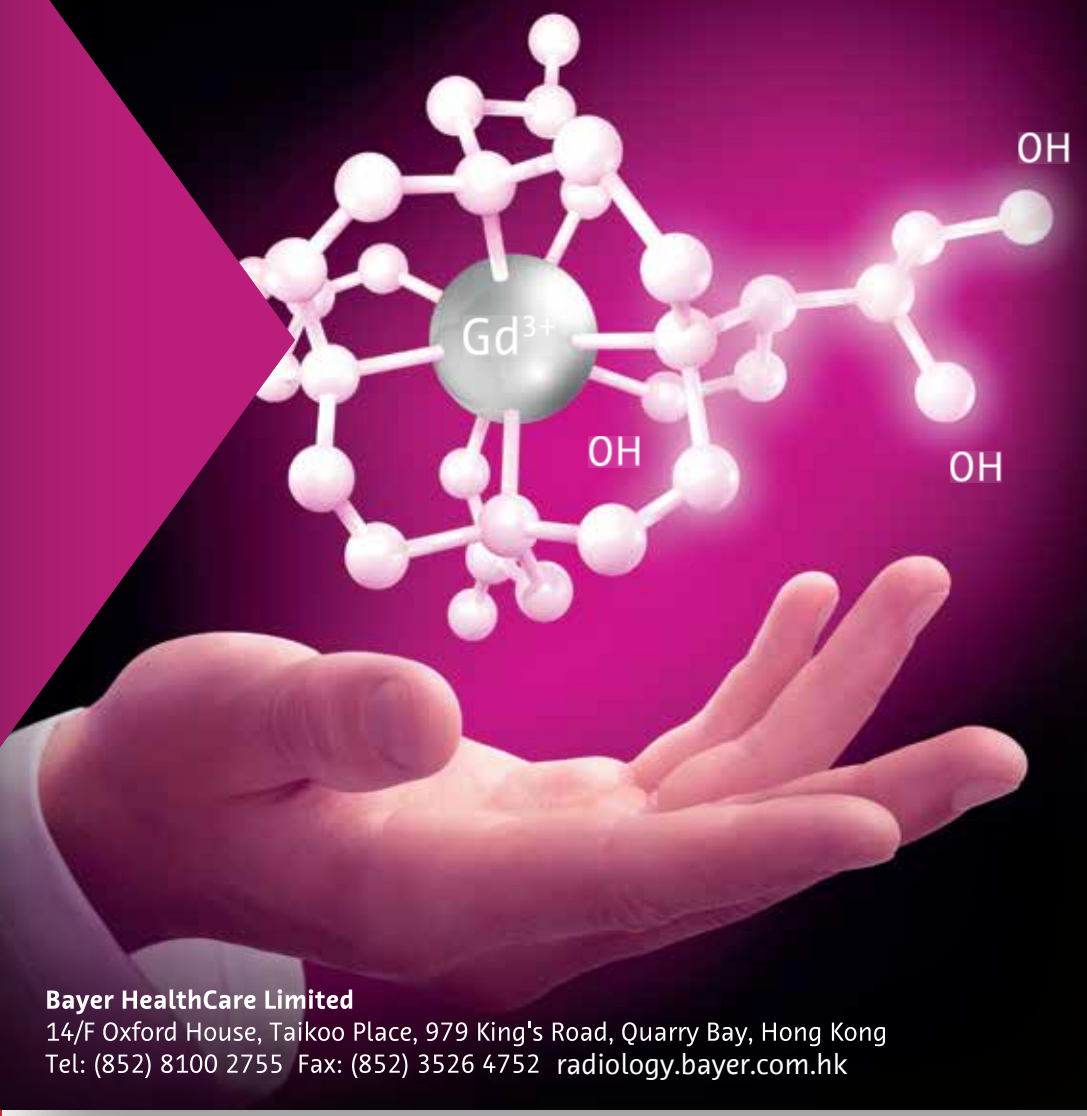

Clinical updates on

ESUR V.10.0 & ACR 2025

on Gadolinium -based contrast media

Latest ACR (2025) Guideline Version

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Clinical updates on ESUR V.10.0 & ACR 2025

