

GADOPENTETATE DIMEGLUMINE- gadopentetate dimeglumine injection
Alvogen, Inc

Gadopentetate dimeglumine

Injection

FOR INTRAVENOUS ADMINISTRATION

Rx only

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs.

- Do not administer gadopentetate dimeglumine to patients with:
 - chronic, severe kidney disease (GFR < 30 mL/min/1.73m²), or
 - acute kidney injury (see CONTRAINDICATIONS).
- Screen patients for acute kidney injury and other conditions that may reduce renal function.

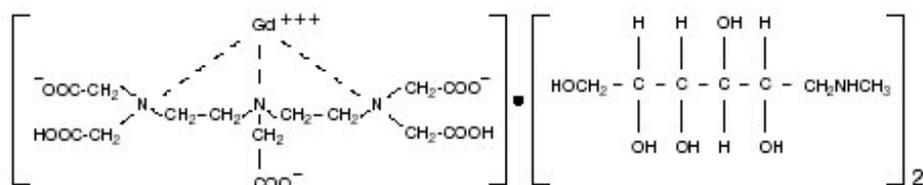
For patients at risk for chronically reduced renal function (for example, age >60 years, hypertension or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.

Do not exceed the recommended gadopentetate dimeglumine dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration (see WARNINGS AND PRECAUTIONS).

DESCRIPTION

Gadopentetate dimeglumine Injection is the N-methylglucamine salt of the gadolinium complex of diethylenetriamine pentaacetic acid, and is an injectable contrast medium for magnetic resonance imaging (MRI). Gadopentetate dimeglumine Injection is provided as a sterile, clear, colorless to slightly yellow aqueous solution for intravenous injection.

Gadopentetate dimeglumine Injection is a 0.5-mol/L solution of 1-deoxy-1-(methylamino)-D-glucitol dihydrogen [N,N-bis[2-[bis(carboxymethyl)amino]ethyl] glycinato(5-)]gadolate(2-)(2:1) with a molecular weight of 938, an empirical formula of C₂₈H₅₄GdN₅O₂₀, and has the following structural formula:



Each mL contains 469.01 mg gadopentetate dimeglumine, 0.99 mg meglumine, 0.40 mg

diethylenetriamine pentaacetic acid and water for injection. Gadopentetate dimeglumine Injection contains no antimicrobial preservative.

Gadopentetate dimeglumine Injection has a pH of 6.5 to 8.0. Pertinent physicochemical data are noted below:

PARAMETER		
Osmolality (mOsmol/kg water)	at 37° C	1,960
Viscosity (CP)	at 20° C	4.9
	at 37° C	2.9
Density (g/mL)	at 25° C	1.195
Specific Gravity	at 25° C	1.208
Octanol: H ₂ O Coefficient	at 25° C, pH7 log P _{ow} = - 5.4	

Gadopentetate dimeglumine Injection has an osmolality 6.9 times that of plasma which has an osmolality of 285 mOsmol/kg water. Gadopentetate dimeglumine Injection is hypertonic under conditions of use.

CLINICAL PHARMACOLOGY

Pharmacokinetics

The pharmacokinetics of intravenously administered gadopentetate dimeglumine in normal subjects conforms to a two compartment open-model with mean distribution and elimination half-lives (reported as mean ± SD) of about 0.2 ± 0.13 hours and 1.6 ± 0.13 hours, respectively.

Upon injection, the meglumine salt is completely dissociated from the gadopentetate dimeglumine complex. Gadopentetate is exclusively eliminated in the urine with 83 ± 14% (mean ± SD) of the dose excreted within 6 hours and 91 ± 13% (mean ± SD) by 24 hours, post-injection. There was no detectable biotransformation or decomposition of gadopentetate dimeglumine.

The renal and plasma clearance rates (1.76 ± 0.39 mL/min/kg and 1.94 ± 0.28 mL/min/kg, respectively) of gadopentetate are essentially identical, indicating no alteration in elimination kinetics on passage through the kidneys and that the drug is essentially cleared through the kidney. The volume of distribution (266 ± 43 mL/kg) is equal to that of extracellular water and clearance is similar to that of substances which are subject to glomerular filtration.

