Medtronic

ITB Therapy℠

For Severe Spasticity

Commonly Billed Codes

January 2010

Medtronic provides this information for your convenience only. It is not intended as a recommendation regarding clinical practice. It is the responsibility of the provider to determine coverage and submit appropriate codes, modifiers, and charges for the services that were rendered. This document provides assistance for FDA approved or cleared indications. Where reimbursement is requested for a use of a product that may be inconsistent or not expressly specified in the FDA cleared or approved labeling (e.g., instructions for use, operator's manual or package insert) consult with your billing advisors or payers for advice on handling such billing issues. Some payers may have policies that make it inappropriate to submit claims for such items or related service. Contact your Medicare contractor or other payer for interpretation of coverage, coding, and payment policies.

Coverage and Authorization Services is available to respond to your coding questions at 800-292-2903.

ICD-9-CM[1] Diagnosis Codes

Diagnosis codes are used by both physicians and hospitals to document the indication for the procedure. ITB Therapy is directed at reducing spasticity. Although ICD-9-CM provides codes for these symptoms, the principal diagnosis is the underlying cause as shown.

Spasticity of Spinal Origin	**340**	Multiple sclerosis
	342.1X	Spastic hemiplegia
	344.0X	Spastic quadriplegia
	344.1	Spastic paraplegia, non-infantile or congenital
	344.2	Spastic diplegia of upper limbs
	344.3X	Spastic monoplegia of lower limb
	344.4X	Spastic monoplegia of upper limb
	344.5	Spastic monoplegia, unspecified
	344.9	Spastic paralysis, unspecified
Spasticity of Cerebral Origin: Cerebral Palsy[2]	**343.0**	Infantile cerebral palsy, diplegic (congenital diplegia, congenital paraplegia)
	343.1	Infantile cerebral palsy, hemiplegic (congenital hemiplegia)
	343.2	Infantile cerebral palsy, quadriplegic (tetraplegic)
	343.3	Infantile cerebral palsy, monoplegic
	343.4	Infantile cerebral palsy, infantile hemiplegia (postnatal)
	343.8	Other specified infantile cerebral palsy
	343.9	Infantile cerebral palsy, unspecified
	344.89	Spastic cerebral palsy, not congenital or infantile

Chart continued on next page

ICD-9-CM[1] Diagnosis Codes *continued*

Spasticity of Cerebral Origin: Late Effects of Brain Injury	**342.1X**	Spastic hemiplegia
	344.0X	Spastic quadriplegia
	344.1	Spastic paraplegia
	344.2	Spastic diplegia of upper limbs
	344.3X	Spastic monoplegia of lower limb
	344.4X	Spastic monoplegia of upper limb
	344.5	Spastic monoplegia, unspecified
	344.9	Spastic paralysis, unspecified
Spasticity of Cerebral Origin: Late Effects of Cerebrovascular Accident	**438.20**	Hemiplegia/hemiparesis, affecting unspecified side
	438.21	Hemiplegia/hemiparesis, affecting dominant side
	438.22	Hemiplegia/hemiparesis, affecting nondominant side
	438.30	Monoplegia of upper limb, affecting unspecified side
	438.31	Monoplegia of upper limb, affecting dominant side
	438.32	Monoplegia of upper limb, affecting nondominant side
	438.40	Monoplegia of lower limb, affecting unspecified side
	438.41	Monoplegia of lower limb, affecting dominant side
	438.42	Monoplegia of lower limb, affecting nondominant side
	438.50	Other paralytic syndrome (includes quadriplegia), affecting unspecified side
	438.51	Other paralytic syndrome (includes quadriplegia), affecting dominant side
	438.52	Other paralytic syndrome (includes quadriplegia), affecting nondominant side
	438.84	Ataxia, late effect of cerebrovascular disease
	438.89	Other late effects of cerebrovascular disease
Attention to Device[3]	**V53.09**	Fitting and adjustment of devices related to nervous system
Symptom Codes[4]	**781.0**	Abnormal involuntary movements, spasms, tremors
	781.2	Abnormality of gait (gait dysfunction)
	781.3	Lack of coordination (ataxia, muscular incoordination)

1. The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) is maintained by the National Center for Health Statistics and the Centers for Medicare and Medicaid Services.
2. Cerebral palsy codes also classify cerebral spastic infantile paralysis, congenital spastic paralysis (cerebral) and spastic paralysis due to birth injury.
3. Code V53.09 is used as the principal diagnosis when patients are seen for routine device replacement and maintenance. A secondary diagnosis code is then used for the underlying condition.
4. Some payers may require these symptom codes as a secondary diagnosis. Please contact the payer to obtain proper billing instructions.

ICD-9-CM[1] Procedure Codes

Hospitals use ICD-9-CM procedure codes for inpatient services.

Catheter Insertion	**03.90**	Insertion of catheter into spinal canal for infusion of therapeutic or palliative substances
Lioresal® Intrathecal (baclofen injection)	**03.92**	Injection of other agent into spinal canal
Pump Implantation	**86.06**	Insertion of totally implantable infusion pump
Pump Removal	**86.05**	Incision with removal of foreign body or device from skin and subcutaneous tissue
Catheter Removal (surgical)	**03.99**	Other operation on spinal cord and spinal canal structures

1. The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) is maintained by the National Center for Health Statistics and the Centers for Medicare and Medicaid Services.

HCPCS II Device Codes[1]

These codes are used by the entity that purchased and supplied the medical device, DME, or supply to the patient. For implantable devices, that is typically the facility.

For specific Medicare hospital outpatient billing instructions for Medicare devices, see the Device C-Codes for Medicare.

Entire System (Catheter and Programmable Pump)	**E0783**	Infusion pump system, implantable, programmable (includes all components, e.g., pump, catheter, connectors, etc.)
Programmable Pump only (replacement)	**E0786**	Implantable programmable infusion pump, replacement (excludes implantable intraspinal catheter)
Intraspinal Catheter only (replacement)	**E0785**	Implantable intraspinal (epidural/intrathecal) catheter used with implantable infusion pump, replacement

1. Healthcare Common Procedure Coding System (HCPCS) Level II codes are maintained by the Centers for Medicare and Medicaid Services. More information can be found at: http://www.cms.hhs.gov/MedHCPCSGenInfo/01_Overview.asp#TopOfPage.

Device C-Codes[1] (Medicare)

Hospitals assign C-codes when billing Medicare for medical devices in the outpatient setting. Although other payers may also accept C-codes, regular HCPCS II device codes are generally used for billing non-Medicare payers. For Medicare, billing C-codes is mandatory for medical devices utilized in the hospital outpatient setting.

ASCs, however, usually should not assign or report HCPCS II device codes for devices on claims sent to Medicare. Medicare generally does not make a separate payment for devices in the ASC. Instead, payment is "packaged" into the payment for the ASC procedure. ASCs are specifically instructed not to bill HCPCS II device codes to Medicare for devices that are packaged.[2]

Infusion Pump	**C1772**	Infusion pump, programmable (implantable)
Intrathecal Catheter	**C1755**	Catheter, intraspinal

1. Device C-codes are HCPCS Level II codes and also maintained by the Centers for Medicare and Medicaid Services. A complete list of C-codes is available at: http://www.cms.hhs.gov/HCPCSReleaseCodeSets/ANHCPCS/list.asp#TopOfPage.
2. ASC should report all charges incurred. However, only charges for non-packaged items should be billed as separate line items. For example, the ASC should report its charge for the infusion pump. However, because the infusion pump is a packaged item, the charge should not be reported on its own line. Instead, the ASC should bill a single line for the implantation procedure with a single total charge, including not only the charge associated with the operating room but also the charges for the infusion pump and all other packaged items. Because of a Medicare requirement to pay the lesser of the ASC rate or the line-item charge, breaking these packaged charges out onto their own lines can result in incorrect payment to the ASC. (See the Medicare Claims Processing Manual, Chapter 14, section 40; see also MLN Matters SE0742 p. 9-10.)

Device Edits (Medicare)

Medicare's Consolidated Device Edits require that when specific CPT® procedure codes for device implantation are billed, associated HCPCS II codes for the devices must also be billed.[1] When a hospital outpatient bill is received that contains one of the specific CPT procedure codes without one of the required HCPCS II codes, the claim is returned to the provider for correction.

CPT Procedure Code	CPT Code Description[2]	Associated HCPCS II Code	HCPCS II Code Description
62362	Implantation or replacement of device for intrathecal or epidural drug infusion; programmable pump, including preparation of pump, with or without programming	**C1772**	Infusion pump, programmable, implantable

1. Device edits can be found at: http://www.cms.hhs.gov/HospitalOutpatientPPS/02_device_procedure.asp#TopOfPage. The edits are updated once a quarter.
2. CPT copyright 2009 American Medical Association. All rights reserved. CPT is a registered trademark of the American Medical Association. No fee schedules, basic units, relative values, or related listings are included in CPT. The AMA assumes no liability for the data contained herein. Applicable FARS/DFARS restrictions apply to government use.

HCPCS II Drug Codes[1]

These codes are used by the entity that purchased and supplied the drug to the patient. These HCPCS II codes can be used by physicians and hospitals for billing both Medicare and non-Medicare payers.

ASC may also use these HCPCS II codes for billing non-Medicare payers. For Medicare, however, special instructions apply.

ASCs usually should not assign or report HCPCS II codes for drugs on claims sent to Medicare. Medicare generally does not make separate payment for drugs but instead "packages" it into the payment for the ASC procedure. ASC are specifically instructed not to bill HCPCS II drug codes to Medicare for drugs that are packaged.[2] However, both of the drugs below are not packaged and for this reason, either drug should be coded separately.

Lioresal® Intrathecal (baclofen injection)	**J0475**	Injection, baclofen, 10 mg
	J0476	Injection, baclofen, 50 mcg for intrathecal trial

1. Healthcare Common Procedure Coding System (HCPCS) Level II codes are maintained by the Centers for Medicare and Medicaid Services. More information can be found at: http://www.cms.hhs.gov/MedHCPCSGenInfo/01_Overview.asp#TopOfPage.
2. ASCs should report all charges incurred but only charges for non-packaged items should be billed as separate line items. Because of a Medicare requirement to pay the lesser of the ASC rate or the line-item charge, breaking these packaged charges out onto their own lines can result in incorrect payment to the ASC. However, Lioresal (baclofen) is not packaged, for either the 10mg injection or the intrathecal trial form. The charges associated with Lioresal (baclofen) should be broken out and billed as their own line item along with the HCPCS II code. (See the Medicare Claims Processing Manual, Chapter 14, section 40; see also MLN Matters SE0742 p. 9-10.)