Gadolinium Contrast Media

[E]ESUR Guidelines on Contrast Media Version 10.0; 2018 [A]ACR Manual Contrast Media 2025

CA: Contrast Agent; CM: Contrast Medium; GBCA: Gadolinium-Based Contrast Agent; ICM: Iodine-Based Contrast Media

Provided by

PP-PF-RAD-HK-0070-1

Acute Adverse Reactions - Classification

Definition: An adverse reaction which occurs within 1 hour of contrast agent injection.[E]

- The same acute adverse reactions are seen after ICM and GBCAs [E]
- The incidence is highest after ICM[E]

ESUR V.10.0

	Hypersensitivity / Allergy-like	Grade (Ring and Messmer classification	Chemotoxic
Mild	Mild urticaria Mild itching Erythema	Grade 1 Grade 1 Grade 1	Nausea/mild vomiting Warmth/chills Anxiety Vasovagal reaction which resolves spontaneously
Moderate	Marked urticaria Mild bronchospasm Facial / laryngeal edema	Grade 1 Grade 2 Grade 2	Vasovagal reaction
Severe	Hypotensive shock Respiratory arrest Cardiac arrest	Grade 3 Grade 4 Grade 4	Arrythmia Convulsion

ACR 2025

Allergic-like	Physiologic
Mild Signs and symptoms are self-limited without evidence of progression.	
Limited urticaria/pruritis Cutaneous edema Limited "itchy"/Scratchy" throat Nasal Congestion Sneezing/Conjunctivitis/rhinorrhea	Limited nausea / vomiting Transient flushing/ warmth / chills Headache / dizziness / anxiety / altered taste Mild hypertension Vasovagal reaction that resolves spontaneously
Moderate Signs and symptoms are more pronounced and commonly require medical management.	
Diffuse urticaria / pruritis Diffuse erythema, stable vital signs Facial edema without dyspnea Throat tightness or hoarseness without dyspnea Wheezing / bronchospasm, mild or no hypoxia	Protracted nausea/vomiting Hypertensive urgency Isolated chest pain Vasovagal reaction that requires and is responsive to treatement
Severe Signs and symptoms are often life-threatening and can result in permanent morbidity or death if not managed appropriately.	
Diffuse edema, or facial edema with dyspnea Diffuse erythema with hypotension Laryngeal edema with stridor and/or hypoxia Wheezing / bronchospasm, significant hypoxia Anaphylactic shock (hypotension + tachycardia)	Vasovagal reaction resistant to treatment Arrhythmia Convulsions, seizures Hypertensive emergency

GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Acute Adverse Reactions

Allergic-Like Reactions

Allergic-like reactions to GBCA manifest similarly to true allergic reactions seen with other drugs and allergens, but because an antigen-antibody response cannot be always identified, allergic-like contrast reactions are classified as “anaphylactoid”, “allergic-like”, or “idiosyncratic”. Allergic-like contrast reactions are likely independent of dose and concentration above a certain unknown threshold.

Physiologic Reactions

Physiologic reactions to GBCA likely relate to specific molecular attributes that lead to direct chemotoxicity, osmotoxicity (adverse effects due to hyperosmolality), or molecular binding to certain activators. Physiologic reactions are frequently dose and concentration dependent.

Incidence of Acute Adverse Reactions by GBCA

ESUR (V.10.0)

- The risk of a reaction is not related to the osmolality of the contrast agent: the low doses used make the osmolar load very small.
- There is no difference in the incidence of acute adverse reactions among the gadolinium-based extracellular agents.