In vitro laboratory results indicate that gadopentetate does not bind to human plasma protein. *In vivo* protein binding studies have not been done.

Renal Impairment

Gadopentetate dimeglumine is excreted via the kidneys, even in patients with impaired renal function. In patients with impaired renal function, the serum half-life of gadopentetate dimeglumine is prolonged. Mean serum elimination half-lives of a single intravenous dose of gadopentetate dimeglumine (0.1 mmol/kg) were 2.6 ± 1.2 h, 4.2 ± 2.0 h and 10.8 ± 6.9 h, for mildly (creatinine clearance, CLCR = 60 to < 90 mL/min), moderately (CLCR = 30 to < 60 mL/min) and severely (CLCR = < 30 mL/min) impaired patients, respectively, as compared with 1.6 ± 0.1 h in healthy subjects.

Pharmacodynamics

Gadopentetate dimeglumine is a paramagnetic agent and, as such, it develops a magnetic moment when placed in a magnetic field. The relatively large magnetic moment produced by the paramagnetic agent results in a relatively large local magnetic field, which can enhance the relaxation rates of water protons in the vicinity of the paramagnetic agent.

In magnetic resonance imaging (MRI), visualization of normal and pathological brain tissue depends in

part on variations in the radiofrequency signal intensity that occur with 1) changes in proton density; 2) alteration of the spin-lattice or longitudinal relaxation time (T₁); and 3) variation of the spin-spin or transverse relaxation time (T₂). When placed in a magnetic field, gadopentetate dimeglumine decreases the T₁ and T₂ relaxation time in tissues where it accumulates. At usual doses the effect is primarily on the T₁ relaxation time.

Gadopentetate dimeglumine does not cross the intact blood-brain barrier and, therefore, does not accumulate in normal brain or in lesions that do not have an abnormal blood-brain barrier, e.g., cysts, mature post-operative scars, etc. However, disruption of the blood-brain barrier or abnormal vascularity allows accumulation of gadopentetate dimeglumine in lesions such as neoplasms, abscesses, and subacute infarcts. The pharmacokinetic parameters of gadopentetate dimeglumine in various lesions are not known.

CLINICAL TRIALS

Gadopentetate dimeglumine Injection was administered to 1272 patients in open label controlled clinical studies. The mean age of these patients was 46.4 years (range 2 to 93 years). Of these patients, 55% (700) were male and 45% (572) were female. Of the 1271 patients who received Gadopentetate dimeglumine Injection and for whom race was reported, 82.1% (1043) were Caucasian, 9.7% (123) were Black, 5.3% (67) were Hispanic, 2.1% (27) were Oriental/Asian, and 0.9% (11) were other. Of the 1272 patients, 550 patients were evaluated in blinded reader studies. These evaluated the use of contrast enhancement in magnetic resonance imaging of lesions in the head and neck, brain, spine and associated tissues, and body (excluding the heart). Of the 550 patients, all patients had a reason for an MRI and efficacy assessments were based on pre-and post- Gadopentetate dimeglumine Injection film quality, film contrast, lesion configuration (border, size, and location), and the number of lesions. The protocols did not include systematic verification of specific diseases or histopathologic confirmation of findings.