Lioresal® Intrathecal (baclofen injection) Billing and Refill Kit Information

Kit #/ Model #	NDC	Ampules (number x volume)	Concentration	Total Volume In Kit	Total Drug Qty	HCPCS II Codes and Description	Billing Units Per Kit (1 unit = 10 mg)
8563S Screening Kit	58281-0562-01	1 x 1 ml	50 mcg/ml	1 ml	.05 mg	**J0476** Injection, baclofen, 50 mcg for intrathecal trial	1
8561	58281-0560-01	1 x 20 ml	500 mcg/ml	20 ml	10 mg	**J0475** Injection, baclofen, 10 mg	1
8562	58281-0561-02	2 x 5 ml	2000 mcg/ml	10 ml	20 mg	**J0475** Injection, baclofen, 10 mg	2
8564	58281-0563-01	1 x 20 ml	2000 mcg/ml	20 ml	40 mg	**J0475** Injection, baclofen, 10 mg	4
8565	58281-0560-02	2 x 20 ml	500 mcg/ml	40 ml	20 mg	**J0475** Injection, baclofen, 10 mg	2
8566	58281-0563-02	2 x 20 ml	2000 mcg/ml	40 ml	80 mg	**J0475** Injection, baclofen, 10 mg	8

Physician Coding and Payment — Effective January 1, 2010 – February 28, 2010

CPT® Procedure Codes

Physicians use CPT codes for all services. Under Medicare's Resource-Based Relative Value Scale (RBRVS) methodology for physician payment, each CPT code is assigned a point value, the relative value unit (RVU), which is then converted to a flat payment amount.

Procedure	CPT Code and Description[1]	2010 Medicare RVUs[2]		2010 Medicare National Average[3]	
		For physician services provided in:[4]			
		Physician Office[5]	Facility[5]	Physician Office[5]	Facility[5]
Screening Test	**62311** Injection, single (not via indwelling catheter), not including neurolytic substances, with or without contrasts (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal)	5.02	2.27	$181	$82
	62319 Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal)	5.49	2.54	$198	$92
Implantation, Revision, or Replacement of Catheter[6,7]	**62350** Implantation, revision, or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; without laminectomy	N/A	10.19	N/A	$368
	62351 Implantation, revision, or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; with laminectomy	N/A	22.19	N/A	$801
Implantation or Replacement of Pump[6,7]	**62362** Implantation or replacement of device for intrathecal or epidural drug infusion; programmable pump, including preparation of pump, with or without programming	N/A	10.68	N/A	$385
Removal of Catheter or Pump[6,7]	**62355** Removal of previously implanted intrathecal or epidural catheter	N/A	7.68	N/A	$277
	62365 Removal of subcutaneous reservoir or pump, previously implanted for intrathecal or epidural infusion	N/A	8.46	N/A	$305
Drug/Refill Kit[8] **(ASP Drug Pricing Updated Quarterly—See Footnote)**	**J0475** Injection, baclofen, 10 mg	—	—	ASP+6%	—
	J0476 Injection, baclofen, 50 mcg for intrathecal trial	—	—	ASP+6%	—

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Physician Coding and Payment — CPT® Procedure Codes *continued*

Procedure	CPT Code and Description[1]	2010 Medicare RVUs[2]		2010 Medicare National Average[3]	
		For physician services provided in:[4]			
		Physician Office[5]	Facility[5]	Physician Office[5]	Facility[5]
Fluoroscopy for Catheter Placement and Injection[9]	**77003** Fluoroscopic guidance and localization of needle or catheter tip for spine or paraspinous diagnostic or therapeutic injection procedures (epidural, subarachnoid)	1.60	N/A	$58	N/A
	77003-26 Fluoroscopic guidance and localization of needle or catheter tip for spine or paraspinous diagnostic or therapeutic injection procedures (epidural, subarachnoid)	0.79	0.79	$29	$29
Refill/ Analysis/ Programming[10]	**95990** Refilling and maintenance of implantable pump or reservoir for drug delivery, spinal (intrathecal, epidural) or brain (intraventricular)	1.75	N/A	$63	N/A
	95991 Refilling and maintenance of implantable pump or reservoir for drug delivery, spinal (intrathecal, epidural) or brain (intraventricular), administered by physician	2.58	1.03	$93	$37
	62367 Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); without reprogramming[11]	1.04	0.66	$38	$24
	62368 Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming[11]	1.49	1.03	$54	$37
Catheter Dye Study[12]	**61070** Puncture of reservoir for injection procedure	N/A	2.15	N/A	$78
	75809-26 Shuntogram for investigation of previously placed indwelling non-vascular shunt (indwelling infusion pump)	0.66	0.66	$24	$24
Pump Rotor Study	**62368** Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming	1.49	1.03	$54	$37
	76000 Fluoroscopy	2.69	N/A	$97	N/A
	76000-26 Fluoroscopy	0.24	0.24	$9	$9

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Physician Coding and Payment — CPT® Procedure Codes *continued*

Procedure	CPT Code and Description[1]	2010 Medicare RVUs[2]		2010 Medicare National Average[3]	
		For physician services provided in:[4]			
		Physician Office[5]	Facility[5]	Physician Office[5]	Facility[5]
Evaluation and Management **Note:** An office visit can only be billed separately when a full-scale, separately identifiable evaluation and management service takes place in addition to analysis and programming. The use of evaluation and management codes may require a -25 modifier and must meet separate coding requirements as well as documentation requirements.	**99211 – 99215** Office or other outpatient visit	0.53 – 3.68	0.25 – 2.92	$19 – $133	$9 – $105
	99217 – 99220 Observation care	N/A	1.77 – 4.10	N/A	$64 – $148
	99221 – 99223 Initial hospital care	N/A	2.64 – 5.26	N/A	$95 – $190
	99354 – 99355 Prolonged service, office	2.58 – 2.59	2.43 – 2.45	$93	$88
	99356 – 99357 Prolonged service, inpatient	N/A	2.38	N/A	$86

1. CPT copyright 2009 American Medical Association. All rights reserved. CPT is a registered trademark of the American Medical Association. No fee schedules, basic units, relative values, or related listings are included in CPT. The AMA assumes no liability for the data contained herein. Applicable FARS/DFARS restrictions apply to government use.
2. Medicare Program; Payment Policies Under the Physician Fee Schedule and Other Revisions to Part B (for CY 2010), 74 Fed. Reg. 61738-62188 (finalized November 25, 2009). The total RVU as shown here is the sum of three components: physician work RVU, 2010 transitioned practice expense RVU, and malpractice RVU.
3. Medicare national average payment is determined by multiplying the sum of the three RVUs by the conversion factor. The conversion factor for CY 2010 is $28.4061 as published in the Medicare Program; Payment Policies Under the Physician Fee Schedule and Other Revisions to Part B (for CY 2010), 74 Fed. Reg 61968 (finalized November 25, 2009). However, Congress approved a 60-day freeze on the 2010 Medicare physician payments, beginning on January 1, 2010, and ending on February 28, 2010, as found in bill H.R. 3326 and available at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_cong_bills&docid=f:h3326enr.txt.pdf. Therefore, the payment rates shown are computed using the conversion of $36.0846. Final payment to the physician is adjusted by the Geographic Practice Cost Indices (GPCI). Because GPCI varies by area, each physician's specific reimbursement will vary from the national average payment shown. Also note that any applicable coinsurance, deductible, and other amounts that are patient obligations are included in the national average payment amount shown.
4. The RVUs shown are for the physician's services and payment is made to the physician. However, there are different RVUs and payments depending on the setting in which the physician rendered the service. "Facility" includes physician services rendered in hospitals, ASCs, and SNFs. Physician RVUs and payments are generally lower in the "Facility" setting because the facility is incurring the cost of some of the supplies and other materials. Physician RVUs and payments are generally higher in the "Office" setting because the physician incurs all costs there.
5. "N/A" shown in Physician Office setting indicates that Medicare has not developed RVUs in the office setting because the service is typically performed in a facility (e.g., in a hospital). However, if the local contractor determines that it will cover the service in the office, then it is paid using the facility RVUs at the facility rate, per the Medicare Program; Payment Policies Under the Physician Fee Schedule and Other Revisions to Part B (for CY 2010), 74 Fed. Reg 62015 (finalized November 25, 2009). "NA" shown in the Facility setting indicates that the service is not paid to the physician in a hospital or ASC, because the service is expected to be performed by employees of the hospital or ASC instead.
6. In a replacement, National Correct Coding Initiative (NCCI) edits do not allow removal of the old device to be coded together with implantation of the new device.
7. Surgical procedures are subject to a "global period." The global period defines other physician services which are generally considered part of the surgery package. The services are not separately coded, billed or paid when rendered by the physician who performed the surgery. These services include: preoperative visits the day before or the day of the surgery, postoperative visits related to recovery from the surgery for 10 days or 90 days depending on the specific procedure, treatment of complications unless they require a return visit to the operating room, and minor postoperative services such as dressing changes and suture removal.
8. CMS updates Average Sales Price (ASP) drug pricing on a quarterly basis. ASP values are publicly available at http://www.cms.hhs.gov/McrPartBDrugAvgSalesPrice. For 2010, the payment amount is based on ASP plus 6% per 42CFR 414, SubpartK; Section 112(a) Medicare, Medicaid, and SCHIP Extension Act of 2007 (MMSEA) and Medicare Claims Processing Manual (Chapter 17, section 20.1.3, drugs furnished incident to professional service). Check with your local Medicare contractor or other payer regarding coding and billing instructions for the KD modifier for "drug or biological infused through DME."
9. Some carriers or payers may consider the work of fluoroscopy to be included in the related procedure codes (i.e., 62311, 62319, and 62350) while others may consider fluoroscopy separately payable. According to guidelines by the American Association of Neurological Surgeons, use of fluoroscopy to place the catheter is inherent to 62350 and should not be coded separately. Although National Correct Coding Initiative (NCCI) edits prohibit use of fluoroscopy code 76000 with 62350, they do not prohibit use of fluoroscopy code 77003 with 62350. Similarly, NCCI edits exist for use of fluoroscopy codes 76000, 76001, and 77002 with injection codes 62311 and 62319, but there is no edit for fluoroscopy code 77003. Check with the carrier or payer for specific billing and coverage guidelines.
10. Use the Refill/Analysis/Programming codes only for follow-up services. NCCI edits do not allow these codes to be assigned at the time of pump implantation. Also note that according to published material from the AMA, it is appropriate to code both 62367 – 62368 for device analysis with 95990 – 95991 for refilling when performed at the same encounter.
11. Code 62367 is used for pump interrogation only (e.g., determining the current programming, assessing the device's functions such as its battery voltage and settings, and retrieving or downloading stored data for review). Code 62368 is used when the pump is both interrogated and reprogrammed. In the context of a refill, the AMA has published material indicating that pumps require reprogramming at the time of refilling and that it is appropriate to use 62368 for resetting the pump to its original parameters after a refill.
12. The AMA has published material confirming the use of 61070 and 75809 for implanted pump catheter dye studies. However, use of 64999, (unlisted procedure, nervous system) or code 95999 (unlisted neurological diagnostic procedure) may be preferred by some carriers or payers.

