XEOMIN® in Dystonia* and Spasticity** Treatment
Educational Material for Physicians
31 May 2012

* XEOMIN® is indicated for the symptomatic treatment of blepharospasm, cervical dystonia of a predominantly rotational form (spasmodic torticollis) in adults
** XEOMIN® is indicated for the symptomatic treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
Introduction
Introduction

With this PowerPoint presentation, Merz Pharmaceuticals provides a training module for physicians as part of the Risk Management Plan (RMP) for XEOMIN®

The goal of the training module is to ensure the safe use of XEOMIN® with special regard to the indications blepharospasm, spasmodic torticollis and post-stroke spasticity of the upper limb* in adults

To achieve this goal, this training module provides comprehensive information concerning: contraindications, risk factors, potential undesirable effects, appropriate patient counseling, treatment planning and documentation, as well as application procedures for treatment of blepharospasm, spasmodic torticollis and post-stroke spasticity of the upper limb*

* XEOMIN® is indicated for the symptomatic treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
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* XEOMIN® is indicated for the symptomatic treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
Treatment With XEOMIN® in General
The treatment process with XEOMIN® can be subdivided into five steps: consultation, treatment planning, reconstitution, administration and follow-up discussion.

In each step specific tasks need to be performed. Details are given on the following slides.
Treatment in General – Tasks in Consultation 1

- Discuss condition and treatment strategy
- Agree on treatment goals
- Provide detailed information about the planned treatment
- Check for contraindications
- Check for drug interactions
- Consider special warnings
- Consider precautions in aggravating circumstances
- Advise about emergency measures: patients should seek immediate medical care if swallowing, speech or respiratory disorders arise
- Draw attention to undesirable effects specific to indication
- Hand out patient information brochure
- Obtain patient’s informed consent (ideally in writing)
The check for contraindications

- Hypersensitivity to Botulinum neurotoxin type A or to any of the excipients
- Generalized disorders of muscle activity (e.g. myasthenia gravis, Lambert-Eaton syndrome)
- Infection at the proposed injection site

The check for drug interactions with Botulinum neurotoxin

- Aminoglycoside antibiotics
- Medicinal products interfering with neuromuscular transmission, e.g. tubocurarine-type muscle relaxants
- 4-aminochinolines

may potentiate effect
may reduce effect
Consideration of special warnings

- Undesirable effects distant from the injection site due to toxin spread; patients should seek immediate medical care if swallowing, speech or respiratory disorders arise

- Botulinum toxin should only be used under specialist supervision in patients with underlying neurological disorders, including swallowing difficulties, as the risk of undesirable effects is increased; the benefit of treatment should be considered to outweigh the risk

- Extreme caution in patients with a history of dysphagia and aspiration

- An anaphylactic reaction may occur rarely; adrenaline and other medical aids for treating anaphylaxis should be available
Consideration of precautions for use in patients
  - With bleeding disorders
  - Receiving anticoagulant therapy
  - Suffering from ALS or other diseases that result in peripheral neuromuscular dysfunction
  - Showing pronounced weakness or atrophy in targeted muscles
  - With altered anatomy due to prior surgical procedures
  - When injecting at sites close to sensitive structures (e.g. carotid artery, lung apices)

During pregnancy or lactation the use of Botulinum neurotoxin cannot be recommended due to the lack of adequate clinical data
Post-Marketing Experience
Flu-like symptoms and hypersensitivity reactions like swelling, oedema (also apart from injection site), erythema, pruritus, rash (local and generalised) and breathlessness have been reported
Plan and document the treatment, e.g. using an indication-specific report form (below: an example for the indication post-stroke spasticity of the upper limb*)

* XEOMIN® is indicated for the symptomatic treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
Treatment in General – Tasks in Treatment Planning 2