Of the above 550 patients, 97 patients received 0.1 mmol/kg Gadopentetate dimeglumine Injection IV in two clinical trials of gadopentetate dimeglumine MRI contrast enhancement for body imaging. Of these 97, 68 had MRIs of the internal organs/structures of the abdomen or thorax (excluding the heart); 8 had breast images and 22 had images of appendages. The results of MRIs before and after gadopentetate dimeglumine use were compared blindly. Overall additional lesions were identified in 22/97 (23%) of the patients after Gadopentetate dimeglumine Injection. The mean number of lesions identified before (1.49/patient) and after gadopentetate dimeglumine (1.75/patient) were similar. Seven (8%) of the patients had lesions seen before gadopentetate dimeglumine that were not seen after gadopentetate dimeglumine. Overall, after Gadopentetate dimeglumine Injection, 41% of the images had a higher contrast score than before injection; and 18% of the images had a higher contrast score before Gadopentetate dimeglumine Injection than after Gadopentetate dimeglumine Injection. Gadopentetate dimeglumine MRI of the 8 patients with breast images were not systematically compared to the results to mammography, breast biopsy or other modalities. In the 22 patients with appendage images (e.g., muscle, bone and intraarticular structures), gadopentetate dimeglumine MRI was not systematically evaluated to determine the effects of contrast biodistribution in these different areas.

Of the above 550 patients, 66 patients received gadopentetate dimeglumine 0.1 mmol/kg IV in clinical trials of gadopentetate dimeglumine MRI contrast enhancement of lesions in the head and neck. A total of 66 MRI images were evaluated blindly by comparing each pair of MRI images, before and after Gadopentetate dimeglumine Injection. In these paired images, 56/66 (85%) had greater enhancement after gadopentetate dimeglumine and 40/66 (61%) had better lesion configuration or border delineation after gadopentetate dimeglumine. Overall, there was better contrast after gadopentetate dimeglumine in 55% of the images, comparable enhancement in 44 (36%) before and after gadopentetate dimeglumine, and better enhancement in 9% without gadopentetate dimeglumine.

In the studies of the brain and spinal cord, gadopentetate dimeglumine 0.1 mmol/kg IV provided contrast enhancement in lesions with an abnormal blood brain barrier.

In two studies, a total of 108 patients were evaluated to compare the dose response effects of 0.1

mmol/kg and 0.3 mmol/kg of gadopentetate dimeglumine in CNS MRI. Both dosing regimens had similar imaging and general safety profiles; however, the 0.3 mmol/kg dose did not provide additional benefit to the final diagnosis (defined as number of lesions, location and characterization).

INDICATIONS AND USAGE

Central Nervous System

Gadopentetate dimeglumine Injection is indicated for use with magnetic resonance imaging (MRI) in adults, and pediatric patients (2 years of age and older) to visualize lesions with abnormal vascularity in the brain (intracranial lesions), spine and associated tissues. Gadopentetate dimeglumine Injection has been shown to facilitate visualization of intracranial lesions including but not limited to tumors.

Extracranial/Extraspinal Tissues

Gadopentetate dimeglumine is indicated for use with MRI in adults and pediatric patients (2 years of age and older) to facilitate the visualization of lesions with abnormal vascularity in the head and neck.

Body

Gadopentetate dimeglumine Injection is indicated for use in MRI in adults and pediatric patients (2 years of age and older) to facilitate the visualization of lesions with abnormal vascularity in the body (excluding the heart).

CONTRAINDICATIONS

Gadopentetate dimeglumine is contraindicated in patients with:

- Chronic, severe kidney disease (glomerular filtration rate, GFR < 30 mL/min/1.73m²), or
- Acute kidney injury, or
- History of severe hypersensitivity reactions to gadopentetate dimeglumine.

WARNINGS AND PRECAUTIONS

Nephrogenic Systemic Fibrosis (NSF)

Gadolinium-based contrast agents (GBCAs) increase the risk for nephrogenic systemic fibrosis (NSF) among patients with impaired elimination of the drugs. Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast enhanced MRI or other modalities. The GBCA-associated NSF risk appears highest for patients with chronic, severe kidney disease (GFR < 30 mL/min/1.73m²) as well as patients with acute kidney injury. Do not administer gadopentetate dimeglumine to these patients. The risk appears lower for patients with chronic, moderate kidney disease (GFR 30- 59 mL/min/1.73m²) and little, if any, for patients with chronic, mild kidney disease (GFR 60- 89 mL/min/1.73m²). NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs. Report any diagnosis of NSF following gadopentetate dimeglumine administration to Strides Arcolab Limited (1-877-244-9825 or www.stridesarco.com) or FDA (1-800-FDA-1088 or www.fda.gov/medwatch).