Hospital Outpatient Coding and Payment — Effective January 1, 2010 – December 31, 2010

CPT® Procedure Codes

Hospitals use CPT codes for outpatient services. Under Medicare's APC methodology for hospital outpatient payment, each CPT code is assigned to one of about 800 ambulatory payment classes. Each APC has a relative weight that is then converted to a flat payment amount. Multiple APCs can be assigned for each claim depending on the number of procedures coded.

Procedure	CPT Code and Description[1]	APC[2]	APC Title[2]	SI[2,3]	Relative Weight[2]	2010 Medicare National Average[2,4]
Screening Test	**62311** Injection, single (not via indwelling catheter), not including neurolytic substances, with or without contrasts (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal)	0207	Level III Nerve Injections	T	7.2002	$485
	62319 Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal)	0207	Level III Nerve Injections	T	7.2002	$485
Implantation, Revision, or Replacement of Catheter[5]	**62350** Implantation, revision, or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; without laminectomy	0224	Implantation of Catheter/ Reservoir/ Shunt	T	41.0288	$2,766
	62351 Implantation, revision, or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; with laminectomy	0208	Laminotomies and Laminectomies	T	49.2256	$3,318
Implantation or Replacement of Pump[5]	**62362** Implantation or replacement of device for intrathecal or epidural drug infusion; programmable pump, including preparation of pump, with or without programming	0227	Implantation of Drug Infusion Device	T	198.6572	$13,391
Removal of Catheter or Pump[5]	**62355** Removal of previously implanted intrathecal or epidural catheter	0203	Level IV Nerve Injections	T	13.2439	$893
	62365 Removal of subcutaneous reservoir or pump, previously implanted for intrathecal or epidural infusion	0221	Level II Nerve Procedures	T	37.2806	$2,513
Fluoroscopy for Catheter Placement and Injection[6]	**77003** Fluoroscopic guidance and localization of needle or catheter tip for spine or paraspinous diagnostic or therapeutic injection procedures (epidural, subarachnoid)	N/A	N/A	N	N/A	N/A

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Hospital Outpatient Coding and Payment — CPT® Procedure Codes *continued*

Procedure	CPT Code and Description[1]	APC[2]	APC Title[2]	SI[2,3]	Relative Weight[2]	2010 Medicare National Average[2,4]
Drug[7] **(ASP Drug Pricing Updated Quarterly—See Footnote)**	**J0475** Injection, baclofen, 10 mg	9032	Baclofen, 10 mg injection	K	N/A	ASP+4%
	J0476 Injection, baclofen, 50 mcg for intrathecal trial	1631	Baclofen, intrathecal trial	K	N/A	ASP+4%
Refill/ Analysis/ Programming[8]	**95990** Refilling and maintenance of implantable pump or reservoir for drug delivery, spinal (intrathecal, epidural) or brain (intraventricular)	0439	Level V Drug Administration	S	1.8808	$127
	95991 Refilling and maintenance of implantable pump or reservoir for drug delivery, spinal (intrathecal, epidural) or brain (intraventricular), administered by physician	0439	Level V Drug Administration	S	1.8808	$127
	62367 Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); without reprogramming[9]	0691	Level IV Electronic Analysis of Devices	S	2.5406	$171
	62368 Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming[9]	0691	Level IV Electronic Analysis of Devices	S	2.5406	$171
Catheter Dye Study[10]	**61070** Puncture of reservoir for injection procedure	0121	Level I Tube or Catheter Changes and Repositioning	T	6.3742	$430
	75809 Shuntogram for investigation of previously placed indwelling non-vascular shunt (indwelling infusion pump)[11]	N/A	N/A	Q2	N/A	N/A
Pump Rotor Study	**62368** Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming	0691	Level IV Electronic Analysis of Devices	S	2.5406	$171
	76000 Fluoroscopy[12]	N/A	N/A	Q1	N/A	N/A

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Hospital Outpatient Coding and Payment — CPT® Procedure Codes *continued*

Procedure	CPT Code and Description[1]	APC[2]	APC Title[2]	SI[2,3]	Relative Weight[2]	2010 Medicare National Average[2,4]
Evaluation and Management **Note:** A clinic visit can only be billed separately when a full-scale, separately identifiable evaluation and management service takes place in addition to refilling, analyzing, and programming the pump. The use of evaluation and management codes may require a -25 modifier and must meet separate coding requirements as well as documentation requirements.	**99201** Office or other outpatient visit, new patient, problem focused	0604	Level 1 Hospital Clinic Visits	V	0.8593	$58
	99202 Office or other outpatient visit, new patient, straightforward	0605	Level 2 Hospital Clinic Visits	V	1.0337	$70
	99203 Office or other outpatient visit, new patient, low complexity	0606	Level 3 Hospital Clinic Visits	V	1.3222	$89
	99204 Office or other outpatient visit, new patient, moderate complexity	0607	Level 4 Hospital Clinic Visits	V	1.6830	$113
	99205 Office or other outpatient visit, new patient, high complexity[13]	0608	Level 5 Hospital Clinic Visits	V	2.4853	$168
	99211 Office or other outpatient visit, established patient, minimal	0604	Level 1 Hospital Clinic Visits	V	0.8593	$58
	99212 Office or other outpatient visit, established patient, straightforward	0605	Level 2 Hospital Clinic Visits	V	1.0337	$70
	99213 Office or other outpatient visit, established patient, low complexity	0605	Level 2 Hospital Clinic Visits	V	1.0337	$70
	99214 Office or other outpatient visit, established patient, moderate complexity	0606	Level 3 Hospital Clinic Visits	V	1.3222	$89
	99215 Office or other outpatient visit, established patient, high complexity[13]	0607	Level 4 Hospital Clinic Visits	V	1.6830	$113

Chart continued on next page

Hospital Outpatient Coding and Payment — CPT® Procedure Codes *continued*

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2. Changes to the Hospital Outpatient Prospective Payment System and CY 2010 Payment Rates, 74 Fed. Reg. 60316-60983 (finalized November 20, 2009).
3. Status Indicator (SI) shows how a code is handled for payment purposes. K = non-pass-through drugs, paid under separate APC; N = packaged into other services, not separately payable; S = always paid at 100% of rate; T = paid at 50% of rate when billed with another higher-weighted T procedure; V = visit, paid at 100% of rate. See notes 11 and 12 for status indicators Q1 and Q2.
4. Medicare average payment is determined by multiplying the APC weight by the conversion factor ($67.406 for 2010) as published in the Changes to the Hospital Outpatient Prospective Payment System and CY 2010 Payment Rates, 74 Fed. Reg. 60419 (finalized November 20, 2009). The payment is adjusted by the Wage Index for each hospital's specific geographic locality. Therefore, payment will vary from the stated national average Medicare payment levels.
5. In a replacement, National Correct Coding Initiative (NCCI) edits do not allow removal of the old device to be coded together with implantation of the new device.
6. It is questionable if fluoroscopy can be coded separately with injections and catheter implantation. According to guidelines by the American Association of Neurological Surgeons, use of fluoroscopy to place the catheter is inherent to 62350 and should not be coded separately. Although National Correct Coding Initiative (NCCI) edits prohibit use of fluoroscopy code 76000 with 62350, they do not prohibit use of fluoroscopy code 77003 with 62350. Similarly, NCCI edits prohibit use of fluoroscopy codes 76000, 76001, and 77002 with injection codes 62311 and 62319, but there is no edit for fluoroscopy code 77003. Check with the payer for specific guidelines.
7. J0475 and J0476 are both designated as a "specified covered outpatient drug." Each is assigned to an APC and generates separate payment. CMS updates Average Sales Price (ASP) drug pricing on a quarterly basis. ASP values are publicly available at http://www.cms.hhs.gov/McrPartBDrugAvgSalesPrice. For 2010, the payment amount is based on ASP plus 4% per the Changes to the Hospital Outpatient Prospective Payment System and CY 2010 Payment Rates, 74 Fed. Reg. 60517 (finalized November 20, 2009).
8. Use the Refill/Analysis/Programming codes only for follow-up services. Do not assign these codes at the time of implantation. NCCI edits do not allow these codes to be assigned at the time of pump implantation. Also note that according to published material from the AMA, it is appropriate to code both 62367 – 62368 for device analysis with 95990–95991 for refilling when performed at the same encounter.
9. Code 62367 is used for pump interrogation only (e.g., determining the current programming, assessing the device's functions such as its battery voltage and settings, and retrieving or downloading stored data for review). Code 62368 is used when the pump is both interrogated and reprogrammed. In the context of a refill, the AMA has published material indicating that pumps require reprogramming at the time of refilling and that it is appropriate to use 62368 for resetting the pump to its original parameters after a refill.
10. The AMA has published material confirming the use of 61070 and 75809 for implanted pump catheter dye studies. However, use of 64999 (unlisted procedure, nervous system) or code 95999 (unlisted neurological diagnostic procedure) may be preferred by some payers.
11. Status Q2 indicates that code 75809 is conditionally packaged. Although separately payable in certain circumstances, code 75809 is designated as "packaged" into the primary service when submitted with another code with status indicator "T." In a catheter dye study, its companion code is 61070. Because code 61070 is status "T," code 75809 is "packaged" and not separately payable in this scenario.
12. Status Q1 indicates that code 76000 is conditionally packaged. Although payable in a separate APC in certain unusual circumstances, it is designated as "packaged" into the primary service when submitted with another code with status indicator "S," "T," "V," or "X." In a pump rotor study, its companion code is 62368. Because code 62368 is status "S," code 76000 is "packaged" and not separately payable in this scenario.
13. More broadly, these codes have status indicator Q3. Status indicator Q3 shows that the higher level clinic visits may be part of a composite APC if billed with observation services. Otherwise, however, within the context of services related to ITB Therapy℠, the codes will typically be paid separately under the APCs, status indicators, and rates shown.

Hospital Inpatient Coding and Payment — Effective October 1, 2009 – September 30, 2010

MS-DRG Assignments

Under Medicare's MS-DRG methodology for hospital inpatient payment, each inpatient stay is assigned to one of about 745 diagnosis-related groups, based on the ICD-9-CM codes assigned to the diagnoses and procedures. Each MS-DRG has a relative weight that is then converted to a flat payment amount. Only one MS-DRG is assigned by inpatient stay, regardless of the number of procedures performed. The MS-DRGs shown are those typically assigned for the scenarios.