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Renal Safety - Nephrogenic Systemic Fibrosis (NSF)

A diagnosis of NSF should only be made if the Yale NSF Registry clinical and histopathological criteria are met (J Am Acad Dermatol 2011; 65: 1095-1106) – ***ESUR V.10.0***

	Patient related factors	Contrast medium related factors
ESUR (V.10.0)	• Reduced renal function, particularly if eGFR < 15mL/min/1.73m^2 • Patients on dialysis.	• Gadodiamide was responsible for most reported NSF cases. • NSF also occurred after gadopentetate dimeglumine and gadoversetamide. • Risk increases with increasing CA dose, but NSF may occur after a single dose.
ACR 2025	• Patients with end-stage CKD (CKD5, eGFR < 15mL/min/1.73m^2) and severe CKD (CKD4, eGFR 15-29 mL/min/1.73m^2) after exposure to Group I GBCAs. • Patients with AKI • High dose and multiple exposures **Specific groups of patients:** *Patients with CKD 4or5 (eGFR<30mL/min/1.73m^2) not on chronic dialysis* • Group I agents are contraindicated in this setting. A group II agent should be used. *Patients with CKD 3 (eGFR 30 to 59mL/min/1.73 m^2)* • No special precautions are necessary *Patients with CKD 1or2 (eGFR 60 to 119mL/min/1.73m^2)* • Any GBCA can be administered safely to these patients *Patients with acute kidney injury (AKI)* • Group I agents should be avoided in patients with known or suspected AKI and a group II agent is preferred. *Children* • Group II agents should be used	• Patients receiving group I GBCAs should be considered at risk of developing NSF if any of the following conditions apply to the patient: √ On dialysis (of any form) √ Severe or end-stage CKD (CKD 4 or 5, eGFR < 30mL/min/1.73m^2) without dialysis √ AKI

Group I: Gadodiamide, Gadopentetate dimeglumine (Magnevist®), Gadoversetamide
Group II: Gadobenate dimeglumine, Gadobutrol (Gadovist®), Gadoterate acid, Gadoteridol
Group III: Gadoxetate disodium (Primovist®)

CA: Contrast Agent CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Renal Safety - Classification of Gd CM relative to NSF by ESUR

GADOLINIUM-BASED CONTRAST AGENTS:
Risk classification (based on laboratory data) and recommendations

Highest risk of NSF

Contrast agents

Gadodiamide
Ligand: Non-ionic linear chelate (DTPA-BMA)

Gadopentetate dimeglumine (Magnevist®)
Ligand: lonic linear chelate (DTPA)

Gadoversetamide
Ligand: Non-ionic linear chelate (DTPA-BMEA)

Recommendations

- European Medicines Agency (EMA) has suspended intravenous use of all high-risk agents (Gadodiamide, Magnevist®) and the Marketing Authorization Holder has withdrawn Gadoversetamide from the European market.
- EMA states that Magnevist® may be used for arthrography.
- CMSC supports these recommendations.

Renal Safety - Classification of Gd CM relative to NSF by ESUR

Intermediate risk of NSF

Contrast agents

Gadobenate dimeglumine
Ligand: lonic linear chelate (BOPTA)

Gadoxetate disodium (Primovist®, Eovist®)
Ligand: lonic linear chelate (EOB-DTPA)

Recommendations

- EMA states that intermediate risk agents (Gadobenate dimeglumine, Primovist®) are approved for hepato-biliary imaging only
- CMSC supports this recommendation.

Renal Safety - Classification of Gd CM relative to NSF by ESUR

Lowest risk of NSF

Contrast agents

Gadobutrol (Gadovist®, Gadavist®)
Ligand: Non-ionic cyclic chelate (BT-DO3A)

Gadoterate meglumine
Ligand: lonic cyclic chelate (DOTA)

Gadoteridol
Ligand: Non-ionic cyclic chelate (HP-DO3A)

Recommendations

- These agents should be used with CAUTION in patients with GFR < 30 ml/min. There should be at least 7 days between two injections.
- Pregnant women: these agents can be used to give essential diagnostic information.
- Lactating women: discarding the breast milk in the 24 hours after contrast medium is not considered necessary, but the patient can discuss with the doctor whether she wishes to do this.
- Laboratory testing of renal function (eGFR) is **not mandatory**

Recommendations for all patients

- Never deny a patient a clinically well-indicated enhanced MR-examination.
- In all patients use the smallest amount of contrast medium necessary for a diagnostic result.
- Always record the name and dose of the contrast agent used in the patient records.