Screen patients for acute kidney injury and other conditions that may reduce renal function. Features of acute kidney injury consist of rapid (over hours to days) and usually reversible decrease in kidney function, commonly in the setting of surgery, severe infection, injury or drug-induced kidney toxicity. Serum creatinine levels and estimated GFR may not reliably assess renal function in the setting of acute kidney injury. For patients at risk for chronically reduced renal function (for example, age > 60 years, diabetes mellitus or chronic hypertension), estimate the GFR through laboratory testing.

Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of a GBCA and degree of renal impairment at the time of exposure. Record the specific GBCA and the dose administered to a patient. When administering gadopentetate dimeglumine, do not exceed the recommended dose and allow a sufficient period of time for elimination of the drug prior to re-administration (see **CLINICAL PHARMACOLOGY** and **DOSAGE AND ADMINISTRATION**).

Hypersensitivity Reactions

Anaphylactoid and anaphylactic reactions with cardiovascular, respiratory and/or cutaneous manifestations rarely resulting in death have occurred. The risk of hypersensitivity reactions is higher in patients with a history of reaction to contrast media, bronchial asthma, or allergic disorders. Hypersensitivity reactions can occur with or without prior exposure to GBCAs.

Have appropriately trained personnel administer gadopentetate dimeglumine in a facility that has immediate availability of resuscitative equipment. If a hypersensitivity reaction occurs, stop Gadopentetate dimeglumine Injection and immediately begin appropriate therapy.

Observe closely patients with a history of drug reactions, allergy or other hypersensitivity disorders, during and up to several hours after Gadopentetate dimeglumine Injection.

Renal Failure

In patients with renal impairment, acute renal failure (acute kidney injury) requiring dialysis or worsening renal function has occurred, mostly within 48 hrs of Gadopentetate dimeglumine Injection. The risk of acute renal failure is higher with increasing dose of contrast. Use the lowest possible dose, evaluate renal function in patients with renal impairment, and allow sufficient time for contrast elimination before re-administration. Elimination half-life in patients with mild or moderate renal impairment is 3 to 4 hours. Elimination half-life in patients with severe renal impairment is about 11 hours. Gadopentetate dimeglumine is cleared by glomerular filtration and is dialyzable. After 3 dialysis sessions of 3 hours each, about 97% of the administered dose is eliminated from the body; each dialysis session removes about 70% of the circulating drug (see **CLINICAL PHARMACOLOGY, Pharmacokinetics**).

Injection Site Reactions

Skin and soft tissue necrosis, thrombosis, fasciitis, and compartment syndrome requiring surgical intervention (e.g., compartment release or amputation) have occurred very rarely at the site of contrast injection or the dosed limb. Total volume and rate of Gadopentetate dimeglumine Injection, extravasation of contrast agent, and patient susceptibility might contribute to these reactions. Phlebitis and thrombophlebitis may be observed generally within 24 hours after Gadopentetate dimeglumine Injection and resolve with supportive treatment. Determine the patency and integrity of the intravenous line before administration of Gadopentetate dimeglumine Injection. Assessment of the dosed limb for the development of injection site reactions is recommended.

Interference with Visualization of Lesions Visible with Non-Contrast MRI

As with any paramagnetic contrast agent, Gadopentetate dimeglumine Injection might impair the visualization of lesions seen on non-contrast MRI. Therefore, caution should be exercised when gadopentetate dimeglumine MRI scans are interpreted without a companion non-contrast MRI scan.

Patient Counseling Information

Patients scheduled to receive Gadopentetate dimeglumine Injection should be instructed to inform their physician if they are pregnant, breastfeeding, or have a history of renal insufficiency, asthma or allergic respiratory disorders. Additionally instruct patients to inform their physician if they:

- Have a history of kidney and/or liver disease, or

- Have recently received a GBCA.