Procedure	Scenario	MS-DRG[1]	MS-DRG Title[2]	Relative Weight[1]	FY10 Medicare National Average[3]
Screening Test[4]	Spasticity due to specified forms of cerebral palsy and spastic paraplegia, quadriplegia, and diplegia	052	Spinal Disorders and Injuries W CC/MCC	1.4836	$8,386
		053	Spinal Disorders and Injuries W/O CC/MCC	0.8382	$4,738
	Spasticity due to late effects of CVA and spastic hemiplegia	056	Degenerative Nervous System Disorders W MCC	1.6952	$9,582
		057	Degenerative Nervous System Disorders W/O MCC	0.9028	$5,103
	Spasticity due to multiple sclerosis	058	Multiple Sclerosis and Cerebellar Ataxia W MCC	1.5512	$8,768
		059	Multiple Sclerosis and Cerebellar Ataxia W CC	0.9581	$5,415
		060	Multiple Sclerosis and Cerebellar Ataxia W/O CC/MCC	0.7083	$4,003
	Spasticity due to mixed or unspecified cerebral palsy, unspecified spastic paralysis, and spastic monoplegia	091	Other Disorders of Nervous System W MCC	1.5465	$8,742
		092	Other Disorders of Nervous System W CC	0.9167	$5,182
		093	Other Disorders of Nervous System W/O CC/MCC	0.6691	$3,782

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Hospital Inpatient Coding and Payment — MS-DRG Assignments *continued*

Procedure	Scenario	MS-DRG[1]	MS-DRG Title[2]	Relative Weight[1]	FY10 Medicare National Average[3]
Implantation and Replacement	Entire system implant or replacement, pump (86.06) plus catheter (03.90)	040	Peripheral/Cranial Nerve and Other Nervous System Procedures W MCC	3.9518	$22,337
		041	Peripheral/Cranial Nerve and Other Nervous System Procedures W CC or Peripheral Neurostimulator	2.1249	$12,011
		042	Peripheral/Cranial Nerve and Other Nervous System Procedures W/O CC/MCC	1.6448	$9,297
	Pump only implant or replacement (86.06)	040	Peripheral/Cranial Nerve and Other Nervous System Procedures W MCC	3.9518	$22,337
		041	Peripheral/Cranial Nerve and Other Nervous System Procedures W CC or Peripheral Neurostimulator	2.1249	$12,011
		042	Peripheral/Cranial Nerve and Other Nervous System Procedures W/O CC/MCC	1.6448	$9,297
	Catheter only implant or replacement (03.90)	This code is not considered a significant procedure for the purpose of DRG assignment. A non-surgical (i.e., medical) DRG is assigned to the stay according to the principal diagnosis. The most common DRGs are those displayed above for the screening trial.			
Removal (without replacement)[5]	Entire system removal, pump (86.05) and catheter (03.99)[6]	028	Spinal Procedures W MCC	5.1090	$28,878
		029	Spinal Procedures W CC or Spinal Neurostimulator	2.7768	$15,696
		030	Spinal Procedures W/O CC/MCC	1.6019	$9,055
	Pump only removal (86.05)	This code is not considered a significant procedure for the purpose of DRG assignment. A non-surgical (i.e., medical) DRG is assigned to the stay according to the principal diagnosis. The most common DRGs are those displayed above for the screening trial.			
	Catheter only removal (03.99)[6]	028	Spinal Procedures W MCC	5.1090	$28,878
		029	Spinal Procedures W CC or Spinal Neurostimulator	2.7768	$15,696
		030	Spinal Procedures W/O CC/MCC	1.6019	$9,055

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Hospital Inpatient Coding and Payment — MS-DRG Assignments *continued*

1. Changes to the Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and Fiscal Year 2010 Rates, 74 Fed. Reg. 43754 – 44236 (finalized August 27, 2009).
2. W MCC in MS-DRG titles refers to secondary diagnosis codes that are designated as major complications or comorbidities. MS-DRGs W MCC have at least one major secondary complication or comorbidity. Similarly, W CC in MS-DRG titles refers to secondary diagnosis codes designated as other (non-major) complications or comorbidities, and MS-DRGs W CC have at least one other (non-major) secondary complication or comorbidity. MS-DRGs W/O CC/MCCs have no secondary diagnoses that are designated as complications or comorbidities, major or otherwise. Note that some secondary diagnoses are only designated as CCs or MCCs when the conditions were present on admission, and do not count as CCs or MCCs when the conditions were acquired in the hospital during the stay.
3. Payment is based on the average standardized operating amount ($5,223.14) plus the capital standard amount ($429.26) as published in Changes to the Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and Fiscal Year 2010 Rates, 74 Fed. Reg. 44031 (finalized August 27, 2009), and corrected via Changes to the Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and Fiscal Year 2010 Rates; Corrections, 74 Fed. Reg. 51499 (finalized October 7, 2009). The payment rate shown is the standardized amounts for facilities with a wage index greater than one. The average standard amounts shown also assume facilities receive the full quality update. The payment will also be adjusted by the Wage Index for your specific geographic locality. Therefore, payment for your area will vary from the stated Medicare national average payment levels shown.
4. The ICD-9-CM procedure codes for screening injections are not considered "significant procedures" for the purpose of MS-DRG assignment. As shown, a non-surgical (i.e., medical) MS-DRG is assigned to the stay according to the principal diagnosis.
5. Device removal without replacement is typically performed as an outpatient. It is shown here for the occasional scenario where removal takes place due to a complication that requires inpatient admission. For coding purposes, an intrathecal pump is classified as a nervous system device. When it is removed for complications or because it is no longer needed, the principal diagnosis is either various nervous system complication codes or code V53.09. Both map to the nervous system MS-DRGs shown.
6. To use 03.99, removal of the catheter must be surgical (i.e., by incision).

ASC Coding and Payment — Effective January 1, 2010 – December 31, 2010

CPT® Procedure Codes

ASCs use CPT codes for their services. Medicare payment for procedures performed in an ambulatory surgery center is based on Medicare's ambulatory patient classification (APC) methodology for hospital outpatient payment. Each CPT code designated as a covered procedure in an ASC is assigned the same relative weight, or a comparable weight, as under the hospital outpatient APC system. This is then converted to a flat payment amount using a conversion factor unique to ASCs. Multiple procedures can be paid for each claim. Certain ancillary services, such as imaging, are also covered when they are integral to covered surgical procedures, although they may not be separately payable. In general, there is no separate payment for drugs and devices; their payment is packaged into the payment for the procedure.

Procedure	CPT Code and Description[1]	Payment Indicator[2,3,4]	Multiple Procedure Discounting[5]	Relative Weight[2,4]	2010 Medicare National Average[2,4,6]
Screening Test[7]	**62311** Injection, single (not via indwelling catheter), not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal)	A2	Y	7.0685	$296
	62319 Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal)	A2	Y	7.0685	$296
	62350 Implantation, revision, or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; without laminectomy	A2	Y	31.9867	$1,339
Implantation, Revision, or Replacement of Catheter[8]	**62350** Implantation, revision, or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; without laminectomy	A2	Y	31.9867	$1,339
Implantation or Replacement of Pump[8]	**62361** Implantation or replacement of device for intrathecal or epidural drug infusion; non-programmable pump	H8	Y	291.6404	$12,212
	62362 Implantation or replacement of device for intrathecal or epidural drug infusion; programmable pump, including preparation of pump, with or without programming	H8	Y	291.6404	$12,212

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ASC Coding and Payment — CPT® Procedure Codes *continued*

Procedure	CPT Code and Description[1]	Payment Indicator[2,3,4]	Multiple Procedure Discounting[5]	Relative Weight[2,4]	2010 Medicare National Average[2,4,6]
Removal of Catheter or Pump[8]	**62355** Removal of previously implanted intrathecal or epidural catheter	A2	Y	12.0502	$505
	62365 Removal of subcutaneous reservoir or pump, previously implanted for intrathecal or epidural infusion	A2	Y	29.2974	$1,227
Fluoroscopy for Catheter Placement and Injection[9]	**77003** Fluoroscopic guidance and localization of needle or catheter tip for spine or paraspinous diagnostic or therapeutic injection procedures (epidural, subarachnoid)	N1	N/A	N/A	N/A
Drug[10] **(ASP Drug Pricing Updated Quarterly—See Footnote)**	**J0475** Injection, baclofen, 10 mg	K2	N/A	N/A	ASP+4%
	J0476 Injection, baclofen, 50 mcg for intrathecal trial	K2	N/A	N/A	ASP+4%

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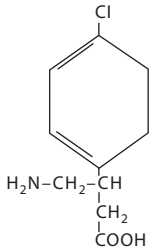
2. Changes to the Ambulatory Surgical Center Payment System and CY 2010 Payment Rates, 74 Fed. Reg. 60316-60983 (finalized November 20, 2009), and corrected by Changes to the Ambulatory Surgical Center Payment System and CY 2010 Payment Rates, 74 Fed. Reg. 69502-69676 (corrected December 31, 2009).
3. The Payment Indicator shows how a code is handled for payment purposes. A2 = surgical procedure, subject to transitional weight; H8 = device-intensive procedure, subject to transitional weight; K2 = drugs paid separately when provided integral to a surgical procedure on ASC list; N1 = packaged service, no separate payment.
4. Calendar Year 2008 was the first year in which Medicare payment to ambulatory surgery centers was based on hospital outpatient APCs. For some procedures, transitional payment formulas are in effect until 2011, blending factors from the prior ASC system and the APC system. The transition may cause weights for some procedures to vary significantly from year to year through 2011 until final rates are achieved. As shown, rates for 2010 are determined by multiplying the 2010 weight by the ASC conversion factor ($41.873 for 2010). For all procedures, the payment is then adjusted by the Wage Index for each facility's specific geographic locality. Therefore, payment will vary from the stated national average Medicare payment levels. Also note that any applicable coinsurance, deductible, and other amounts that are patient obligations are included in the national average payment amount shown.
5. When multiple procedures are coded and billed, payment is usually made at 100% of the rate for the first procedures and 50% of the rate for the second and all subsequent procedures. These procedures are marked "Y." However, procedures marked "N" are not subject to this discounting and are paid at 100% of the rate regardless of whether they are submitted with other procedures.
6. Medicare should be billed using a CMS-1500 form.
7. When epidural or intrathecal injection is performed without a catheter, code 62311 is used. When a trial catheter is placed and is not tunneled, code 62319 is used. However, when the trial catheter is tunneled, it is unclear whether to use 62319 or 62350. By definition, 62350 captures a tunneled catheter and an external pump; it can be further argued that a tunneled catheter meets the requirement for "long-term" because it anticipates a successful trial in which medication will eventually be administered through the pump. Alternately, it can argued that a trial is temporary by nature and 62319 indicates a temporary catheter. Check with the payer for specific guidelines.
8. In a replacement, National Correct Coding Initiative (NCCI) edits do not allow removal of the old device to be coded together with implantation of the new device.
9. It is questionable if fluoroscopy can be coded separately with injections and catheter implantation. According to guidelines by the American Association of Neurological Surgeons, use of fluoroscopy to place the catheter is inherent to 62350 and should not be coded separately. Although National Correct Coding Initiative (NCCI) edits prohibit use of fluoroscopy code 76000 with 62350, they do not prohibit use of fluoroscopy code 77003 with 62350. Similarly, NCCI edits prohibit use of fluoroscopy codes 76000, 76001, and 77002 with injection codes 62311 and 62319, but there is no edit for fluoroscopy code 77003. Check with the payer for specific coding guidelines. If fluoroscopy is coded, it is packaged into payment for the lead placement and is not separately payable.
10. Although most drugs are packaged and not separately payable, both code J0475 and code J0476 are designated as an "ASC covered ancillary service integral to covered surgical procedures for Calendar Year 2010." Both codes generate separate payment. CMS updates Average Sales Price (ASP) drug pricing on a quarterly basis. ASP values are publicly available at http://www.cms.hhs.gov/McrPartBDrugAvgSalesPrice. For 2010, the payment amount is based on ASP plus 4% per the Federal Register, Volume 74, Number 223, November 20, 2009; CMS-1414-FC, p. 60512.

