Botulinum Toxin Injection

Description of Procedure or Service

Description

Botulinum is a family of toxins produced by the anaerobic organism Clostridia botulinum. Four formulations of botulinum toxin have been approved by the U.S. Food and Drug Administration (FDA). Labeled indications of these agents differ; however, all are FDA-approved for treating cervical dystonia in adults. Botulinum toxin products are also used for a range of off-label indications.

Background

There are 7 distinct serotypes designated as type A, B, C-1, D, E, F, and G. In the U.S., 4 preparations of botulinum are commercially available, 3 using type A serotype and 1 using type B. The drug names of the botulinum toxin products were changed in 2009; trade names and product formulations did not change. The 3 formulations of botulinum toxin type A are currently called onabotulinumtoxinA (Botox®), abobotulinumtoxinA (Dysport®), and incobotulinumtoxinA (Xeomin®). Botox has been available for the longest time in the United States and has been the most widely used. Xeomin, the newest product marketed in the U.S., consists of the pure neurotoxin without complexing proteins and is the only product that is stable at room temperature for up to 4 years. Myobloc® contains botulinum toxin type B; the current name of this drug is rimabotulinumtoxinB.

All 4 products are approved by the U.S. Food and Drug Administration (FDA) for the treatment of cervical dystonia in adults; this is the only FDA-approved indication for Myobloc. Dystonia is a general term describing a state of abnormal or disordered tonicity of muscle. As an example, esophageal achalasia is a dystonia of the lower esophageal sphincter, while cervical dystonia is also known as torticollis. Spasticity is a subset of dystonia, describing a velocity-dependent increase in tonic-stretch reflexes with exaggerated tendon jerks. Spasticity typically is associated with injuries to the central nervous system. Spasticity is a common feature of cerebral palsy. OnabotulinumtoxinA is also approved for treatment of urinary incontinence due to neurogenic conditions causing detrusor overactivity in patients unresponsive to or intolerant to anticholinergic medication. Most recently, in 2013, onabotulinumtoxinA received FDA approval for treatment of overactive bladder (OAB) in adults who are unresponsive to or intolerant to anticholinergic medication.

The newest product, Xeomin, is approved for treating blepharospasm.

Two products, Botox (marketed as Botox Cosmetic) and Dysport, are approved for temporarily improving the appearance of glabellar (frown) lines in adults younger than 65 years of age.

The botulinum toxin products have also been used for a wide variety of off-label indications, ranging from achalasia, spasticity after strokes, cerebral palsy, and anal fissures.
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Regulatory Status

Botox® (Allergan, Irvine, CA) was approved by the FDA in 1991, Myobloc® (Solstice Neurosciences) in 2000, Dysport® (Medicis Pharmaceutical Corporation, Scottsdale, AZ) in 2009, and Xeomin® (Merz Pharmaceuticals) in 2010.

Related Policies

Hyperhidrosis, Treatment of

***Please note that the US Food & Drug Administration (FDA) now requires a boxed warning and a Risk Evaluation and Mitigation Strategy (REMS) for all Botulinum Toxin products. Refer to the FDA Website for additional information located at http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/ucm174949.htm.

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for Botulinum Toxin Injection when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Botulinum Toxin Injection is covered

The use of botulinum toxin may be considered medically necessary for the following:

1. Cervical dystonia (spasmodic torticollis; applicable whether congenital, due to child birth injury, or traumatic injury). For this use, cervical dystonia must be associated with sustained head tilt or abnormal posturing with limited range of motion in the neck AND a history of recurrent involuntary contraction of one or more of the muscles of the neck, e.g., sternocleidomastoid, splenius, trapezius, or posterior cervical muscles*. (See additional details in Policy Guidelines section.)
2. Strabismus*
3. Blepharospasm or facial nerve (VII) disorders (including hemifacial spasm)*
4. Upper limb spasticity*
5. Prevention (treatment) of chronic migraine headache in the following situations*:
   (See Policy Guidelines)
   a. Initial 6-month trial: Adult patients who meet established diagnostic criteria for chronic migraine headache and have symptoms that persist despite trials of at least 2 agents used to prevent migraines or reduce migraine frequency representing different classes of medications. (Patients who have contraindications to preventive medications are not required to undergo a trial of these agents).
   b. Continuation of treatment beyond 6 months:
      • Migraine headache frequency reduced by at least 7 days per month compared to pre-
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- Migraine headache duration reduced at least 100 hours per month compared to pre-treatment level.