- Record patient data, diagnosis, severity of the disorder, case history and the current findings, plus earlier treatments and their effects in the report form.
- Identify the muscles to be treated (possibly taking into account EMG, ultrasonography or CT findings) and mark them on the picture provided in the report form.
- Decide on the quantities of XEOMIN® to be injected into the individual muscles and record them in the report form.
- Decide on the volume of sodium chloride solution for XEOMIN® reconstitution and record in the report form.
Treatment in General – Tasks in Reconstitution 1

- XEOMIN® is supplied in vials as a lyophilizate (freeze-dried powder) and must therefore be reconstituted to form a solution before injection. Only sterile, unpreserved physiological saline (0.9% sodium chloride) should be used as solvent.
Treatment in General – Tasks in Reconstitution 2

- Reconstitution and dilution should be performed in accordance with good clinical practice guidelines, particularly with respect to asepsis.
- It is good practice to perform reconstitution and syringe preparation over plastic-lined paper towels to catch any spillage.
Treatment in General – Tasks in Reconstitution 3

- An appropriate amount of solvent is drawn up into a syringe
- The exposed portion of the rubber stopper of the vial is cleaned with alcohol (70%) prior to insertion of the needle if necessary
- The solvent must then be injected gently into the vial. Because of the vacuum in the XEOMIN® vial, the solvent should be sucked into it without exerting any pressure on the piston of the syringe
Possible dilutions are indicated in the table below.

<table>
<thead>
<tr>
<th>Solvent added (NaCl 9 mg/ml [0.9%] solution for injection)</th>
<th>50 U vial*: Resulting dose in units per 0.1 ml</th>
<th>100 U vial: Resulting dose in units per 0.1 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 ml</td>
<td>20.0 U</td>
<td>-</td>
</tr>
<tr>
<td>0.5 ml</td>
<td>10.0 U</td>
<td>20.0 U</td>
</tr>
<tr>
<td>1.0 ml</td>
<td>5.0 U</td>
<td>10.0 U</td>
</tr>
<tr>
<td>2.0 ml</td>
<td>2.5 U</td>
<td>5.0 U</td>
</tr>
<tr>
<td>4.0 ml</td>
<td>1.25 U</td>
<td>2.5 U</td>
</tr>
<tr>
<td>8.0 ml</td>
<td>-</td>
<td>1.25 U</td>
</tr>
</tbody>
</table>

* May not be marketed in all European countries where the 100 U vial is available
Treatment in General – Tasks in Reconstitution 5

- After injecting the solvent into the vial, the solution should be shaken around gently until all lyophilised solid material on the surfaces of the vial and its stopper is dissolved.
- Reconstituted XEOMIN® is a clear colourless solution free of particles.
- XEOMIN® should be discarded if the vacuum is lost or if the reconstituted solution has a cloudy appearance or contains floccular or particulate matter.
Treatment in General – Tasks in Administration 1

- If necessary, localise the muscles to be injected, e.g. with electromyography (EMG)
- Use 25-30 gauge needles for injection into superficial muscles
- With deeper musculature it may be necessary to use larger needles (e.g. 22 gauge)
- The optimum dosage and number of injection sites in the treated muscle should be determined by the physician individually for each patient. A titration of the dose should be performed.
Treatment in General – Tasks in Administration 2

Doses

- The doses of XEOMIN® (units) to be applied depend on the indication to be treated and on the specific condition of the patient. Later in this module you will be shown injection schedules for three specific cases.

- Due to unit differences in the LD_{50} assay, Xeomin units are specific to Xeomin. Therefore unit doses recommended for Xeomin are not interchangeable with those for other preparations of Botulinum toxin.