GBCAs increase the risk of NSF among patients with impaired elimination of drugs. To counsel patients at risk of NSF:

- Describe the clinical manifestation of NSF
- Describe procedures to screen for the detection of renal impairment

Instruct the patients to contact their physician if they develop signs or symptoms of NSF following gadopentetate dimeglumine administration, such as burning, itching, swelling, scaling, hardening and tightening of the skin; red or dark patches on the skin; stiffness in joints with trouble moving, bending or straightening the arms, hands, legs or feet; pain in the hip bones or ribs; or muscle weakness.

LABORATORY TEST FINDINGS

Transitory changes in serum iron, bilirubin and transaminase levels were observed in clinical trials.

Gadopentetate dimeglumine Injection does not interfere with serum and plasma calcium measurements determined by colorimetric assays.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long term animal studies have not been performed to evaluate the carcinogenic potential of gadopentetate dimeglumine.

A comprehensive battery of *in vitro* and *in vivo* studies in bacterial and mammalian systems suggest that gadopentetate dimeglumine is not mutagenic or clastogenic and does not induce unscheduled DNA repair in rat hepatocytes or cause cellular transformation of mouse embryo fibroblasts. However, the drug did show some evidence of mutagenic potential *in vivo* in the mouse dominant lethal assay at doses of 6 mmol/kg, but did not show any such potential in the mouse and dog micronucleus tests at intravenous doses of 9 mmol/kg and 2.5 mmol/kg, respectively.

When administered intra-peritoneally to male and female rats daily prior to mating, during mating and during embryonic development for up to 74 days (males) or 35 days (females), gadopentetate caused a decrease in number of corpora lutea at the 0.1 mmol/kg dose level. After daily dosing with 2.5 mmol/kg suppression of food consumption and body weight gain (males and females) and a decrease in the weights of testes and epididymis were also observed.

In a separate experiment in rats, daily injections of gadopentetate dimeglumine over 16 days caused spermatogenic cell atrophy at a dose level of 5 mmol/kg but not at a dose level of 2.5 mmol/kg. This atrophy was not reversed within a 16-day observation period following the discontinuation of the drug.

Pregnancy

Category C

Gadopentetate dimeglumine retarded fetal development slightly when given intravenously for 10 consecutive days to pregnant rats at daily doses of 0.25, 0.75, and 1.25 mmol/kg (2.5, 7.5 and 12.5 times the human dose based on body weight) and when given intravenously for 13 consecutive days to pregnant rabbits at daily doses of 0.75 and 1.25 mmol/kg (7.5 and 12.5 times the human dose respectively, based on body weight) but not at daily doses of 0.25 mmol/kg. No congenital anomalies were noted in rats or rabbits.

Adequate and well controlled studies were not conducted in pregnant women. Gadopentetate dimeglumine Injection should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

Gadopentetate dimeglumine is excreted in human milk. Gadopentetate dimeglumine Injection was administered intravenously to 18 lactating women with normal renal function at a dose of 0.1 mmol/kg body weight. In these women, less than 0.04% of the administered gadolinium was excreted into the breast milk during the 24-hour period following dosing. Breast milk obtained during the 24 hours following dosing revealed the average cumulative amount of gadolinium excreted in breast milk was 0.57+/-0.71 micromoles. The amount transferred from a 70 kg woman (receiving 0.1 mmol/kg body weight) to an infant by breastfeeding over a period of 24 hrs translates into less than 3 micromoles of gadolinium.

The overall duration of excretion of gadolinium into breast milk is unknown. The extent of the absorption of Gadopentetate dimeglumine Injection in infants and its effect on the breast-fed child remains unknown.

Pediatric Use

The use of gadopentetate dimeglumine in imaging the central nervous system, extracranial/extraspinal tissues, and body have been established in the pediatric population from the ages of 2 to 16 years on the basis of adequate and well controlled clinical trials in adults and safety studies in this pediatric population. (see **CLINICAL TRIALS** for details).