6. Dystonia/spasticity resulting in functional impairment (interference with joint function, mobility, communication, nutritional intake) with or without pain. Examples include but are not limited to patients with any of the following:
   a. Focal dystonias:
      - Focal upper limb dystonia (e.g., organic writer’s cramp)
      - Oromandibular dystonia (orofacial dyskinesia, Meige syndrome)
      - Laryngeal dystonia (adductor spasmodic dysphonia)
      - Idiopathic (primary or genetic) torsion dystonia
      - Symptomatic (acquired) torsion dystonia
   b. Spastic conditions
      - Cerebral palsy
      - Spasticity related to stroke
      - Acquired spinal cord or brain injury
      - Hereditary spastic paraparesis
      - Spastic hemiplegia
      - Neuromyelitis optica
      - Multiple sclerosis or Schilder’s disease

7. Esophageal achalasia in patients who have not responded to dilation therapy or who are considered poor surgical candidates.

8. Sialorrhea (drooling) associated with Parkinson disease.

9. Chronic anal fissure.

10. Urinary incontinence due to detrusor overreactivity* associated with neurogenic causes (e.g., spinal cord injury, multiple sclerosis), that is inadequately controlled with anticholinergics.

11. Overactive bladder* (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication.

*FDA-approved indication for at least one of the agents.

***Use of botulinum toxin for off-label indications should only be done when the treating physician has determined that the benefits of the treatment clearly outweigh the risks of the therapy.

When Botulinum Toxin Injection is not covered

With the exception of cosmetic indications, the use of botulinum toxin is considered investigational for all other indications not specifically mentioned above, including, but not limited to:

- headaches, except as noted above for prevention (treatment) of chronic migraine headache
- chronic low back pain
- joint pain
- mechanical neck disorders
- neuropathic pain after neck dissection
- myofascial pain syndrome
- temperomandibular joint disorders
- trigeminal neuralgia
- pain after hemorrhoidectomy or lumpectomy
- tremors such as benign essential tremor (upper extremity)
- tinnitus
- sialorrhea (drooling) except that associated with Parkinson disease.
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- chronic motor tic disorder, and tics associated with Tourette syndrome (motor tics)
- lateral epicondylitis
- benign prostatic hyperplasia
- interstitial cystitis
- detrusor sphincteric dyssynergia (after spinal cord injury)
- piriformis
- prevention of pain associated with breast reconstruction after mastectomy
- Hirschsprung’s disease
- gastroparesis
- facial wound healing
- internal anal sphincter (IAS) achalasia
- depression

The use of botulinum toxin is not medically necessary as a treatment of wrinkles or other cosmetic indications.

The use of assays to detect antibodies to botulinum toxin is considered investigational.

Policy Guidelines

This drug may require prior review. In cases for which botulinum toxin has been approved in the past, medical records may be required yearly to document ongoing effectiveness. For the indication of prevention of chronic migraine headaches, medical records may be required to document effectiveness after the initial 6-month trial and periodically thereafter.

Prevention (treatment) of chronic migraine headache. Botulinum toxin is considered medically necessary for the prevention (treatment) of chronic migraine in the following situations, i.e., patients were diagnosed with chronic migraine who failed trials of other medications.

According to the International Headache Classification (ICHD-2) diagnostic criteria for migraine without aura are:

A. At least 5 attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following characteristics:
   1. unilateral location
   2. pulsating quality
   3. moderate or severe pain intensity
   4. aggravation by or causing avoidance of routine activity (e.g., walking or climbing stairs)
D. During headache at least one of the following:
   1. nausea and/or vomiting
   2. photophobia and phonophobia
E. Not attributed to another disorder

According to the International Headache Classification (ICHD-2), diagnostic criteria for migraines with aura are:

A. At least 2 attacks fulfilling criteria B-D
B. Aura consisting of at least one of the following, but no motor weakness:
   1. fully reversible visual symptoms including positive features (e.g., flickering lights, spots or lines) and/or negative features (i.e., loss of vision)
   2. fully reversible sensory symptoms including positive features (i.e., pins and needles) and/or negative features (i.e., numbness)
   3. fully reversible dysphasic speech disturbance
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C. At least two of the following:
   1. homonymous visual symptoms and/or unilateral sensory symptoms
   2. at least one aura symptom develops gradually over ≥5 minutes and/or different aura symptoms occur in succession over ≥5 minutes
   3. each symptom lasts ≥5 and ≤60 minutes
D. Headache fulfilling criteria B-D for Migraine without aura begins during the aura or follows aura within 60 minutes
E. Not attributed to another disorder

Chronic migraine is defined as headaches that occur on ≥15 days per month for at least 3 months; with greater than or equal to 8 meeting criteria for migraines; provided there is no medication overuse. For complete classification of primary migraine and non-migraine headaches, please see the International Headache Classification (ICHD-2) at http://ihs-classification.org/en/.