- Non-inferiority of XEOMIN® efficacy as compared to a comparator product containing the conventional Botulinum toxin type A complex onabotulinumtoxinA (900 kD) was shown in two comparative single-dosing Phase III studies in blepharospasm and cervical dystonia, one in patients with blepharospasm (study MRZ 60201-0003, n=300) and one in patients with cervical dystonia (study MRZ 60201-0013, n=463). Study results also suggest that XEOMIN® and this comparator product have a similar efficacy and safety profile in patients with blepharospasm or cervical dystonia when used in a dosing conversion ratio of 1:1.
Treatment in General – Tasks in Follow-up discussion

- Remind the patient that the duration of the toxin’s action is about 3-4 months in the registered indications and that the period between each treatment session should be at least 10-12 weeks, depending on the indication.
- Inform the patient that undesirable effects should be reported.
- Remind the patient that some undesirable effects require immediate medical attention: She/he should seek medical help immediately if swallowing, speech or respiratory disorders occur.
- Previously akinetic or sedentary patients should be reminded to gradually resume activities following the injection of XEOMIN®.
Symptomatic Treatment of Blepharospasm
Treating Blepharospasm – Case Introduction

- 60-year-old female patient suffering from bilateral clonic blepharospasm
- Severity on the Jankovic Rating Scale (see Appendix): 4
Treating Blepharospasm – Consultation 1

- Discuss diagnosed disorder (clonic blepharospasm)* and treatment strategy (local XEOMIN® therapy)*
- Agree on treatment goals (reducing disability caused by clonic eyelid closure)*
- Check for contraindications (none present)*
- Check for drug interactions (none present)*
- Consider and discuss special warnings (the history of the patient does not point to an increased risk for the occurrence of undesirable effects)*
- Explain treatment procedure and hand over patient brochure
- Obtain patient’s informed consent for the treatment

* Information in parentheses refers to the case introduced on the previous page
Treating Blepharospasm – Consultation 2

- Draw attention to possible undesirable effects (common reported undesirable effects for XEOMIN® are ptosis and dry eyes) and tell patient to report them.
- The full list of undesirable effects is listed in the Summary of Product Characteristics (SmPC, see Appendix).
- Consider precautions for use:
  - Caution in patients at risk of developing an angle closure glaucoma.
  - Vigorous treatment of any epithelial defect with protective eyedrops, ointments, soft bandage contact lenses, or closure of the eye by patching or similar means.
  - Testing of corneal sensation in patients with previous eye operations (no aggravating circumstances are known in the presented case).
Treating Blepharospasm – Treatment Planning 1

- XEOMIN® treatment of the patient starts with identifying and assessing the affected muscles
- XEOMIN® is injected into the medial and lateral orbicularis oculi of the upper lid and the lateral orbicularis oculi of the lower lid
- Additional sites in the brow area, the lateral orbicularis and in the upper facial area may also be injected if spasms here interfere with vision
Treating Blepharospasm – Treatment Planning 2

- Regarding doses, the recommendation for the initial treatment is 1.25-2.5 units at each site. The total initial dose should not exceed 25 units per eye. Total dosing should not exceed 100 units every 12 weeks.

- At repeat treatment sessions, the dose may be increased up to two-fold if the response to the initial treatment is considered insufficient – usually defined as an effect that does not last longer than 2 months.

- However, there appears to be no additional benefit obtainable from injecting more than 5.0 units per site.
After assessing the patient, the results are recorded in the relevant report form (below an injection schedule for the case at hand).

<table>
<thead>
<tr>
<th>Muscles</th>
<th>Units XEOMIN®</th>
<th>Number of injection sites</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>L</td>
<td>R</td>
</tr>
<tr>
<td>Orbicularis oculi</td>
<td>7.5</td>
<td>7.5</td>
<td>3</td>
</tr>
<tr>
<td>Frontalis</td>
<td>2.5</td>
<td>2.5</td>
<td>2</td>
</tr>
<tr>
<td>Corrugator supercili</td>
<td>2.5</td>
<td>2.5</td>
<td>1</td>
</tr>
<tr>
<td>Procerus</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Treating Blepharospasm – Administration