Renal Safety - Classification of Gd CM relative to NSF by ACR

NEW

TABLE 1. ACR Manual Classification of Gadolinium-Based Agents Relative to Nephrogenic Systemic Fibrosis (NSF)

Group I: Agents associated with the greatest number of NSF cases:
- Gadodiamide (Omniscan® GE Healthcare)
- Gadopentetate dimeglumine (Magnevist® Bayer HealthCare Pharmaceuticals)
- Gadoversetamide (OptiMARK® Guerbet)

Group II: Agents associated with few, if any, unconfounded cases of NSF:
- Gadobenate dimeglumine (MultiHance® Bracco Diagnostics)
- Gadobutrol (Gadavist® Bayer HealthCare Pharmaceuticals; Gadovist® in many countries*)
- Gadoteric acid (Dotarem® Guerbet, Clariscan GE Healthcare)
- Gadoteridol (ProHance® Bracco Diagnostics)
- Gadopiclenol* (Elucirem® Guerbet, Vueway® Bracco Diagnostics)
- Gadoxetate disodium (Eovist® - Bayer HealthCare Pharmaceuticals registered in USA; Primovist® in many countries*)

Group III: Agents for which data remains limited regarding NSF risk, but for which few, if any unconfounded cases of NSF have been reported:
- No agents currently in this category (as of April 2024)

*As of January 2025, gadopiclenol's (Elucirem®- Guerbet, Vueway® - Bracco Diagnostics) NSF risk data in severe kidney disease patients is less established, leaving its classification as a group II or III agent to local discretion.

Reference:
1. ACR Manual on Contrast Media, 2025

*Gadovist® and Primovist® are registered trade names in Hong Kong and Macau

Renal Safety - Suggested Indications for Renal Function Assessment before Intravascular Administration of GBCAs

ESUR (V.10.0)

EMA has suspended intravenous use of all GBCAs with highest risk of NSF: Gadodiamide, Gadopentetate dimeglumine, Gadoversetamide

GBCAs with intermediate risk of NSF: Gadobenate dimeglumine, Gadoxetate disodium (Primovist®) are approved for hepato-biliary imaging only.

GBCAs with lowest risk of NSF: Gadobutrol (Gadovist®), Gadoterate meglumine, Gadoteridol

- Should be used with caution in patients with GFR < 30mL/min/1.73m^2, Pregnant and lactating women
- Laboratory testing of renal function (eGFR) is **not mandatory.**

ACR 2025

eGFR Evaluation of Renal Function to Group I or Group III GBCA Administration

Patient Condition	eGFR Requirement
Patient on dialysis (any type)	No eGFR required — eGFR is not helpful in this situation.
Patient with AKI	No eGFR required — eGFR is not helpful in this situation.
Inpatient	Obtain eGFR within 2 days of the MRI study.
Outpatient/ED with no prior eGFR at the time the MR exam is scheduled	If NO risk factors** , no eGFR required. WITH risk factors**, obtain eGFR.*
Outpatient/ED with most recent prior eGFR of 45 or above	If NO risk factor** and eGFR of 60 or above, no new eGFR required. WITH risk factors** and/or eGFR 45-59, if most recent prior eGFR is within 6 weeks of the MRI, no new eGFR is needed; otherwise obtain a new eGFR.*
Outpatient/ED with most recent prior eGFR of 44 or below	Obtain eGFR within 2 days of the MRI study

* If the new eGFR is to be obtained expressly for evaluation of suitability for administration of GBCA, obtaining the eGFR within 2 days of the MRI exam would avoid the situation where the new eGFR might be less than 45 and require another eGFR within two days of the MRI exam, as per the last line in the table.