Safety and efficacy in the pediatric population under the age of 2 years have not been established. Gadopentetate dimeglumine is eliminated primarily by the kidney. In a study with pediatric patients aged 2 months to < 2 years the pharmacokinetics (body weight-normalized clearance, body weight-normalized distribution volume, and terminal half-life) gadopentetate were similar to adults. (see **INDICATIONS** and **DOSAGE AND ADMINISTRATION**).

ADVERSE REACTIONS

Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The mean age of the 1272 patients who received Gadopentetate dimeglumine Injection in pre-market clinical trials was 46.4 years (range 2 to 93 years). Of these patients, 55% (700) were male and 45% (572) were female. Of the 1271 patients who received Gadopentetate dimeglumine Injection and for whom race was reported, 82.1% (1043) were Caucasian, 9.7% (123) were Black, 5.3% (67) were Hispanic, 2.1% (27) were Oriental/Asian, and 0.9% (11) were other.

The most common adverse reaction was headache (4.8%). The majority of headaches were transient and of mild to moderate severity. Other adverse reactions that occurred in $\geq 1\%$ of patients included: nausea (2.7%), injection site coldness/localized coldness (2.3%) and dizziness (1%).

The following additional adverse reactions occurred in less than 1% of the patients:

General Disorders: injection site reactions, including phlebitis, pain, localized warmth, localized edema, and burning sensation; substernal chest pain, back pain, pyrexia, asthenia, feeling cold, generalized warmth, fatigue, and chest tightness, and anaphylactoid reactions characterized by cardiovascular, respiratory and/or cutaneous symptoms, such as dyspnea, bronchospasm, and cough (see **WARNINGS AND PRECAUTIONS**.)

Cardiovascular: Hypotension, hypertension, tachycardia, migraine, syncope, vasodilatation, pallor.

Gastrointestinal: Abdominal discomfort, teeth pain, increased salivation, abdominal pain, vomiting, diarrhea.

Nervous System: Agitation, anxiety, thirst, somnolence, diplopia, loss of consciousness, convulsions (including grand mal), paresthesia.

Respiratory System: Throat irritation, rhinitis, sneezing.

Skin: Rash, sweating (hyperhidrosis), pruritus, urticaria (hives), facial edema.

Special Senses: Conjunctivitis, taste abnormality, dry mouth, lacrimation, eye irritation, eye pain, ear pain.

Postmarketing Experience

The following additional adverse reactions have been identified during postmarketing use of gadopentetate dimeglumine. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The most serious reactions were nephrogenic systemic fibrosis (see **Boxed Warning**) and acute reactions including cardiac or respiratory arrest, anaphylactic shock, shock, respiratory distress, and laryngeal edema. Life threatening and/or fatal adverse reactions have been reported. The most frequently reported adverse reactions in the postmarketing experience were nausea, vomiting, urticaria and rash.

General Disorders and Administration Site Conditions: Nephrogenic systemic fibrosis (see **Warnings and Precautions**), body temperature decreased, tremor, shivering (chills).

Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions that may be fatal and include cardiac or respiratory arrest, respiratory distress, cyanosis, laryngeal edema, laryngospasm, pharyngeal edema, and angioedema (see **Warnings and Precautions**).

Delayed hypersensitivity reactions have been reported up to several hours after administration of gadopentetate dimeglumine.

Renal and Urinary: Acute renal failure, worsening renal impairment (see **Warnings and Precautions**), urinary incontinence, urinary urgency.

Vascular: Thrombophlebitis, deep vein thrombophlebitis, compartment syndrome requiring surgical intervention.

Cardiac: Cardiac arrest, heart rate decreased, arrhythmia.

Ear and Labyrinth Disorders: Hearing impaired.

Eye Disorders: Visual disturbance.

Musculoskeletal and Connective Tissue Disorder: Arthralgia.

Nervous System Disorders: Coma, parosmia, speech disorder.

Respiratory System: Respiratory arrest, pulmonary edema.

Skin: Erythema multiforme, pustules (rash pustular).

OVERDOSAGE

Systemic consequences associated with overdosage of Gadopentetate dimeglumine Injection have not been reported.