Cervical dystonia is a movement disorder (nervous system disease) characterized by sustained muscle contractions. This results in involuntary, abnormal, squeezing and twisting muscle contractions in the head and neck region. These muscle contractions result in sustained abnormal positions or posturing. Sideways or lateral rotation of the head and twisting of the neck is the most common finding in cervical dystonia. Muscle hypertrophy occurs in most patients. When using botulinum toxin to treat cervical dystonia, the postural disturbance and pain must be of a severity to interfere with activities of daily living; and the symptoms must have been unresponsive to a trial of standard conservative therapy. In addition, before using botulinum toxin, alternative causes of symptoms such as cervicogenic headaches must have been considered and excluded.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 46505, 52287, 64611, 64612, 64615, 64616, 64617, 64642, 64643, 64644, 64645, 64646, 64647, 64653, 67345, 95873, 95874, J0585, J0586, J0587, J0588, S2340, S2341

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Independent Review by Senior Director of Health Affairs - 5/94


TEC Bulletin - 2/26/96


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Corporate Pharmacist - 5/99


BCBSA Medical Policy Reference Manual, 8/18/00, 5.01.05


BCBSA Medical Policy Reference Manual, 5.01.05, 5/31/01


TEC Assessment, Botulinum Toxin for Treatment of Primary Chronic Headache Disorders. October 10, 2002

BCBSA Medical Policy Reference Manual, 5.01.05, 12/18/02


BCBSA Medical Policy Reference Manual, 5.01.05, 11/9/04

BCBSA Medical Policy Reference Manual, 5.01.05, 12/14/05

BCBSA Medical Policy Reference Manual, 5.01.05, 4/25/06


BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.05, 12/12/06.
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U.S. Food & Drug Administration (FDA). Early communication about an ongoing safety review Botox and Botox Cosmetic (Botulinum toxin Type A) and Myobloc (Botulinum toxin Type B). Retrieved 2/25/2008 from http://www.fda.gov/cder/drug/early_comm/botulinium_toxins.htm.


Senior Medical Director - 9/2009


Aurora SK, Dodick DW, Turkel CC et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 1 trial. Cephalagia 2010; 30(7):804-17.


Medical Director – 1/2011


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Senior Medical Director – 5/2013


Policy Implementation/Update Information

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/85</td>
<td>Original Policy National Association - Investigational for blepharospasm</td>
</tr>
<tr>
<td>4/96</td>
<td>Revised: Added additional covered indications and investigational indications, TEC Bulletin 2/96</td>
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<tr>
<td>4/97</td>
<td>Reaffirmed</td>
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<tr>
<td>5/99</td>
<td>Reaffirmed</td>
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<tr>
<td>7/99</td>
<td>Reformatted, Description of Procedure or Service changed, Medical Term Definitions added.</td>
</tr>
<tr>
<td>4/2000</td>
<td>Statement added to section, &quot;When Botulinum-A Toxin Injection is not covered&quot;, which says, &quot;1) For conditions other than those listed above.&quot; System coding changes.</td>
</tr>
<tr>
<td>7/00</td>
<td>Added Gustatory sweating (Frey’s Syndrome) as a covered indication. Specialty Matched Consultant Advisory Panel.</td>
</tr>
<tr>
<td>9/00</td>
<td>Medical Policy Advisory Group review. Approved. No change in criteria.</td>
</tr>
<tr>
<td>10/00</td>
<td>Revised. Criteria changes. Botulinum now eligible for coverage for achalasia, chronic anal fissure, and investigational for headache or migraine, myofascial pain syndrome, or tremors such as benign essential tremor, chronic motor tic disorder and tics associated with Tourette syndrome. Medical Policy Advisory Group - Approved.</td>
</tr>
<tr>
<td>04/01</td>
<td>Changes in formatting.</td>
</tr>
<tr>
<td>10/01</td>
<td>Policy name changed from Botulinum A Toxin Injection. Revised description to include type...</td>
</tr>
</tbody>
</table>
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B Botulinum (Myobloc) and FDA labeled indications to include cervical dystonia. System application guidelines revised.

3/02 System coding changes. Added code J0587 to policy and removed code J3490.

5/02 Revised under when it is covered, number 3. a. to include, "and/or". Codes 64612-64614, and 67345 added to Billing and Coding section.

8/03 Description section revised for clarity. Added spasmodic dysphonia under "When Covered" section. Added chronic low back pain under "When Not Covered" section. Reformatted "When Covered" and "When Not Covered" sections for ease of reading. Removed codes 64040 and 67399 from Billing and Coding section. Added Codes S2340 and S2341 to Billing and Coding section. Added references.