** Risk Factors:
1. History of renal disease, including:
   a. Prior dialysis. b. Renal transplant. c. Single kidney. d. Kidney surgery. e. Renal cancer. f. History of CKD or prior history of AKI.
2. Diabetes mellitus (optional)

Calculating eGFR for adults
The recommended method for calculating eGFR for adults from the National Kidney Foundation is the 2021 CKD- EPI equations which use serum creatinine, age and sex. Race is not a variable in the calculation. The updated Schwartz equation should be used for children (also see Chapter on Contrast Media in Children).

EMA:European Medicines Agency; GBCA: Gadolinium-Based Contrast Agent

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Renal Safety - Patients on Dialysis

	ESUR (V.10.0)	ACR 2025
Patients on hemodialysis	**ICM** • Correlation of time of the CM injection with the hemodialysis session is **unnecessary.** • Extra hemodialysis session to remove CM is **unnecessary.** **GBCA** • Correlation of time of the CA injection with the hemodialysis session is recommended. • **Extra hemodialysis** session to remove CA **as soon as possible** after it has been administered is recommended.	**ICM** • Patients with anuric end-stage chronic kidney disease who do not have a functioning transplant can receive intravascular iodinated contrast medium without risk of further renal damage because their kidneys are no longer functioning. • However, there is a theoretical risk of converting an oliguric patient on dialysis to an anuric patient on dialysis by exposing him or her to intravascular iodinated contrast medium. (Inconclusive) • Therefore, patients undergoing dialysis who make more than 1-2 cups of urine/day (100 mL) should be considered nonanuric and treated as high-risk patients similar to patients with AKI or eGFR less than 30 mL/min/1.73m^2 who are not undergoing hemodialysis. • Patients should not have acute dialysis nor continuous renal replacement therapy initiated or alter their schedule solely based on iodinated contrast media administration regardless of renal function due to the risks, costs and lack of benefit **GBCA** • In patients with end-stage renal disease on chronic dialysis, injection of Group I agents is contraindicated. **Group II agent is recommended.** • Elective GBCA-enhanced MRI examinations be performed before regularly scheduled dialysis. • Due to the risks of catheter placement and infection, the possibility of worsening kidney function in patients with AKI and CKD, and the perceived very low risk of NSF from group II and III GBCM agents, dialysis should not be initiated or altered in patients receiving a group II GBCM (i.e. daily dialysis or multiple per-day dialysis sessions) # Peritoneal dialysis may provide less NSF risk reduction compared to hemodialysis, but this has not been adequately studied
Patients on continuous ambulatory peritoneal dialysis	**ICM** • Hemodialysis to remove the CM is **unnecessary.** **GBCA** • The need for hemodialysis should be discussed with the referring physician.	

Group I: Gadodiamide, Gadopentetate dimeglumine (Magnevist®), Gadoversetamide
Group II: Gadobenate dimeglumine, Gadobutrol (Gadovist®), Gadoterate acid, Gadoteridol

CA: Contrast Agent CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Patient Selection & Preparation Strategies Before CM Administration

Primary Considerations

Allergy [P]	• Patients with **a history of previous allergic-like/ unknown-type reaction** to CM → 8 times higher risk of developing acute adverse reactions for GBCAs → An approximately 5-fold increased risk of developing a future allergic-like reaction if exposed to the same class of CM again. → Greatest risk factor for predicting future adverse events • Patients with **unrelated allergies** are at a 2- to 3-fold increased risk of an allergic-like contrast reaction. → Patients with shellfish or povidone-iodine allergies are at no greater risk from ICM than are patients with other allergies. • **No cross-reactivity** between different classes of CM. (e.g GBCA v.s ICM)
Asthma [P]	• A history of **asthma increases the likelihood** of an allergic-like contrast reaction. → Patients with asthma may be more prone to develop **bronchospasm**. Due to the modest increased risk, restricting contrast medium use or premedicating solely on the basis of a history of asthma is not recommended.
Renal Insufficiency	• **Renal Function Assessment** should be available/ obtained before the injection of CM in all patients considered at risk for CIN and NSF.
Cardiac Status [P]	• **Patients with severe cardiac disease** may be at increased risk of a **non-allergic cardiac event** if a contrast reaction occurs. → These include symptomatic patients and also patients with severe aortic stenosis, cardiac arrhythmias, primary pulmonary hypertension, or severe but compensated cardiomyopathy.
Anxiety	• Contrast reactions are **more common in anxious patients**. → Reassuring an anxious patient before CM injection may mitigate the likelihood of a mild contrast reaction.