LIORESAL® INTRATHECAL
(baclofen injection)

Abrupt discontinuation of intrathecal baclofen, regardless of the cause, has resulted in sequelae that include high fever, altered mental status, exaggerated rebound spasticity, and muscle rigidity, that in rare cases has advanced to rhabdomyolysis, multiple organ-system failure and death.
Prevention of abrupt discontinuation of intrathecal baclofen requires careful attention to programming and monitoring of the infusion system, refill scheduling and procedures, and pump alarms. Patients and caregivers should be advised of the importance of keeping scheduled refill visits and should be educated on the early symptoms of baclofen withdrawal. Special attention should be given to patients at apparent risk (e.g. spinal cord injuries at T-6 or above, communication difficulties, history of withdrawal symptoms from oral or intrathecal baclofen). Consult the technical manual of the implantable infusion system for additional postimplant clinician and patient information (see WARNINGS)

DESCRIPTION
LIORESAL INTRATHECAL (baclofen injection) is a muscle relaxant and antispastic. Its chemical name is 4- amino- 3-(4- chlorophenyl) butanoic acid, and its structural formula is:



Baclofen is a white to off- white, odorless or practically odorless crystalline powder, with a molecular weight of 213.66. It is slightly soluble in water, very slightly soluble in methanol, and insoluble in chloroform.

LIORESAL INTRATHECAL is a sterile, pyrogen-free, isotonic solution free of antioxidants, preservatives or other potentially neurotoxic additives indicated only for intrathecal administration. The drug is stable in solution at 37° C and compatible with CSF. Each milliliter of LIORESAL INTRATHECAL contains baclofen U. S. P. 50 mcg, 500 mcg or 2000 mcg and sodium chloride 9 mg in Water for Injection; pH range is 5.0 - 7.0. Each ampule is intended for SINGLE USE ONLY. Discard any unused portion. **DO NOT AUTOCLAVE**.

CLINICAL PHARMACOLOGY
The precise mechanism of action of baclofen as a muscle relaxant and antispasticity agent is not fully understood. Baclofen inhibits both monosynaptic and polysynaptic reflexes at the spinal level, possibly by decreasing excitatory neurotransmitter release from primary afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect. Baclofen is a structural analog of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), and may exert its effects by stimulation of the $GABA_B$ receptor subtype.
LIORESAL INTRATHECAL when introduced directly into the intrathecal space permits effective CSF concentrations to be achieved with resultant plasma concentrations 100 times less than those occurring with oral administration.
In people, as well as in animals, baclofen has been shown to have general CNS depressant prop- erties as indicated by the production of sedation with tolerance, somnolence, ataxia, and respiratory and cardiovascular depression.
Pharmacodynamics of LIORESAL INTRATHECAL:
Intrathecal Bolus:
Adult Patients: The onset of action is generally one-half hour to one hour after an intrathecal bolus. Peak spasmolytic effect is seen at approximately four hours after dosing and effects may last four to eight hours. Onset, peak response, and duration of action may vary with individual patients depending on the dose and severity of symptoms.
Pediatric Patients: The onset, peak response and duration of action is similar to those seen in adult patients.
Continuous Infusion:
LIORESAL INTRATHECAL'S antispastic action is first seen at 6 to 8 hours after initiation of continuous infusion. Maximum activity is observed in 24 to 48 hours.
Continuous Infusion: No additional information is available for pediatric patients.
Pharmacokinetics of LIORESAL INTRATHECAL:
The pharmacokinetics of CSF clearance of LIORESAL INTRATHECAL calculated from intrathecal bolus or continuous infusion studies approximates CSF turnover, suggesting elimination is by bulk-flow removal of CSF.
Intrathecal Bolus: After a bolus lumbar injection of 50 or 100 mcg LIORESAL INTRATHECAL in seven patients, the average CSF elimination half-life was 1.51 hours over the first four hours and the average CSF clearance was approximately 30 ml/ hour.
Continuous Infusion: The mean CSF clearance for LIORESAL INTRATHECAL (baclofen injection) was approximately 30 ml/ hour in a study involving ten patients on continuous intrathecal infusion.
Concurrent plasma concentrations of baclofen during intrathecal administration are expected to be low (0- 5 ng/ ml).
Limited pharmacokinetic data suggest that a lumbar-cisternal concentration gradient of about 4: 1 is established along the neuroaxis during baclofen infusion. This is based upon simultaneous CSF sampling via cisternal and lumbar tap in 5 patients receiving continuous baclofen infusion at the lumbar level at doses associated with therapeutic efficacy; the interpatient variability was great. The gradient was not altered by position.
Six pediatric patients (age 8- 18 years) receiving continuous intrathecal baclofen infusion at doses of 77- 400 mcg/ day had plasma baclofen levels near or below 10 ng/ ml.

INDICATIONS
LIORESAL INTRATHECAL is indicated for use in the management of severe spasticity. Patients should first respond to a screening dose of intrathecal baclofen prior to consideration for long term infusion via an implantable pump. For spasticity of spinal cord origin, chronic infusion of LIORESAL INTRATHECAL via an implantable pump should be reserved for patients unresponsive to oral baclofen therapy, or those who experience intolerable CNS side effects at effective doses. Patients with spasticity due to traumatic brain injury should wait at least one year after the injury before consideration of long term intrathecal baclofen therapy. LIORESAL INTRATHECAL (baclofen injection) is intended for use by the intrathecal route in single bolus test doses (via spinal catheter or lumbar puncture) and, for chronic use, only in implantable pumps approved by the FDA specifically for the administration of LIORESAL INTRATHECAL into the intrathecal space.
Spasticity of Spinal Cord Origin: Evidence supporting the efficacy of LIORESAL INTRATHECAL was obtained in randomized, controlled investigations that compared the effects of either a single intrathecal dose or a three day intrathecal infusion of LIORESAL INTRATHECAL to placebo in patients with severe spasticity and spasms due to either spinal cord trauma or multiple sclerosis. LIORESAL INTRATHECAL was superior to placebo on both principal outcome measures employed: change from baseline in the Ashworth rating of spasticity and the frequency of spasms.
Spasticity of Cerebral Origin: The efficacy of LIORESAL INTRATHECAL was investigated in three controlled clinical trials; two enrolled patients with cerebral palsy and one enrolled patients with spasticity due to previous brain injury. The first study, a randomized controlled cross- over trial of 51 patients with cerebral palsy, provided strong, statistically significant results; LIORESAL INTRATHECAL was superior to placebo in reducing spasticity as measured by the Ashworth Scale. A second cross- over study was conducted in 11 patients with spasticity arising from brain injury. Despite the small sample size, the study yielded a nearly significant test statistic (p= 0.066) and provided directionally favorable results. The last study, however, did not provide data that could be reliably analyzed.
LIORESAL INTRATHECAL therapy may be considered an alternative to destructive neurosurgical procedures. Prior to implantation of a device for chronic intrathecal infusion of LIORESAL INTRATHECAL, patients must show a response to LIORESAL INTRATHECAL in a screening trial (see Dosage and Administration).

CONTRAINDICATIONS
Hypersensitivity to baclofen. LIORESAL INTRATHECAL is not recommended for intravenous, intramuscular, subcutaneous or epidural administration.

WARNINGS
LIORESAL INTRATHECAL is for use in single bolus intrathecal injections (via a catheter placed in the lumbar intrathecal space or injection by lumbar puncture) and in implantable pumps approved by the FDA specifically for the intrathecal administration of baclofen. Because of the possibility of potentially life- threatening CNS depression, cardiovascular collapse, and/ or respiratory failure, physicians must be adequately trained and educated in chronic intrathecal infusion therapy.
The pump system should not be implanted until the patient's response to bolus LIORESAL INTRATHECAL injection is adequately evaluated. Evaluation (consisting of a screening procedure: see Dosage and Administration) requires that LIORESAL INTRATHECAL be administered into the intrathecal space via a catheter or lumbar puncture. Because of the risks associated with the screening procedure and the adjustment of dosage following pump implantation, these phases must be conducted in a medically supervised and adequately equipped environment following the instructions outlined in the Dosage and Administration section.
Resuscitative equipment should be available.
Following surgical implantation of the pump, particularly during the initial phases of pump use, the patient should be monitored closely until it is certain that the patient's response to the infusion is

acceptable and reasonably stable.

On each occasion that the dosing rate of the pump and/ or the concentration of LIORESAL INTRATHECAL (baclofen injection) in the reservoir is adjusted, close medical monitoring is required until it is certain that the patient's response to the infusion is acceptable and reasonably stable.

It is mandatory that the patient, all patient caregivers, and the physicians responsible for the patient receive adequate information regarding the risks of this mode of treatment. All medical personnel and caregivers should be instructed in 1) the signs and symptoms of overdose, 2) procedures to be followed in the event of overdose and 3) proper home care of the pump and insertion site.

Overdose: Signs of overdose may appear suddenly or insidiously. Acute massive overdose may present as coma. Less sudden and/ or less severe forms of overdose may present with signs of drowsiness, lightheadedness, dizziness, somnolence, respiratory depression, seizures, rostral pro- gression of hypotonia and loss of consciousness progressing to coma. Should overdose appear likely, the patient should be taken immediately to a hospital for assessment and emptying of the pump reservoir. In cases reported to date, overdose has generally been related to pump malfunction or dosing error. (See Drug Overdose Symptoms and Treatment.)

Extreme caution must be used when filling an FDA approved implantable pump. Such pumps should only be refilled through the reservoir refill septum. However, some pumps are also equipped with a catheter access port that allows direct access to the intrathecal catheter. Direct injection into this catheter access port may cause a life-threatening overdose.

Withdrawal: Abrupt withdrawal of intrathecal baclofen, regardless of the cause, has resulted in sequelae that included high fever, altered mental status, exaggerated rebound spasticity and muscle rigidity that in rare cases progressed to rhabdomyolysis, multiple organ-system failure, and death. In the first 9 years of post-marketing experience, 27 cases of withdrawal temporally related to the cessation of baclofen therapy were reported; six patients died. In most cases, symptoms of withdrawal appeared within hours to a few days following interruption of baclofen therapy. Common reasons for abrupt interruption of intrathecal baclofen therapy included malfunction of the catheter (especially disconnection), low volume in the pump reservoir, and end of pump battery life; human error may have played a causal or contributing role in some cases. Prevention of abrupt discontinuation of intrathecal baclofen requires careful attention to programming and monitoring of the infusion system, refill scheduling and procedures, and pump alarms. Patients and caregivers should be advised of the importance of keeping scheduled refill visits and should be educated on the early symptoms of baclofen withdrawal.