- The basis for the administration procedure is the determined injection schedule
- Like determined in the treatment plan, XEOMIN® is injected into the medial and lateral orbicularis oculi of the upper lid and the lateral orbicularis oculi of the lower lid, additional sites may also be injected if necessary
- Sterile 27-30 gauge needles are suitable for the injection
- An injection volume of approximately 0.05 to 0.1 ml is recommended
- Injections near the levator palpebrae superioris should be avoided to reduce the occurrence of ptosis
- Medial injections into the lower lid should be avoided as to reduce the risk of diplopia due to toxin spread into the inferior oblique muscle
- The risk of ecchymosis can be limited by immediate gentle pressure at the injection site
Treating Blepharospasm – Follow-up Discussion

- Inform the patient that an onset of effect can be expected after about 4 days, but that a later onset is possible.
- Remind the patient that undesirable effects (e.g. ptosis, dry eyes, paraesthesia, headache, conjunctivitis, dry mouth, skin rash, muscle weakness, inflicted injury) may occur temporarily. These should be reported at the next appointment.
- The patient should seek medical help immediately if swallowing, speech or respiratory disorders occur.
- Inform the patient that the period between treatment sessions should be at least 12 weeks.
The case in this chapter was designed as an example. It must be kept in mind that every case and every patient is unique. The individual features of each case must always be assessed and then taken into account when planning the treatment.

Before treating patients with XEOMIN®, the product's current SmPC should be consulted.
Symptomatic Treatment of Spasmodic Torticollis
Treating Spasmodic Torticollis – Case Introduction

- 63-year-old male patient suffering from cervical dystonia with a predominantly rotatory component (spasmodic torticollis to the right)
- Severity on the TWSTRS severity scale: 13 (for TWSTRS scale see Appendix)
Treating Spasmodic Torticollis – Consultation 1

- Discuss diagnosed disorder (tonic spasmodic torticollis)* and treatment strategy (local XEOMIN® therapy)*
- Agree on treatment goals (reducing disfigurement caused by involuntary head rotation)*
- Check for contraindications (none present)*
- Check for drug interactions (none present)*
- Consider and discuss special warnings, e.g. the possible toxin spread into the oesophageal musculature. This may cause dysphagia, with the risk of aspiration and dyspnoea. Medical intervention may then be necessary
- Explain treatment procedure and hand over patient brochure
- Obtain patient's informed consent for the treatment

* Information in parentheses refers to the case introduced on the previous page.
Treating Spasmodic Torticollis – Consultation 2

- Draw attention to possible undesirable effects and tell patient to report them. Common reported undesirable effects for XEOMIN® are dysphagia, muscle weakness, and back pain.
- The full list of undesirable effects is listed in the SmPC (see Appendix).
- Consider precautions for use:
  - Limiting the dose injected into the sternocleidomastoid to less than 100 units may decrease the occurrence of dysphagia.
  - Patients with smaller neck muscle mass are at greater risk for developing dysphagia and should be treated with greater care.
  - Patients who require bilateral injections into the sternocleidomastoid muscles are at greater risk for dysphagia.
In the management of spasmodic torticollis, XEOMIN® dosing must be tailored to the individual patient, based on the patient’s head and neck position, location of possible pain, muscle hypertrophy, patient’s body weight, and response to the injection.

XEOMIN® is usually injected into the sternocleidomastoid, levator scapulae, scalenus, splenius capitis and/or the trapezius muscle(s). This list is not exhaustive as any of the muscles responsible for controlling head position may be involved and therefore require treatment.

If difficulties arise isolating single muscles, injections should be performed using electromyographic guidance.
Treating Spasmodic Torticollis – Treatment Planning 2

- Regarding doses, no more than 50 units should be given at any one injection site.
- Normally, in practice, the total dose administered does not exceed 200 U. Doses of up to 300 units may be given.
- The period between each treatment session should be at least 10 weeks.
- Multiple injection sites permit XEOMIN® more uniform coverage of the innervated areas of the dystonic muscle and are especially useful in larger muscles.
- The sternocleidomastoid should not be injected bilaterally as there is an increased risk of adverse reactions (in particular dysphagia) when bilateral injections or doses in excess of 100 units are administered into this muscle.
After assessing the patient, the results are recorded in the relevant report form (below an injection schedule for the case at hand)