2/17/05 Added the following statement to "When Covered" and "Policy Guidelines" sections: Refer to separate policy number MED1215, titled "Hyperhidrosis, Treatment of" regarding Botulinum toxin injection guidelines for patients with primary Hyperhidrosis. Key word added.

1/19/06 Added 2006 CPT codes 46505, 64653, 95873, 95874 to Billing/Coding section.

9/18/06 Under "When Covered" section, added "Botulinum toxin may be considered medically necessary as a treatment of incontinence due to detrusor overreactivity caused by spinal cord injury that is inadequately controlled with anticholinergic therapy." Under "When not Covered" section, 3.c. now reads "headache including migraine, chronic tension, chronic daily, and cervicodystonic headaches". Added 3.i. sialorrhea (drooling); 3.j. lateral epicondylitis; 3.k. benign prostatic hyperplasia; 3.l. detrusor overactivity not due to spinal cord injury; 3.m. detrusor sphincteric dyssynergia. Medical term definitions added. Reference sources added.


8/27/07 Under "When Covered" section: 1.c.- added "such as hemifacial spasm"; 1.d.- added "(see "Policy Guidelines" section for use of Botulinum Toxin for this indication)"; 2.i.- added "or to demyelinating conditions such as multiple sclerosis."

8/27/07 Under "When Covered" section: Revised to "lower esophageal achalasia where the patient has not responded to dilation therapy or where the patient is considered a poor surgical candidate." Under "When not Covered" section: 3.a.- end of sentence revised to "and cervicogenic or "cervicodystonic"; added 3.l. priformis syndrome. Under "Policy Guidelines" section: Added A.1-5: Use of Botulinum Toxin for Cervical Dystonia (Spasmocic Torticollis): ALL of the following criteria must be met: 1) Postural disturbance and pain must be of moderate or greater severity as documented by interference with specific activities of daily living and unresponsive to a trial of appropriate standard conservative therapy that may include non-narcotic analgesics, muscle relaxants and physical modalities; AND 2) There are clonic and/or tonic involuntary contractions of multiple neck muscles (that is, sternocleidomastoid, splenius, trapezius and/or posterior cervical muscles); AND 3) There is sustained head torsion and/or tilt with limited range of motion in the neck; AND 4) The duration of the condition must be greater than six months; AND 5) Alternative causes of the patient's symptoms have been considered and ruled out including chronic neuroleptic treatment, cervicogenic headaches, myofascial pain syndrome, contractures or other neuromuscular conditions. Added B. Contraindications for use of Botulinum toxin: 1) Absolute: a. Inflammation or infection at the site of injection. b. Allergy...
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to the drug. 2) Relative: a. Inability of patient to cooperate b. Coagulopathy c. Disease of
euromuscular transmission: i. Myasthenia Gravis ii. Eaton Lambert Syndrome iii.
Amyotrophic lateral sclerosis iv. Peripheral neuropathy v. Motor neuron disease d. Concurrent
use of medications that affect neuromuscular transmission such as aminoglycoside antibiotics.

4/7/08  Added FDA warning information to the "Description" section; "Please note that the US Food
& Drug Administration (FDA) has issued a warning regarding the use of botulinum toxin. It
has been reported that there have been serious systemic adverse reactions including respiratory
distress and death from botulinum toxins types A and B. The adverse events have occurred in
both FDA approved and unapproved uses. Most of the adverse events have occurred in
children treated for cerebral palsy associated limb spasticity. Safety, efficacy and dosage have
not be established of the use of Botulinum toxins for limb spasticity of cerebral palsy or any
condition in children under the age of 12. Also added the following to the "When Covered"
section; "The treating physician should carefully review the above FDA issued warning. Use
of botulinum toxin for off-label indications should only be done when the treating physician
does not think that the benefits of the treatment clearly outweigh the risks of the therapy."
References added.

7/14/08  Specialty Matched Consultant Advisory review 5/29/08. Added comment; "(See "Policy
Guidelines" section for use of Botulinum Toxin for this indication)" to 3.a. under the "When
Covered" section. Changed the wording in #5 under the "When Covered" section to read
"either idiopathic or due to neurogenic causes" and added "multiple sclerosis" as an example.
Added additional examples of non-covered indications under the "When Covered" section.
These are "c. joint pain, d. mechanical neck disorders, e. neuropathic pain after neck
dissection, g. pain after hemorrhoidectomy or lumpectomy, and n. interstitial cystitis." No
change to policy intent. Added "Myoclonus and Tics" to "Definition" section. References
added.