All patients receiving intrathecal baclofen therapy are potentially at risk for withdrawal. Early symptoms of baclofen withdrawal may include return of baseline spasticity, pruritus, hypotension, and paresthesias. Some clinical characteristics of the advanced intrathecal baclofen withdrawal syndrome may resemble autonomic dysreflexia, infection (sepsis), malignant hyperthermia, neuroleptic- malignant syndrome, or other conditions associated with a hypermetabolic state or widespread rhabdomyolysis.

Rapid, accurate diagnosis and treatment in an emergency-room or intensive- care setting are important in order to prevent the potentially life-threatening central nervous system and systemic effects of intrathecal baclofen withdrawal. The suggested treatment for intrathecal baclofen withdrawal is the restoration of intrathecal baclofen at or near the same dosage as before therapy was interrupted. However, if restoration of intrathecal delivery is delayed, treatment with GABA-ergic agonist drugs such as oral or enteral baclofen, or oral, enteral, or intravenous benzodiazepines may prevent potentially fatal sequelae. Oral or enteral baclofen alone should not be relied upon to halt the progression of intrathecal baclofen withdrawal.

Seizures have been reported during overdose and with withdrawal from LIORESAL INTRATHECAL as well as in patients maintained on therapeutic doses of LIORESAL INTRATHECAL.

Fatalities :

Spasticity of Spinal Cord Origin: There were 16 deaths reported among the 576 U.S. patients treat- ed with LIORESAL INTRATHECAL (baclofen injection) in pre- and post- marketing studies evaluated as of December 1992. Because these patients were treated under uncontrolled clinical settings, it is impossible to determine definitively what role, if any, LIORESAL INTRATHECAL played in their deaths. As a group, the patients who died were relatively young (mean age was 47 with a range from 25 to 63), but the majority suffered from severe spasticity of many years duration, were nonambulatory, had various medical complications such as pneumonia, urinary tract infections, and decubiti, and/ or had received multiple concomitant medications. A case- by- case review of the clinical course of the 16 patients who died failed to reveal any unique signs, symptoms, or laboratory results that would suggest that treatment with LIORESAL INTRATHECAL caused their deaths. Two patients, however, did suffer sudden and unexpected death within 2 weeks of pump implantation and one patient died unexpectedly after screening.

One patient, a 44 year-old male with MS, died in hospital on the second day following pump implantation. An autopsy demonstrated severe fibrosis of the coronary conduction system. A second patient, a 52 year-old woman with MS and a history of an inferior wall myocardial infarction, was found dead in bed 12 days after pump implantation, 2 hours after having had documented normal vital signs. An autopsy revealed pulmonary congestion and bilateral pleural effusions. It is impossible to determine whether LIORESAL INTRATHECAL contributed to these deaths. The third patient underwent three baclofen screening trials. His medical history included SCI, aspiration pneumonia, septic shock, disseminated intravascular coagulopathy, severe metabolic acidosis, hepatic toxicity, and status epilepticus. Twelve days after screening (he was not implanted), he again experienced status epilepticus with subsequent significant neurological deterioration. Based upon prior instruction, extraordinary resuscitative measures were not pursued and the patient died.

Spasticity of Cerebral Origin: There were three deaths occurring among the 211 patients treated with LIORESAL INTRATHECAL in pre- marketing studies as of March 1996. These deaths were not attributed to the therapy.

PRECAUTIONS

Children should be of sufficient body mass to accommodate the implantable pump for chronic infu- sion. Please consult pump manufacturer's manual for specific recommendations.

Safety and effectiveness in pediatric patients below the age of 4 have not been established.

Screening

Patients should be infection-free prior to the screening trial with LIORESAL INTRATHECAL (baclofen injection) because the presence of a systemic infection may interfere with an assessment of the patient's response to bolus LIORESAL INTRATHECAL.

Pump Implantation

Patients should be infection-free prior to pump implantation because the presence of infection may increase the risk of surgical complications. Moreover, a systemic infection may complicate dosing.

Pump Dose Adjustment and Titration

In most patients, it will be necessary to increase the dose gradually over time to maintain effectiveness; a sudden requirement for substantial dose escalation typically indicates a catheter complication (i. e., catheter kink or dislodgement).

Reservoir refilling must be performed by fully trained and qualified personnel following the directions provided by the pump manufacturer. Refill intervals should be carefully calculated to prevent depletion of the reservoir, as this would result in the return of severe spasticity and possibly symptoms of withdrawal.

Strict aseptic technique in filling is required to avoid bacterial contamination and serious infection. A period of observation appropriate to the clinical situation should follow each refill or manipulation of the drug reservoir.

Extreme caution must be used when filling an FDA approved implantable pump equipped with an injection port that allows direct access to the intrathecal catheter. Direct injection into the catheter through the catheter access port may cause a life-threatening overdose.

Additional considerations pertaining to dosage adjustment: It may be important to titrate the dose to maintain some degree of muscle tone and allow occasional spasms to: 1) help support circulatory function, 2) possibly prevent the formation of deep vein thrombosis, 3) optimize activities of daily living and ease of care.

Except in overdose related emergencies, the dose of LIORESAL INTRATHECAL should ordinarily be reduced slowly if the drug is discontinued for any reason.

An attempt should be made to discontinue concomitant oral antispasticity medication to avoid possible overdose or adverse drug interactions, either prior to screening or following implant and initiation of chronic LIORESAL INTRATHECAL infusion. Reduction and discontinuation of oral anti-spasmotics should be done slowly and with careful monitoring by the physician. Abrupt reduction or discontinuation of concomitant antispastics should be avoided.

Drowsiness: Drowsiness has been reported in patients on LIORESAL INTRATHECAL. Patients should be cautioned regarding the operation of automobiles or other dangerous machinery, and activities made hazardous by decreased alertness. Patients should also be cautioned that the central nervous system depressant effects of LIORESAL INTRATHECAL (baclofen injection) may be additive to those of alcohol and other CNS depressants.

Precautions in special patient populations: Careful dose titration of LIORESAL INTRATHECAL is needed when spasticity is necessary to sustain upright posture and balance in locomotion or whenever spasticity is used to obtain optimal function and care.

Patients suffering from psychotic disorders, schizophrenia, or confusional states should be treated cautiously with LIORESAL INTRATHECAL and kept under careful surveillance, because exacerbations of these conditions have been observed with oral administration.

LIORESAL INTRATHECAL should be used with caution in patients with a history of autonomic dys- reflexia. The presence of nociceptive stimuli or abrupt withdrawal of LIORESAL INTRATHECAL (baclofen injection) may cause an autonomic dysreflexic episode.

Because LIORESAL is primarily excreted unchanged by the kidneys, it should be given with caution in patients with impaired renal function and it may be necessary to reduce the dosage.

LABORATORY TESTS

No specific laboratory tests are deemed essential for the management of patients on LIORESAL INTRATHECAL.

DRUG INTERACTIONS

There is inadequate systematic experience with the use of LIORESAL INTRATHECAL in combina- tion with other medications to predict specific drug-drug interactions. Interactions attributed to the combined use of LIORESAL INTRATHECAL and epidural morphine include hypotension and dyspnea.

CARCINOGENESIS, MUTAGENESIS, AND IMPAIRMENT OF FERTILITY

No increase in tumors was seen in rats receiving LIORESAL (baclofen USP) orally for two years at approximately 30- 60 times on a mg/ kg basis, or 10- 20 times on a mg/ m^2 basis, the maximum oral dose recommended for human use. Mutagenicity assays with LIORESAL have not been performed.

PREGNANCY CATEGORY C

LIORESAL (baclofen USP) given orally has been shown to increase the incidence of omphaloceles (ventral hernias) in fetuses of rats given approximately 13 times on a mg/ kg basis, or 3 times on a mg/m^2 basis, the maximum oral dose recommended for human use; this dose also caused reductions in food intake and weight gain in the dams.

This abnormality was not seen in mice or rabbits. There are no adequate and well-controlled studies in pregnant women. LIORESAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS

In mothers treated with oral LIORESAL (baclofen USP) in therapeutic doses, the active substance passes into the breast milk. It is not known whether detectable levels of drug are present in breast milk of

nursing mothers receiving LIORESAL INTRATHECAL. As a general rule, nursing should be undertaken while a patient is receiving LIORESAL INTRATHECAL only if the potential benefit justifies the potential risks to the infant.

PEDIATRIC USE

Children should be of sufficient body mass to accommodate the implantable pump for chronic infusion. Please consult pump manufacturer's manual for specific recommendations.

Safety and effectiveness in pediatric patients below the age of 4 have not been established.

Considerations based on experience with oral LIORESAL (baclofen USP)

A dose-related increase in incidence of ovarian cysts was observed in female rats treated chronically with oral LIORESAL. Ovarian cysts have been found by palpation in about 4% of the multiple sclerosis patients who were treated with oral LIORESAL for up to one year. In most cases these cysts disappeared spontaneously while patients continued to receive the drug. Ovarian cysts are estimated to occur spontaneously in approximately 1% to 5% of the normal female population.

ADVERSE DRUG EVENTS

Spasticity of Spinal Cord Origin:

Commonly Observed in Patients with Spasticity of Spinal Origin — In pre- and post- marketing clin- ical trials, the most commonly observed adverse events associated with use of LIORESAL INTRATHECAL (baclofen injection) which were not seen at an equivalent incidence among placebo- treated patients were: somnolence, dizziness, nausea, hypotension, headache, convulsions and hypotonia.

Associated with Discontinuation of Treatment — 8/ 474 patients with spasticity of spinal cord origin receiving long term infusion of LIORESAL INTRATHECAL in pre- and post- marketing clinical studies in the U. S. discontinued treatment due to adverse events. These include: pump pocket infections (3), meningitis (2), wound dehiscence (1), gynecological fibroids (1) and pump overpressurization (1) with unknown, if any, sequela. Eleven patients who developed coma secondary to overdose had their treatment temporarily suspended, but all were subsequently re-started and were not, therefore, con- sidered to be true discontinuations.

Fatalities — See Warnings.

Incidence in Controlled Trials — Experience with LIORESAL INTRATHECAL (baclofen injection) obtained in parallel, placebo-controlled, randomized studies provides only a limited basis for estimating the incidence of adverse events because the studies were of very brief duration (up to three days of infusion) and involved only a total of 63 patients. The following events occurred among the 31 patients receiving LIORESAL INTRATHECAL (baclofen injection) in two randomized, placebo- controlled trials: hypotension (2), dizziness (2), headache (2), dyspnea (1). No adverse events were reported among the 32 patients receiving placebo in these studies.