<table>
<thead>
<tr>
<th>Muscles</th>
<th>Units XEOMIN®</th>
<th>Number of injection sites</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>R L</td>
<td>R L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sternocleidomastoid</td>
<td>80</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Splenius capitis</td>
<td>60</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Levator scapulae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trapezius</td>
<td>20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Scaleneus anterior</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scaleneus medius</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scaleneus posterior</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Treating Spasmodic Torticollis – Administration

- The basis for the administration procedure is the determined injection schedule
- A suitable sterile needle, e.g. 25-30 gauge / 0.30-0.50 mm, is used for injections into superficial muscles, and an e.g. 22 gauge / 0.70 mm needle may be used for injections into deeper musculature
- An injection volume of approximately 0.1 to 0.5 ml per injection site is recommended
Treating Spasmodic Torticollis – Follow-up Discussion

- Inform the patient that an onset of effect can be expected after about 7 days, but that a later onset is possible.
- Remind the patient that injections of XEOMIN® for the management of spasmodic torticollis may cause mild to severe dysphagia with the risk of aspiration and dyspnoea. Patients or caregivers should seek immediate medical care if swallowing, speech or respiratory disorders arise.
- Other undesirable effects, e.g. headache, tremor, eye pain, dysphonia, diarrhoea, dry mouth, vomiting, colitis, skin rash, erythema, pruritus, increased sweating, muscle weakness, back pain, skeletal pain, myalgia, asthenia, injection site inflammation, injection site tenderness, may occur temporarily.
- Inform the patient that the period between treatment sessions should be at least 10 weeks.
Treating Spasmodic Torticollis – Summary / Disclaimer

- The case in this chapter was designed as an example. It must be kept in mind that every case and every patient is unique. The individual features of each case must always be assessed and then taken into account when planning the treatment.
- Before treating patients with XEOMIN®, the product's current SmPC should be consulted.
Symptomatic Treatment of Post-Stroke Spasticity (PSS) of the Upper Limb*

* XEOMIN® is indicated for the symptomatic treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
Treating PSS – Case Introduction

- 68-year-old male, 9 months post-thrombotic stroke, suffering from spastic wrist flexion, clenched fist and flexed elbow
- Severity on the Ashworth Scale (see Appendix): 3
Treating PSS – Consultation 1

- Discuss diagnosed disorder (post-stroke hyperflexion of the right wrist, the elbow and clenched fist)* and treatment strategy (local XEOMIN® therapy to supplement physical management strategies)*
- Agree on treatment goals (relieve discomfort caused by spastic wrist, elbow flexion and clenched fist, and improve hygiene of the palm)*
- Check for contraindications (none present)*
- Check for drug interactions (none present)*
- Consider and discuss special warnings (the history of the patient does not point to an increased risk for the occurrence of undesirable effects)*
- Explain treatment procedure and hand over patient brochure
- Obtain patient’s informed consent for the treatment

*Information in parentheses refers to the case introduced on the previous page
Treating PSS – Consultation 2

- Draw attention to possible undesirable effects (injection site pain, injection site haematoma, muscular weakness are common) and tell patient to report them
- The full list of undesirable effects is listed in the SmPC (see Appendix)
- Consider precautions for use
  - Combine XEOMIN® with usual standard care regimens in PSS
  - Factors potentially influencing treatment response and post-injection treatment should be considered
    (No aggravating circumstances are known in the present case)
- XEOMIN® is not likely to be effective in improving range of motion at a joint affected by a fixed contracture
Treating PSS – Treatment Planning 1

