be permanent.

5 Administration

5.1 Botulinum toxin must only be administered by staff who have the appropriate qualifications and training in its use.

6 Contraindications and cautions

6.1 Manufacturers have recommendations for contraindications and cautions. All of these should be considered within the clinical context and the most common ones are included here for information.

6.2 Contraindications

- If the patient:
  - has had a previous adverse reaction or allergy to botulinum toxin type A
  - has myasthenia gravis
  - has infection at the injection site
  - is pregnant or lactating

6.3 Cautions

- History of dysphagia or aspiration
- Chronic respiratory disorder
- Generalised disorders of muscle
- a bleeding disorder (or anti-coagulant therapy check most recent INR and follow outpatient standard operational procedure, monitor for signs of bleeding post injection)
- generalised spasticity
- fixed muscle contractures
- marked bony deformity
- lack of engagement with post-treatment adapted therapy programme

7. Interaction with other medicinal products

7.1 No interaction studies have been performed.

7.2 Theoretically, the effect of Botulinum toxin may be potentiated by aminoglycoside antibiotics (oral/parenteral) or other medicinal products that interfere with neuromuscular transmission, e.g. tubocurarine-type muscle relaxants.

7.3 Therefore, the concomitant use with aminoglycosides or spectinomycin requires special care.

8. Adverse Effects

8.1 Potential adverse effects of botulinum toxin type A can be either local or systemic.

- Local adverse effects include:
  - injection site pain
  - dysphagia
  - dysphonia
  - weakness
  - dyspnoea
  - respiratory distress

8.2 Systemic adverse effects are rare and can include:

- influenza – like symptoms
- arrhythmias, myocardial infraction, seizures and possibly antibody formation
- spread reactions (including muscle weakness, dysphagia and aspiration) have been reported rarely with all botulinum toxin products
- anaphylactic reaction may occur rarely – adrenaline and other medical aids for treating anaphylaxis should be available
- rarely acute fatigue syndrome

8.2.1 Systemic side effects can occur within days to weeks following treatment. If injections are misplaced, other muscle groups will be affected, if excessive doses are used, distant muscles may be affected.

8.2.2 Patients and carers should be provided with information about potential side effects as clinically appropriate

9. References

- Map of Medicine accessed via:

  http://app.mapofmedicine.com/mom/58/login_page.html?hideSmartcard=&next=http%3A%2F%2Fapp.mapofmedicine.com%2Fmom%2F58%2Fnode.pdf%3Fdepartment-id%3D6%26specialty-id%3D1030%26pathway-id%3D14626%26page-id%3D14628%26node-id%3D43%26show-quickinfo%3Dtrue%26show-nationalinfo%3Dtrue%26show-localinfo%3Dtrue%26show-note%3Dtrue%26show-publicinfo%3Dtrue on 07/02/2018

- Electronic British National Formulary (January 2018) BMJ Group via https://www.medicinescomplete.com/mc/bnf/current/index.htm on 07/02/2018

- Martindale – The Complete Drug Reference accesses via https://www.medicinescomplete.com/mc/martindale/current/ms-20959-s.htm?q=botulinum&t=search&ss=text&p=1 on 07/02/2018.

- NTW Patient Group Direction 07 – Botulinum Toxin (A+B) October 2017

- Summary of products characteristics – Xeomin via https://www.medicines.org.uk/emc/product/6202/smpc/history accessed on

- Summary of products characteristics – Dysport via: http://www.medicines.org.uk/emc/medicine/870 accessed 07/02/2018.

- Summary of products characteristics – Botox via: http://www.medicines.org.uk/emc/medicine/112 accessed 07/02/2018

- Summary of product characteristics – Neurobloc via: http://www.medicines.org.uk/emc/medicine/20568 accessed 07/02/2018

- Dystonia Society via: https://www.dystonia.org.uk/what-to-do-when-the-botulinum-toxin-is-not-working accessed 07/02/2018

- NTW Medicine Information Enquiry 2487 September 2014 recoded on MI Databank

- Retrospective evaluation of the dose of Dysport and BOTOX in the management of cervical dystonia and blepharospasm: the REAL DOSE study. Marchetti A1, Magar R, Findley L, Larsen JP, Pirtosek Z, Růzicka E, Jech R, Sławek J, Ahmed F. Mov Disord. 2005 Aug;20(8):937-44.

- A new botulinum toxin type A free of complexing proteins for treatment of cervical dystonia, R. Benecke, MD, W. H. Jost, MD, P. Kanovsky, MD, E. Ruzicka, MD, G. Comes, Dipl Stat and S. Grafe, MD Neurology June 14, 2005 vol. 64 no. 11 1949-1951.

Dysport to Xeomin Conversion Ratio 4:1

Dysport Unit	Xeomin Unit
10	2.5
20	5
30	7.5
40	10
50	12.5
60	15
70	17.5
80	20
90	22.5
100	25
110	27.5
120	30
130	32.5
140	35
150	37.5
160	40
170	42.5
180	45
190	47.5
200	50
210	52.5
220	55
230	57.5
240	60
250	62.5
260	65
270	67.5
280	70
290	72.5
300	75
310	77.5
320	80
330	82.5
340	85

Dysport Unit	Xeomin Unit
350	87.5
360	90
370	92.5
380	95
390	97.5
400	100
410	102.5
420	105
430	107.5
440	110
450	112.5
460	115
470	117.5
480	120
490	122.5
500	125
510	127.5
520	130
530	132.5
540	135
550	137.5
560	140
570	142.5
580	145
590	147.5
600	150
610	152.5
620	155
630	157.5
640	160
650	162.5
660	165
670	167.5
680	170

Dysport Unit	Xeomin Unit
690	172.5
700	175
710	177.5
720	180
730	182.5
740	185
750	187.5
760	190
770	192.5
780	195
790	197.5
800	200
810	202.5
820	205
830	207.5
840	210
850	212.5
860	215
870	217.5
880	220
890	222.5
900	225
910	227.5
920	230
930	232.5
940	235
950	237.5
960	240
970	242.5
980	245
990	247.5
1000	250