Events Observed during the Pre- and Post- marketing Evaluation of LIORESAL INTRATHECAL — Adverse events associated with the use of LIORESAL INTRATHECAL reflect experience gained with 576 patients followed prospectively in the United States. They received LIORESAL INTRATHECAL for periods of one day (screening) (N = 576) to over eight years (maintenance) (N = 10). The usual screening bolus dose administered prior to pump implantation in these studies was typically 50 mcg. The maintenance dose ranged from 12 mcg to 2003 mcg per day. Because of the open, uncontrolled nature of the experience, a causal linkage between events observed and the administration of LIORESAL INTRATHECAL cannot be reliably assessed in many cases and many of the adverse events reported are known to occur in association with the underlying conditions being treated. Nonetheless, many of the more commonly reported reactions— hypotonia, somnolence, dizziness, paresthesia, nausea/vomiting and headache— appear clearly drug-related.

Adverse experiences reported during all U.S. studies (both controlled and uncontrolled) are shown in the following table. Eight of 474 patients who received chronic infusion via implanted pumps had adverse experiences which led to a discontinuation of long term treatment in the pre- and post- marketing studies.

INCIDENCE OF MOST FREQUENT (≥1%) ADVERSE EVENTS IN PATIENTS WITH SPASTICITY OF SPINAL ORIGIN IN PROSPECTIVELY MONITORED CLINICAL TRIALS

	Percent of Patients Reporting Events		
	N = 576	**N = 474**	**N = 430**
	Screening[a]	Titration[b]	Maintenance[c]
Adverse Event	**Percent**	**Percent**	**Percent**
Hypotonia	5.4	13.5	25.3
Somnolence	5.7	5.9	20.9
Dizziness	1.7	1.9	7.9
Paresthesia	2.4	2.1	6.7
Nausea and Vomiting	1.6	2.3	5.6
Headache	1.6	2.5	5.1
Constipation	0.2	1.5	5.1
Convulsion	0.5	1.3	4.7
Urinary Retention	0.7	1.7	1.9
Dry Mouth	0.2	0.4	3.3
Accidental Injury	0.0	0.2	3.5
Asthenia	0.7	1.3	1.4
Confusion	0.5	0.6	2.3
Death	0.2	0.4	3.0
Pain	0.0	0.6	3.0
Speech Disorder	0.0	0.2	3.5
Hypotension	1.0	0.2	1.9
Ambylopia	0.5	0.2	2.3
Diarrhea	0.0	0.8	2.3
Hypoventilation	0.2	0.8	2.1
Coma	0.0	1.5	0.9
Impotence	0.2	0.4	1.6
Peripheral Edema	0.0	0.0	2.3
Urinary Incontinence	0.0	0.8	1.4
Insomnia	0.0	0.4	1.6
Anxiety	0.2	0.4	0.9
Depression	0.0	0.0	1.6
Dyspnea	0.3	0.0	1.2
Fever	0.5	0.2	0.7
Pneumonia	0.2	0.2	1.2
Urinary Frequency	0.0	0.6	0.9
Urticaria	0.2	0.2	1.2
Anorexia	0.0	0.4	0.9
Diplopia	0.0	0.4	0.9
Dysautonomia	0.2	0.2	0.9
Hallucinations	0.3	0.4	0.5
Hypertension	0.2	0.6	0.5

[a] Following administration of test bolus
[b] Two month period following implant
[c] Beyond two months following implant
N= total number of patients entering each period
%=% of patients evaluated

In addition to the more common (1% or more) adverse events reported in the prospectively followed 576 domestic patients in pre- and post- marketing studies, experience from an additional 194 patients exposed to LIORESAL INTRATHECAL (baclofen injection) from foreign studies has been reported. The following adverse events, not described in the table, and arranged in decreasing order of frequency, and classified by body system, were reported:

Nervous System: Abnormal gait, thinking abnormal, tremor, amnesia, twitching, vasodilitation, cerebrovascular accident, nystagmus, personality disorder, psychotic depression, cerebral ischemia, emotional lability, euphoria, hypertonia, ileus, drug dependence, incoordination, paranoid reaction and ptosis.

Digestive System: Flatulence, dysphagia, dyspepsia and gastroenteritis.

Cardiovascular: Postural hypotension, bradycardia, palpitations, syncope, arrhythmia ventricular, deep thrombophlebitis, pallor and tachycardia.

Respiratory: Respiratory disorder, aspiration pneumonia, hyperventilation, pulmonary embolus and rhinitis.

Urogenital: Hematuria and kidney failure.

Skin and Appendages: Alopecia and sweating.

Metabolic and Nutritional Disorders: Weight loss, albuminuria, dehydration and hyperglycemia.

Special Senses: Abnormal vision, abnormality of accommodation, photophobia, taste loss and tinnitus.
Body as a Whole: Suicide, lack of drug effect, abdominal pain, hypothermia, neck rigidity, chest pain, chills, face edema, flu syndrome and overdose.
Hemic and Lymphatic System: Anemia.
Spasticity of Cerebral Origin:

Commonly Observed — In pre- marketing clinical trials, the most commonly observed adverse events associated with use of LIORESAL INTRATHECAL (baclofen injection) which were not seen at an equivalent incidence among placebo-treated patients included: agitation, constipation, somnolence, leukocytosis, chills, urinary retention and hypotonia.

Associated with Discontinuation of Treatment — Nine of 211 patients receiving LIORESAL INTRATHECAL in pre-marketing clinical studies in the U.S. discontinued long term infusion due to adverse events associated with intrathecal therapy.

The nine adverse events leading to discontinuation were: infection (3), CSF leaks (2), meningitis (2), drainage (1), and unmanageable trunk control (1).

Fatalities — Three deaths, none of which were attributed to LIORESAL INTRATHECAL, were reported in patients in clinical trials involving patients with spasticity of cerebral origin. See Warnings on other deaths reported in spinal spasticity patients.

Incidence in Controlled Trials — Experience with LIORESAL INTRATHECAL (baclofen injection) obtained in parallel, placebo-controlled, randomized studies provides only a limited basis for estimating the incidence of adverse events because the studies involved a total of 62 patients exposed to a single 50 mcg intrathecal bolus. The following events occurred among the 62 patients receiving LIORESAL INTRATHECAL in two randomized, placebo-controlled trials involving cerebral palsy and head injury patients, respectively: agitation, constipation, somnolence, leukocytosis, nausea, vomiting, nystagmus, chills, urinary retention, and hypotonia.

Events Observed during the Pre- marketing Evaluation of LIORESAL INTRATHECAL — Adverse events associated with the use of LIORESAL INTRATHECAL reflect experience gained with a total of 211 U. S. patients with spasticity of cerebral origin, of whom 112 were pediatric patients (under age 16 at enrollment). They received LIORESAL INTRATHECAL for periods of one day (screening) (N= 211) to 84 months (maintenance) (N= 1). The usual screening bolus dose administered prior to pump implantation in these studies was 50- 75 mcg. The maintenance dose ranged from 22 mcg to 1400 mcg per day. Doses used in this patient population for long term infusion are generally lower than those required for patients with spasticity of spinal cord origin.

Because of the open, uncontrolled nature of the experience, a causal linkage between events observed and the administration of LIORESAL INTRATHECAL cannot be reliably assessed in many cases. Nonetheless, many of the more commonly reported reactions— somnolence, dizziness, headache, nausea, hypotension, hypotonia and coma— appear clearly drug-related.

The most frequent (≥1%) adverse events reported during all clinical trials are shown in the following table. Nine patients discontinued long term treatment due to adverse events.

INCIDENCE OF MOST FREQUENT (≥ 1%) ADVERSE EVENTS IN PATIENTS WITH SPASTICITY OF CEREBRAL ORIGIN IN PROSPECTIVELY MONITORED CLINICAL TRIALS

	Percent of Patients Reporting Events		
	N = 211	**N = 153**	**N = 150**
	Screening[a]	Titration[b]	Maintenance[c]
Adverse Event	**Percent**	**Percent**	**Percent**
Hypotonia	2.4	14.4	34.7
Somnolence	7.6	10.5	18.7
Headache	6.6	7.8	10.7
Nausea and Vomiting	6.6	10.5	4.0
Vomiting	6.2	8.5	4.0
Urinary Retention	0.9	6.5	8.0
Convulsion	0.9	3.3	10.0
Dizziness	2.4	2.6	8.0
Nausea	1.4	3.3	7.3
Hypoventilation	1.4	1.3	4.0
Hypertonia	0.0	0.7	6.0
Paresthesia	1.9	0.7	3.3
Hypotension	1.9	0.7	2.0
Increased Salivation	0.0	2.6	2.7
Back Pain	0.9	0.7	2.0
Constipation	0.5	1.3	2.0
Pain	0.0	0.0	4.0
Pruritus	0.0	0.0	4.0
Diarrhea	0.5	0.7	2.0
Peripheral Edema	0.0	0.0	3.3
Thinking Abnormal	0.5	1.3	0.7
Agitation	0.5	0.0	1.3
Asthenia	0.0	0.0	2.0
Chills	0.5	0.0	1.3
Coma	0.5	0.0	1.3
Dry Mouth	0.5	0.0	1.3
Pneumonia	0.0	0.0	2.0
Speech Disorder	0.5	0.7	0.7
Tremor	0.5	0.0	1.3
Urinary Incontinence	0.0	0.0	2.0
Urination Impaired	0.0	0.0	2.0

[a] Following administration of test bolus
[b] Two month period following implant
[c] Beyond two months following implant
N= Total number of patients entering each period. 211 patients received drug; (1 of 212) received placebo only.

The more common (1% or more) adverse events reported in the prospectively followed 211 patients exposed to LIORESAL INTRATHECAL (baclofen injection) have been reported. In the total cohort, the following adverse events, not described in the table, and arranged in decreasing order of frequency, and classified by body system, were reported:

Nervous System: Akathisia, ataxia, confusion, depression, opisthotonos, amnesia, anxiety, hallucinations, hysteria, insomnia, nystagmus, personality disorder, reflexes decreased, and vasodilitation.
Digestive System: Dysphagia, fecal incontinence, gastrointestinal hemorrhage and tongue disorder.
Cardiovascular: Bradycardia.
Respiratory: Apnea, dyspnea and hyperventilation.
Urogenital: Abnormal ejaculation, kidney calculus, oliguria and vaginitis.
Skin and Appendages: Rash, sweating, alopecia, contact dermatitis and skin ulcer.
Special Senses: Abnormality of accommodation.
Body as a Whole: Death, fever, abdominal pain, carcinoma, malaise and hypothermia.
Hemic and Lymphatic System: Leukocytosis and petechial rash.

DRUG OVERDOSE

Special attention must be given to recognizing the signs and symptoms of overdosage, especially during the initial screening and dose- titration phase of treatment, but also during reintroduction of LIORESAL INTRATHECAL after a period of interruption in therapy.