- Exact dosage and number of injection sites should be tailored to the individual patient based on size, number and location of muscles involved, the severity of spasticity, and presence of local muscle weakness.
- Localisation of the involved muscles with EMG or sonography guidance, or nerve stimulation techniques may be useful.
- Multiple injection sites may allow XEOMIN® to have more uniform contact with the innervation areas of the muscle and are especially useful when larger muscles are injected.
- The maximum total recommended dose is up to 400 units per treatment session.
Dosing should be tailored to the individual patient’s need. Doses for XEOMIN® in upper limb PSS are given below:

<table>
<thead>
<tr>
<th>Clinical pattern</th>
<th>Muscle</th>
<th>Mean initial dose/Units</th>
<th>Repeated treatment dose range/Units</th>
<th>Injection sites per muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexed wrist</td>
<td>Flexor carpi radialis</td>
<td>50</td>
<td>25-100</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Flexor carpi ulnaris</td>
<td>40</td>
<td>20-100</td>
<td>1-2</td>
</tr>
<tr>
<td>Clenched fist</td>
<td>Flexor digitorum superficialis</td>
<td>40</td>
<td>40-100</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Flexor digitorum profundus</td>
<td>40</td>
<td>40-100</td>
<td>2</td>
</tr>
<tr>
<td>Flexed elbow</td>
<td>Brachioradialis</td>
<td>60</td>
<td>25-100</td>
<td>1-3</td>
</tr>
<tr>
<td></td>
<td>Biceps</td>
<td>80</td>
<td>75-200</td>
<td>1-4</td>
</tr>
<tr>
<td></td>
<td>Brachialis</td>
<td>50</td>
<td>25-100</td>
<td>1-2</td>
</tr>
<tr>
<td>Pronated forearm</td>
<td>Pronator quadratus</td>
<td>25</td>
<td>10-50</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Pronator teres</td>
<td>40</td>
<td>25-75</td>
<td>1-2</td>
</tr>
<tr>
<td>Thumb-in-palm</td>
<td>Flexor pollicis longus</td>
<td>20</td>
<td>10-50</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Adductor pollicis</td>
<td>10</td>
<td>5-30</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Flexor pollicis brevis/Opponens pollicis</td>
<td>10</td>
<td>5-30</td>
<td>1</td>
</tr>
</tbody>
</table>
Treating PSS – Treatment Planning 3

- After assessing the patient, the results are recorded in the relevant report form (injection schedule for the case at hand shown below)

**Muscles** | **Units XEOMIN®** | **Number of injection sites** | **Remarks**
--- | --- | --- | ---
1 Flexor carpi radialis | 50 | 2 | 
2 Flexor carpi ulnaris | 40 | 2 | 
3 Flexor digitorum profundus | 40 | 2 | 
4 Flexor digitorum superficialis | 40 | 2 | 
5 Flexor pollicis longus |  |  | 
6 / 7 Opponens pollicis/Flexor pollicis brevis |  |  | 
8 Adductor pollicis |  |  | 

![Hand and forearm diagram highlighting muscles](image-url)
## Treating PSS – Treatment Planning 3 (cont`d)

![Muscle Diagram]

<table>
<thead>
<tr>
<th>Muscles</th>
<th>Units XEOMIN&lt;sup&gt;®&lt;/sup&gt;</th>
<th>Number of injection sites</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>L</td>
<td>R</td>
</tr>
<tr>
<td>9  Biceps brachii</td>
<td>80</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>10  Brachialis</td>
<td>50</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>11  Brachioradialis</td>
<td>60</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>12  Pronator teres</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13  Pronator quadratus</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total dose in this case:** 360 U
Treating PSS – Administration

- The basis for the administration procedure is the determined injection schedule.
- In superficial muscles, a sterile 26 gauge, 37 mm length needle is suitable for administration; for deeper musculature, a sterile 22 gauge, 75 mm length needle is suitable.
Treating PSS – Follow-up Discussion

- Inform the patient that an onset of effect can be expected after about 4 days, but that a later onset is possible.