DOSAGE AND ADMINISTRATION

The recommended dosage of Gadopentetate dimeglumine Injection is 0.2 mL/kg (0.1 mmol/kg) administered intravenously, at a rate not to exceed 10 mL per 15 seconds. Dosing for patients in excess of 286 lbs has not been studied systematically.

DOSE AND DURATION OF Gadopentetate dimeglumine INJECTION BY BODY WEIGHT
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BODY WEIGHT		Total Volume, mL*
lb	kg	
22	10	2
44	20	4
66	30	6
88	40	8
110	50	10
132	60	12
154	70	14
176	80	16
198	90	18
220	100	20
242	110	22
264	120	24
286	130	26
*Rate of injection: 10 mL/15 sec		

Drug Handling:

To ensure complete injection of the contrast medium, the injection should be followed by a 5-mL normal saline flush. The imaging procedure should be completed within 1 hour of injection of Gadopentetate dimeglumine Injection.

As with other gadolinium contrast agents, Gadopentetate dimeglumine Injection has not been established for use in magnetic resonance angiography.

Parenteral products should be inspected visually for particulate matter and discoloration prior to administration. Do not use the solution if it is discolored or particulate matter is present.

Any unused portion must be discarded in accordance with regulations dealing with the disposal of such materials.

HOW SUPPLIED

Gadopentetate dimeglumine Injection is a clear, colorless to slightly yellow solution containing 469.01 mg/mL of gadopentetate dimeglumine. Gadopentetate dimeglumine Injection is supplied in the following sizes:

5 mL single-dose vials, rubber stoppered, in individual cartons,

Boxes of 20 NDC 47781-147-20

10 mL single-dose vials, rubber stoppered, in individual cartons,

Boxes of 20 NDC 47781-147-22

15 mL single-dose vials, rubber stoppered, in individual cartons,

Boxes of 20 NDC 47781-147-27

20 mL single-dose vials, rubber stoppered, in individual cartons,

Boxes of 20 NDC 47781-147-29

STORAGE

Gadopentetate dimeglumine Injection should be stored at controlled room temperature, between 15-30° C (59-86° F) and protected from light. DO NOT FREEZE. Should freezing occur in the vial Gadopentetate dimeglumine Injection should be brought to room temperature before use. If allowed to

stand at room temperature for a minimum of 90 minutes, Gadopentetate dimeglumine Injection should return to a clear, colorless to slightly yellow solution. Before use, examine the product to assure that all solids are redissolved and that the container and closure have not been damaged. Should solids persist, discard vial.

Manufactured for:

Bayer HealthCare Pharmaceuticals Inc.