Symptoms of LIORESAL INTRATHECAL Overdose: Drowsiness, lightheadedness, dizziness, somnolence, respiratory depression, seizures, rostral progression of hypotonia and loss of con- sciousness progressing to coma of up to 72 hr. duration. In most cases reported, coma was reversible without sequelae after drug was discontinued. Symptoms of LIORESAL INTRATHECAL overdose were reported in a sensitive adult patient after receiving a 25 mcg intrathecal bolus.

Treatment Suggestions for Overdose:

There is no specific antidote for treating overdoses of LIORESAL INTRATHECAL (baclofen injection); however, the following steps should ordinarily be undertaken:
1) Residual LIORESAL INTRATHECAL solution should be removed from the pump as soon as possible.
2) Patients with respiratory depression should be intubated if necessary, until the drug is eliminated.

Anecdotal reports suggest that intravenous physostigmine may reverse central side effects, notably drowsiness and respiratory depression. Caution in administering physostigmine is advised, however, because its use has been associated with the induction of seizures and bradycardia.

Physostigmine Doses for Adult Patients: Administer 2 mg of physostigmine intramuscularly or intravenously at a slow controlled rate of no more than 1 mg per minute. Dosage may be repeated if life-threatening signs, such as arrhythmia, convulsions or coma occur.

Physostigmine Doses for Pediatric Patients: Administer 0.02 mg/ kg physostigmine intramuscularly or intravenously, do not give more than 0.5 mg per minute. The dosage may be repeated at 5 to 10 minute intervals until a therapeutic effect is obtained or a maximum dose of 2 mg is attained.

Physostigmine may not be effective in reversing large overdoses and patients may need to be maintained with respiratory support.

If lumbar puncture is not contraindicated, consideration should be given to withdrawing 30- 40 ml of CSF to reduce CSF baclofen concentration.

DOSAGE AND ADMINISTRATION

Refer to the manufacturer's manual for the implantable pump approved for intrathecal infusion for specific instructions and precautions for programming the pump and/ or refilling the reservoir. There are various pumps with varying reservoir volumes and there are various refill kits available. It is important to be familiar with all of these products in order to select the appropriate refill kit for the particular pump in use.

Screening Phase: Prior to pump implantation and initiation of chronic infusion of LIORESAL INTRATHECAL (baclofen injection), patients must demonstrate a positive clinical response to a LIORESAL INTRATHECAL bolus dose administered intrathecally in a screening trial. The screening trial employs LIORESAL INTRATHECAL at a concentration of 50 mcg/ ml. A 1 ml ampule (50 mcg/ ml) is available for use in the screening trial. The screening procedure is as follows. An initial bolus containing 50 micrograms in a volume of 1 milliliter is administered into the intrathecal space by barbotage over a period of not less than one minute. The patient is observed over the ensuing 4 to 8 hours. A positive response consists of a significant decrease in muscle tone and/ or frequency and/ or severity of spasms. If the initial response is less than desired, a second bolus injection may be administered 24 hours after the first. The second screening bolus dose consists of 75 micrograms in 1.5 milliliters. Again, the patient should be observed for an interval of 4 to 8 hours. If the response is still inadequate, a final bolus screening dose of 100 micrograms in 2 milliliters may be administered 24 hours later.

Pediatric Patients: The starting screening dose for pediatric patients is the same as in adult patients, i.e., 50 mcg. However, for very small patients, a screening dose of 25 mcg may be tried first. **Patients who do not respond to a 100 mcg intrathecal bolus should not be considered candidates for an implanted pump for chronic infusion.**

Post- Implant Dose Titration Period: To determine the initial total daily dose of LIORESAL INTRATHECAL following implant, the screening dose that gave a positive effect should be doubled and administered over a 24-hour period, unless the efficacy of the bolus dose was maintained for more than 8 hours, in which case the starting daily dose should be the screening dose delivered over a 24-hour period. No dose increases should be given in the first 24 hours (i.e., until the steady state is achieved).

Adult Patients with Spasticity of Spinal Cord Origin: After the first 24 hours, for adult patients, the daily dosage should be increased slowly by 10- 30% increments and only once every 24 hours, until the desired clinical effect is achieved.

Adult Patients with Spasticity of Cerebral Origin: After the first 24 hours, the daily dose should be increased slowly by 5- 15% only once every 24 hours, until the desired clinical effect is achieved.

Pediatric Patients: After the first 24 hours, the daily dose should be increased slowly by 5-15% only once every 24 hours, until the desired clinical effect is achieved. If there is not a substantive clinical response to increases in the daily dose, check for proper pump function and catheter patency. Patients must be monitored closely in a fully equipped and staffed environment during the screening phase and dose- titration period immediately following implant. Resuscitative equipment should be immediately available for use in case of life- threatening or intolerable side effects.

Maintenance Therapy:

Spasticity of Spinal Cord Origin Patients: The clinical goal is to maintain muscle tone as close to normal as possible, and to minimize the frequency and severity of spasms to the extent possible, without inducing intolerable side effects. Very often, the maintenance dose needs to be adjusted during the first few months of therapy while patients adjust to changes in life style due to the alleviation of spasticity. During periodic refills of the pump, the daily dose may be increased by 10-40%, but no more than 40%, to maintain adequate symptom control. The daily dose may be reduced by 10-20% if patients experience side effects. Most patients require gradual increases in dose over time to maintain optimal response during chronic therapy. A sudden large requirement for dose escalation suggests a catheter complication (i.e., catheter kink or dislodgement).

Maintenance dosage for long term continuous infusion of LIORESAL INTRATHECAL (baclofen injection) has ranged from 12 mcg/ day to 2003 mcg/ day, with most patients adequately maintained on 300 micrograms to 800 micrograms per day. There is limited experience with daily doses greater than 1000 mcg/ day. Determination of the optimal LIORESAL INTRATHECAL dose requires individual titration. The lowest dose with an optimal response should be used.

Spasticity of Cerebral Origin Patients: The clinical goal is to maintain muscle tone as close to nor- mal as possible and to minimize the frequency and severity of spasms to the extent possible, without inducing intolerable side effects, or to titrate the dose to the desired degree of muscle tone for optimal functions. Very often the maintenance dose needs to be adjusted during the first few months of therapy while patients adjust to changes in life style due to the alleviation of spasticity. During periodic refills of the pump, the daily dose may be increased by 5 - 20%, but no more than 20%, to maintain adequate symptom control. The daily dose may be reduced by 10-20% if patients experience side effects. Many patients require gradual increases in dose over time to maintain optimal response during chronic therapy. A sudden large requirement for dose escalation suggests a catheter complication (i.e., catheter kink or dislodgement).

Maintenance dosage for long term continuous infusion of LIORESAL INTRATHECAL (baclofen injection) has ranged from 22 mcg/ day to 1400 mcg/ day, with most patients adequately maintained on 90 micrograms to 703 micrograms per day. In clinical trials, only 3 of 150 patients required daily doses greater than 1000 mcg/ day.

Pediatric Patients: Use same dosing recommendations for patients with spasticity of cerebral origin. Pediatric patients under 12 years seemed to require a lower daily dose in clinical trials. Average daily dose for patients under 12 years was 274 mcg/ day, with a range of 24 to 1199 mcg/ day. Dosage requirement for pediatric patients over 12 years does not seem to be different from that of adult patients. Determination of the optimal LIORESAL INTRATHECAL dose requires individual titration. The lowest dose with an optimal response should be used.

Potential need for dose adjustments in chronic use : During long term treatment, approximately 5% (28/627) of patients become refractory to increasing doses. There is not sufficient experience to make firm recommendations for tolerance treatment; however, this "tolerance" has been treated on occasion, in hospital, by a "drug holiday" consisting of the gradual reduction of LIORESAL INTRATHECAL over a 2 to 4 week period and switching to alternative methods of spasticity management. After the "drug holiday," LIORESAL INTRATHECAL may be restarted at the initial continuous infusion dose.

Stability

Parenteral drug products should be inspected for particulate matter and discoloration prior to administration, whenever solution and container permit.

Delivery Specifications

The specific concentration that should be used depends upon the total daily dose required as well as the delivery rate of the pump. LIORESAL INTRATHECAL may require dilution when used with certain implantable pumps. Please consult manufacturer's manual for specific recommendations.

Preparation Instruction:

Screening

Use the 1 ml screening ampule only (50 mcg/ml) for bolus injection into the subarachnoid space. For a 50mcg bolus dose, use 1 ml of the screening ampule. Use 1.5 ml of 50 mcg/ml baclofen injection for a 75 mcg bolus dose. For the maximum screening dose of 100 mcg, use 2 ml of 50 mcg/ml baclofen injection (2 screening ampules).

Maintenance

For patients who require concentrations other than 500 mcg/ml or 2000 mcg/ml, LIORESAL INTRATHECAL **must be diluted.**

LIORESAL INTRATHECAL **must be diluted** with sterile preservative free Sodium Chloride for Injection, U.S.P.

Delivery Regimen:

LIORESAL INTRATHECAL is most often administered in a continuous infusion mode immediately following implant. For those patients implanted with programmable pumps who have achieved relatively satisfactory control on continuous infusion, further benefit may be attained using more complex schedules of LIORESAL INTRATHECAL delivery. For example, patients who have increased spasms at night may require a 20% increase in their hourly infusion rate. Changes in flow rate should be programmed to start two hours before the time of desired clinical effect.

HOW SUPPLIED

LIORESAL INTRATHECAL (baclofen injection) is available in single use ampules of 10 mg/20 ml (500 mcg/ ml) or 10 mg/ 5 ml (2000 mcg/ml) or 40 mg/20 ml (2000 mcg/ml) packaged in a Refill Kit for intrathecal administration. For screening, LIORESAL INTRATHECAL is available in a single use ampule of 0.05 mg/ 1 ml.

Model 8561 LIORESAL INTRATHECAL Refill Kit contains one ampule of 10 mg/ 20 ml (500 mcg/ml) (NDC 58281-560-01).

Model 8562 LIORESAL INTRATHECAL Refill Kit contains two ampules of 10 mg/ 5 ml (2000 mcg/ml) (NDC 58281-561-02).

Model 8563s LIORESAL INTRATHECAL contains one ampule of 0.05 mg/ 1 ml (NDC 58281-562-01).

Model 8564 LIORESAL INTRATHECAL Refill Kit contains four ampules of 10 mg/ 5 ml (2000 mcg/ml) (NDC 58281-561-04) or one ampule of 40 mg/20 ml (2000 mcg/ml) (NDC 58281-563-01).

Model 8565 LIORESAL INTRATHECAL Refill Kit contains two ampules of 10 mg/ 20 ml (500 mcg/ml) (NDC 58281-560-02).

Model 8566 LIORESAL INTRATHECAL Refill Kit contains eight ampules of 10 mg/ 5 ml (2000 mcg/ml) (NDC 58281-561-08) or two ampules of 40 mg/20 ml (2000 mcg/ml) (NDC 58281-563-02).

STORAGE

Does not require refrigeration.

Do not store above 86° F (30° C).

Do not freeze.

Do not heat sterilize.

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