- Remind the patient that undesirable effects (e.g. dysaesthesia, headache, hypoaesthesia, haematoma, cough, dysphagia, nausea, dry mouth, erythema, muscular weakness, pain in extremity, joint swelling, myalgia, injection site pain, injection site haematoma, feeling hot, asthenia, oedema peripheral) may occur temporarily. These should be reported at the next appointment. However, the patient should seek medical help immediately if swallowing, speech, or respiratory disorders occur.

- Inform the patient that, in general, the treatment effect lasts 12 weeks and that the period between treatment sessions should be at least 12 weeks.
General Summary/Disclaimer

- The case in this chapter was designed as an example. It must be kept in mind that every case and every patient is unique. The individual features of each case must always be assessed and then taken into account when planning the treatment.

- Before treating patients with XEOMIN®, the product’s current SmPC should be consulted.
Self-test
Self-test – Introduction

- On the following pages you may check your knowledge regarding the symptomatic treatment of blepharospasm, spasmodic torticollis and post-stroke spasticity of the upper limb* with XEOMIN®
- Work through the tasks carefully and mark down the correct answers on a piece of paper (or print out the slides and mark the answers there). Then check your answers against the solutions, which are given at the end of this presentation
- For some questions, more than one answer is correct
- If you have difficulties answering the questions, please fill in your gaps by referring to the respective sections in this presentation

* XEOMIN® is indicated for the symptomatic treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
Self-test – Task 1

Which of these statements about the XEOMIN® treatment process and patient selection are correct?

a. The consultation serves to provide the patient with full information about all aspects of the recommended treatment
b. Myasthenia gravis is an absolute contraindication to treatment with XEOMIN®
c. XEOMIN® should be used with caution in patients suffering from diseases that result in peripheral neuromuscular dysfunction
d. 0.9% alcohol is used to prepare an injectable XEOMIN® solution
e. EMG recordings can help to localise involved muscles
Self-test – Task 2

- One vial of XEOMIN® contains 100 units of Botulinum neurotoxin type A (150 kD), free from complexing proteins. How many units per ml do you get after reconstitution with 4.0 ml saline (NaCl)?

a. 40 U/ml  
b. 4 U/ml  
c. 25 U/ml  
d. 20 U/ml
Self-test – Task 3

During consultation a patient mentions that he was recommended to take malaria prophylaxis because of a forthcoming holiday to east Africa. The active substance chloroquine is to be used. The patient would now like to know what he should do

a. No interactions are to be expected from administration of the specified active substance. Prophylaxis can be conducted as planned

b. Administration of the specified active substance may reduce the effect of XEOMIN®. Another active substance should be used instead, as a precautionary measure

c. Administration of the specified active substance may potentiate the effect of XEOMIN®. Another active substance should be used instead, as a precautionary measure
Self-test – Task 4

Which of the following statements regarding the symptomatic treatment of spasmodic torticollis with XEOMIN® are correct?

a. Bilateral injections into the sternocleidomastoid muscle markedly increase the risk of dysphagia.

b. Underlying neurological disorders including swallowing difficulties increase the risk of dysphagia or exaggerated muscle weakness.

c. In spasmodic torticollis management total doses of up to 300 units XEOMIN® may be given per treatment session. However, no more than 50 units should be given at any one injection site.
Self-test – Task 5

Which of the following statements regarding treatment of post-stroke spasticity of the upper limb with XEOMIN® is accurate?

a. Begin physical management of PSS only after an administration procedure for XEOMIN® has been established
b. Exposure to XEOMIN® should not exceed 1 year
c. The total recommended dose of XEOMIN® administered per treatment session in the management of PSS of the upper limb is up to 400 units
Legal Information / Appendix
Legal information

- Number of version: 2.2 (Date: 2012-05-31)
- Copyright notice: This educational material is intended to be used to inform physicians about the safe use of XEOMIN® and potential risks. Any unauthorized copying or distribution is prohibited.
- Contact information:
  Merz Pharmaceuticals GmbH
  Therapeutic Area Neurology (TAN)
  Eckenheimer Landstraße 100
  D-60318 Frankfurt am Main
Appendix – Documents

