Gadovist® 1.0
gadobutrol

Dosing Information*
One contrast agent for every age [1]

General Information

Recommended Dose: Recommended dosage with Gadovist® 1.0 depends on the indication[1].
Generally, a single injection of 0.1 mL/kg body weight (0.1 mmol/kg body weight) is sufficient to answer the clinical questions.[1]

Administration: Administer intravenously as a bolus, manually or by power injector. For brain perfusion studies the use of an autoinjector is recommended.

Maximum Single Dose per Injection: 0.3 mL/kg body weight may be administered at maximum.[1]

Special Populations

- **Pediatric Population (0-17 years of age):** 0.1 mL/kg for all indications[1]
- **Geriatric Population:** No dose adjustments are necessary.[1]
- **Hepatically or Renally Impaired (use with caution in renal impairment):** No dose adjustments are necessary.[1]

Body Weight (BW)		Volume (mL) for each Indication		
		General: CNS, breast, kidney, pediatric* (0-17 years old) Recommended Dose: 0.1 mL/kg BW	**MRA:** 1 Field of View Recommended Dose: 7.5 mL for <75 kg BW 10 mL for ≥75 kg BW	**MRA:** >1 Field of View Recommended Dose: 15 mL for <75 kg BW 20 mL for ≥75 kg BW
lb	kg			
4.4	2	0.2		
8.8	4	0.4		
13	6	0.6		
18	8	0.8		
22	10	1		
33	15	1.5		
66	30	3	7.5	15
88	40	4	7.5	15
110	50	5	7.5	15
132	60	6	7.5	15
154	70	7	7.5	15
176	80	8	10	20
198	90	9	10	20
220	100	10	10	20
242	110	11	10	20
264	120	12	10	20
286	130	13	10	20
308	140	14	10	20

*For children of all ages including term newborns, the recommended dose of GADOVIST 1.0 is 0.1 mL/kg body weight (corresponding to 0.1 mmol/kg body weight of gadobutrol) for all indications.

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gadobutrol

Indications and Usage

GADOVIST 1.0 (gadobutrol) is a medicinal product for diagnostic use only.

GADOVIST 1.0 (gadobutrol) is indicated in adults and children of all ages including term newborns for:

- Contrast enhancement during cranial and spinal MRI investigations and for contrast-enhanced magnetic resonance angiography (CE-MRA).
- Contrast enhanced MRI of the breast to assess the presence and extent of malignant breast disease, and MRI of the kidney.
- GADOVIST 1.0 is particularly suited for cases where the exclusion or demonstration of additional pathology may influence the choice of therapy or patient management, for detection of very small lesions and for visualization of tumors that do not readily take up contrast media.
- GADOVIST 1.0 is also suited for perfusion studies for the diagnosis of stroke, detection of focal cerebral ischemia and tumor perfusion.

Contraindications

Patients who have experienced a life-threatening reaction to GADOVIST 1.0 previously.[1]

Most Serious Warning and Precautions

Gadolinium-based contrast agents (GBCAs) increase the risk for Nephrogenic Systemic Fibrosis (NSF) in patients with:

- acute or chronic severe renal insufficiency (glomerular filtration rate <30 mL/min/1.73m^2), or
- acute renal failure / acute kidney injury

In these patients, avoid use of GBCAs unless the diagnostic information is essential and not available with noncontrast-enhanced magnetic resonance imaging (MRI). NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle, and internal organs. Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests. When administering a GBCA, do not exceed the recommended dose (see DOSAGE AND ADMINISTRATION – Recommended Dose and Dosage Adjustment in the Product Monograph) and allow a sufficient period of time for elimination of the agent from the body prior to any readministration. (See WARNINGS AND PRECAUTIONS – General, Renal and Skin, and ADVERSE REACTIONS – Postmarket Adverse Drug Reactions in the Product Monograph)[1]