1/12/09  Revised "Description" section to add; "Type A (Botox®) is more potent and longer acting
than type B (Myobloc®). Units and dosing are not equivalent and cannot be interchanged."
The word "warning" was removed from the statement; "(FDA) has issued an early
communication regarding an on-going safety review" and added "The FDA plans to
communicate to the public its findings, resulting recommendations, and any regulatory actions
after the review of the data are completed." Updated the "When Covered" section with the
following changes;"2. dystonia/spasticity resulting in functional impairment (interference with
joint function, mobility, communication, nutritional intake)" and statement "The treating
physician should carefully review the above FDA issued warning." Added additional wording
for clarifications to various indications and an additional indication; "2.k. Spinal cord or
traumatic brain injury;". Added additional wording for clarification to various indications in
the "When Not Covered" section and "4. The use of assays to detect antibodies to botulinum
toxin is considered investigational." Added "In cases for which botox has been approved in the
past, medical records are required yearly to document ongoing effectiveness of botox" to the
"Policy Guidelines" section. References added.

10/26/09 Revised "Description" section. Added information related to the FDA approval of Dysport for
cervical dystonia, new established names of Botox and Myobloc, and the FDA requirement of
a boxed warning and a Risk Evaluation and Mitigation Strategy (REMS) for all Botulinum
Toxin products. Changed "paraplegia" to paraparesis" in 2.e. under the "When Covered"
section. Added 3.d. "Sialorrhea (drooling) associated with Parkinson disease" to the "When
covered" section. Changed the wording under the "Policy Guidelines" section in A.2. from
"involuntary contractions of multiple neck muscles" to "involuntary contractions of one or
more neck muscles". Reviewed with the Senior Medical Director 9/16/09. References added.
(btw)
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1/5/10  Added new HCPCS code, J0586, to "Billing/Coding" section. (btw)

6/22/10 Policy Number(s) removed. (amw)


2/1/11 Updated “Description” section to include information regarding FDA approval of onabotulinumtoxinA (Botox) for the prevention of chronic headache. Added #5 to the “When Covered” section to indicate; “5. Prevention (treatment) of chronic migraine headache in the following situations*: (see Policy Guidelines) a. Initial 6-month trial: Adult patients who meet established diagnostic criteria for chronic migraine headache and have symptoms that persist despite trials of at least 2 agents used to prevent migraines or reduce migraine frequency representing different classes of medications. (Patients who have contraindications to preventive medications are not required to undergo a trial of these agents). b. Continuing treatment beyond 6 months: Migraine headache frequency reduced by at least 7 days per month, or Migraine headache duration reduced at least 100 hours per month.” Added the International Headache Classification definition of migraine to “Policy Guidelines” section. References added. Reviewed by Medical Director 1/ 25/2011. (btw)

3/29/11 Added new HCPCS code, Q2040” to “Billing/Coding” section. Removed deleted code, C9278. (btw)

12/20/11 Specialty Matched Consultant Advisory Panel review 11/30/2011. Added the following indications to the “When Not Covered” section for clarification: prevention of pain associated with breast reconstruction after mastectomy, Hirschsprung’s disease, and gastroparesis. Changed wording in number 6 to “Examples include but are not limited to patients with any of the following:”. No change to policy intent. Added 2012 HCPCS code, J0588, to “Billing/Coding” section and deleted Q2040 and C9278. References added. (btw)

11/13/12 Specialty Matched Consultant Advisory Panel review 10/17/2012. No change to policy intent. The definition of “chronic migraine” was updated in the Policy Guidelines to include “with greater than or equal to 8 meeting criteria for migraines; provided there is no medication overuse.” Reference added. (btw)

12/28/12 Effective 1/1/2013, new CPT codes, 52287 and 64615, added to Billing/Coding section. (btw)

2/26/13 Added “urgency, and frequency” and the “*” indicating FDA approval to number 10 under the When Covered section. Medical Director review 2/2/2013. (btw)

5/28/13 Removed “urgency and frequency” from #10 under the When Covered section. Added #11. “Overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication”. Reference added. Senior Medical Director review 5/18/2013. (btw)

12/31/13 Specialty Matched Consultant Advisory Panel review 10/16/2013. Description section updated. Changed the wording in #6 under the When Covered section from “and/or” to “with or without” for clarification. Added Facial wound healing and internal anal sphincter (IAS) achalasia to the When Not Covered section. Added new 2014 CPT codes, 64616, 64617, 64642, 64643, 64644, 64645, 64646, and 64647 to Billing/Coding section. Removed deleted
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codes, 64613 and 64614. Reference added. (btw)


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