- Here you can access the XEOMIN SmPC and the Patient Brochure pertaining to the treatment of dystonic movement disorders and post-stroke spasticity of the upper limb.* Click on the document titles to call them up
- XEOMIN® SmPC
- Patient Brochure

* XEOMIN® is indicated for the symptomatic treatment of blepharospasm, cervical dystonia of a predominantly rotational form (spasmodic torticollis) and for the symptomatic treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults.
Appendix – Self-test solutions

- Task 1: a, b, c, e
- Task 2: c
- Task 3: b (chloroquine is a 4-aminochinoline)
- Task 4: a, b, c
- Task 5: c
## Appendix – Jankovic Rating Scale (JRS)

The JRS consists of a 0 to 4 point severity scale and a 0 to 4 point frequency scale. The overall score is the sum of these two (max. score 8 points)

<table>
<thead>
<tr>
<th>JRS – Severity</th>
<th>JRS – Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Appendix – Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)

- The TWSTRS quantifies overall disease burden with the following subscales
  - Severity Scale (A to F, Maximum = 35)
  - Disability Scale (A to F, Maximum = 30, no details shown)
  - Pain Scale (A to C, Maximum = 20, no details shown)

Severity Scale, part 1/2

<table>
<thead>
<tr>
<th>A. Measurement of the head deviation (maximal excursion)</th>
<th>Possible rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Rotation of head</td>
<td>0-4</td>
</tr>
<tr>
<td>2. Laterocollis</td>
<td>0-3</td>
</tr>
<tr>
<td>3. Antecollis/retrocollis</td>
<td>0-3</td>
</tr>
<tr>
<td>4. Lateral shift</td>
<td>Yes = 1/No = 0</td>
</tr>
<tr>
<td>5. Sagittal shift (forwards or backwards)</td>
<td>Yes = 1/No = 0</td>
</tr>
</tbody>
</table>

### Severity Scale, part 2/2

<table>
<thead>
<tr>
<th></th>
<th>Possible rating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B. Duration factor</strong></td>
<td></td>
</tr>
<tr>
<td>Estimation of the duration of dystonic symptoms (deviation of head) as a percentage</td>
<td>0-5 (weighted x2)</td>
</tr>
<tr>
<td><strong>C. Effect of sensory tricks</strong></td>
<td>Possible rating</td>
</tr>
<tr>
<td>Assessment of the improvement due to sensory tricks</td>
<td>0-2</td>
</tr>
<tr>
<td><strong>D. Shoulder elevation/anterior displacement</strong></td>
<td>Possible rating</td>
</tr>
<tr>
<td>Assessment of the degree of associated movement of the shoulder</td>
<td>0-3</td>
</tr>
<tr>
<td><strong>E. Range of motion (without sensory tricks)</strong></td>
<td>Possible rating</td>
</tr>
<tr>
<td>Assessment of the flexibility of head movements in the opposite direction to the dystonia</td>
<td>0-4</td>
</tr>
<tr>
<td><strong>F. Compensation time</strong></td>
<td>Possible rating</td>
</tr>
<tr>
<td>Measurement of the time for which the patient is able to hold the head in a neutral position looking forward</td>
<td>0-4</td>
</tr>
</tbody>
</table>

Appendix – Ashworth Scale

Significant Muscles: Widely used scale for the quantitative determination of muscle tone during passive movements
Score 0 to 4

<table>
<thead>
<tr>
<th>Score</th>
<th>Ashworth Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No increase in tone</td>
</tr>
<tr>
<td>1</td>
<td>Slight increase in tone</td>
</tr>
<tr>
<td>2</td>
<td>More marked increase in tone, but limb easily flexed</td>
</tr>
<tr>
<td>3</td>
<td>Considerably increased muscle tone, passive movements difficult</td>
</tr>
<tr>
<td>4</td>
<td>Limb rigid in flexion or extension</td>
</tr>
</tbody>
</table>