ADVERSE REACTIONS

CLINICAL TRIALS: CNS Indications - The most common adverse events reported following administration of GADOVIST 1.0 for Central Nervous System (CNS) Indications were: headache (0.9%), vasodilatation (0.6%), nausea (0.5%), injection site pain (0.4%), dizziness (0.3%), rash (0.3%), and dyspnea (0.3%). These reactions were mild to moderate in severity. **MRA Indications** - Most common adverse events were thermal sensations (2.5%) and headache (1.1%). Less common adverse events reported following administration of GADOVIST 1.0 were nausea (0.9%) and vomiting, diarrhea, taste perversion and dizziness in 4 patients each (0.5%). All other events were observed in less than 0.5% of cases. **Pediatric Population** - In children less than 2 years of age, safety is available in 44 subjects. Only one subject (2.3%) experienced a drug-related adverse event (vomiting of mild intensity). Adverse events were reported in 18 subjects (40.9%), the maximum intensity was mild intensity in 13 subjects (29.5%), moderate intensity in 2 subjects (4.5%), and severe intensity serious adverse events in 3 subjects (6.8%; subdural empyema, respiratory failure, and infected cyst). In children from 2 to 17 years of age, most common adverse events were dysgeusia (1.4%) and feeling hot (1.4%). Less common adverse events considered as drug-related that were reported following administration of GADOVIST 1.0 in pediatric patients 0 to 17 years of age (182 subjects evaluated in Phase I/III studies) were: crystal urine (0.5%), headache (0.5%), nausea (0.5%), vomiting (0.5%), rash (0.5%), rash pruritic (0.5%) and pruritus (0.5%), occurring in one patient each; these were predominantly mild in severity. **OTHER CLINICAL TRIALS**: Subsequent to market introduction, additional data from clinical trials with GADOVIST 1.0 has become available. The overall safety profile of GADOVIST 1.0 is based on data from more than 6,300 patients in clinical trials. The most frequently observed adverse drug reactions (≥0.5 %) in patients receiving GADOVIST 1.0 are headache, nausea, and dizziness. Serious adverse drug reactions in patients receiving GADOVIST 1.0 are cardiac arrest, and severe anaphylactoid reactions.

Table – All Adverse Events Considered Drug-Related and Reported by <10% of Patients During Clinical Trials (N > 6,300)*

System Organ Class	Common (≥ 1% and < 10%)	Uncommon (≥ 0.1% and < 1%)	Rare (< 0.1%)
Cardiac disorders		--	tachycardia, palpitations
Gastrointestinal disorders	nausea	vomiting	dry mouth
General disorders and administration site conditions		injection site reaction[b], feeling hot	malaise, feeling cold
Immune system disorders		hypersensitivity / anaphylactoid reaction[ac] (eg, hypotension[c], urticaria, face edema, eyelid edema, flushing)	--
Nervous system disorders	headache	dizziness, dysgeusia, paresthesia	loss of consciousness[a], convulsion, parosmia
Respiratory, thoracic and mediastinal disorders		dyspnea[a]	--
Skin and subcutaneous tissue disorders		erythema pruritus (including generalized pruritus), rash (including generalized, macular, papular, pruritic rash)	--

*Adverse reactions are classified by MedDRA system organ classes (MedDRA SOCs). The most appropriate MedDRA term is used to describe a certain reaction and its synonyms and related conditions. ADR term representation is based on MedDRA version 12.1
a. There have been reports of life-threatening and/or fatal outcomes from this ADR
b. Injection site reactions (various kinds) comprise the following terms: Injection site extravasation, injection site burning, injection site coldness, injection site warmth, injection site erythema or rash, injection site pain, injection site hematoma
c. None of the individual symptom ADRs listed under hypersensitivity/anaphylactoid reaction identified in clinical trials reached a frequency greater than rare (except for urticaria)

References: 1. Gadovist® Product Monograph. Bayer Inc. March 5, 2018

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