Whippany, NJ 07981

Manufactured in Germany

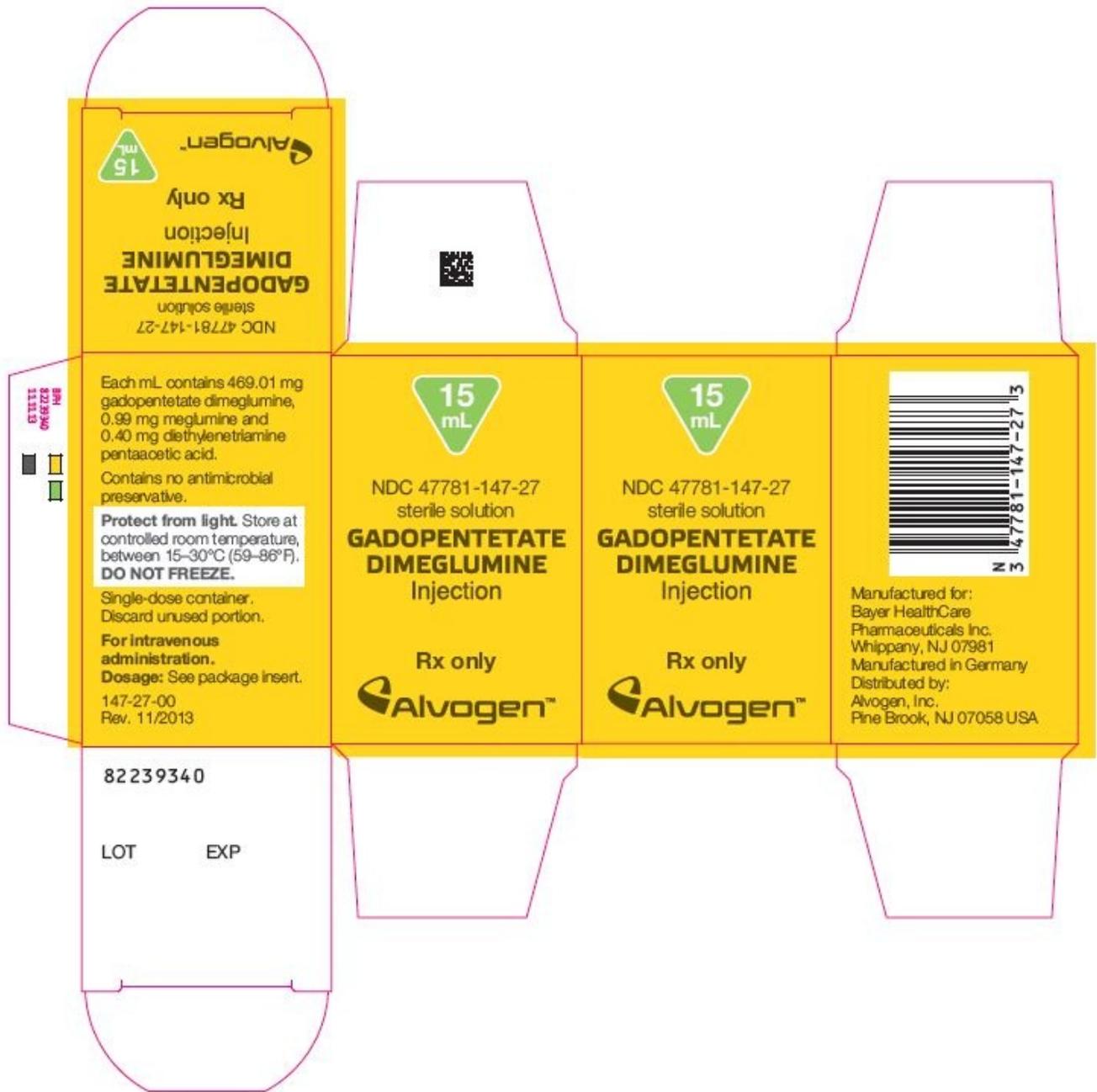
Distributed by:

Alvogen, Inc.

Pine Brook, NJ 07058 USA

Rev. 11/2013

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL



GADOPENTETATE DIMEGLUMINE

gadopentetate dimeglumine injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:47781-147
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
GADOPENTETATE DIMEGLUMINE (UNII: RH248G8V27) (GADOPENTETATE - UNII:V7OK6J19HQ)	GADOPENTETATE DIMEGLUMINE	469.01 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
MEGLUMINE (UNII: 6HG8UB2MUY)	0.99 mg in 1 mL
WATER (UNII: 059QF0K00R)	
PENTETIC ACID (UNII: 7A314HQM0I)	0.4 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:47781-147-29	20 in 1 BOX		
1		1 in 1 CARTON		
1		20 mL in 1 VIAL, SINGLE-DOSE		
2	NDC:47781-147-27	20 in 1 BOX		
2		20 in 1 CARTON		
2		15 mL in 1 VIAL, SINGLE-DOSE		
3	NDC:47781-147-22	20 in 1 BOX		
3		1 in 1 CARTON		
3		10 mL in 1 VIAL, SINGLE-DOSE		
4	NDC:47781-147-20	20 in 1 BOX		
4		1 in 1 CARTON		
4		5 mL in 1 VIAL, SINGLE-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA019596	02/24/2014	

Labeler - Alvogen, Inc (008057330)

Revised: 2/2014

Alvogen, Inc