[P] Due to the modest increased risk, restricting contrast medium use or premedicating solely on the basis of a medical history is not recommended.
CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

NEW

Patient Selection & Preparation Strategies Before CM Administration

Other Historical and Pre-Procedure Considerations

Age and Gender [P]	• Infants, neonates, children, and the elderly < middle-aged patients; Females > males [A] • For pediatric populations, off-label use of Ferumoxytol as an MRI contrast agent is growing. Benefits include prolonged blood pool phase and delayed intracellular uptake, allowing use as a pure intravascular contrast medium.[A]
Beta-Blockers [P]	• The use of ß-blockers **lowers the threshold for contrast reactions, increases the severity of contrast reactions**, and **reduces the responsiveness of treatment with epinephrine**. [A] → Patients on ß-blocker therapy **do not need to discontinue** their medication(s) prior to CM administration.[A] • ß-blockers may impair the management of bronchospasm and the response to adrenaline.[E]
Sickle-Cell Trait/Disease [P]	• CM exposure to patients with sickle cell trait /disease might **increase the risk of an acute sickle crisis**. → No evidence this occurs with modern ICM (LOCM/IOCM) or GBCAs. [A] → Hydrate patients before CM administration [E]
Pheochromocytoma [P]	• **No evidence** that IV administration of modern ICM or GBCA increases the risk of hypertensive crisis in patients with pheochromocytoma.[A]
Myasthenia Gravis [P]	• There is **a questionable relationship** between IV ICM and exacerbations of myasthenic symptoms in patients with myasthenia gravis.[A] → It is **controversial** if ICM should be considered a relative contraindication in patients with myasthenia gravis[A]
Hyperthyroidism [P]	• Patients with a history of **hyperthyroidism can develop thyrotoxicosis** after exposure to ICM, but this complication is rare. [A] Two special situations may affect this: → In patients with **acute thyroid storm**, ICM exposure can potentiate thyrotoxicosis - **ICM should be avoided.** → In patients considering **radioactive iodine therapy / undergoing radioactive iodine imaging of the thyroid gland**, administration of ICM can interfere with uptake of the treatment and diagnostic dose. √ If ICM was administrated, **a washout period** is suggested to minimize this interaction: Hyperthyroidism: 3-4 weeks v.s Hypothyroidism: 6 weeks

[P] Due to the modest increased risk, restricting contrast medium use or premedicating solely on the basis of a medical history is not recommended,
CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

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Good Clinical Practice

Good Clinical Practice

Good Clinical Practice - Premedication

NEW

ESUR (V.10.0) & ACR 2025

ESUR:

Premedication is not recommended because there is not good evidence of its effectiveness.

ACR:

- For patients with mild immediate ICM hypersensitivity, premedication is not recommended; switching the contrast agent is advised if the inciting agent is known and feasible.
- For patients with severe immediate ICM hypersensitivity, consider alternative imaging first. If none are acceptable, premedication and switching the contrast agent are recommended.
- No premedication is necessary for patients with prior chemotoxic reactions or isolated shellfish or iodine allergies, including topical povidone-iodine.

Indications for Premedication by ACR 2025

12- or 13-hour oral premedication	1. Outpatient with a prior allergic-like or unknown-type contrast reaction to the of CM (e.g Iodinated – iodinated). 2. Emergency department patient or inpatient with a prior allergic-like or unknown-type contrast reaction to the same class of CM in whom the use of premedication is not anticipated to adversely delay care decisions or treatment.
Accelerated IV premedication	1. Outpatient with a prior allergic-like or unknown-type contrast reaction to the same class of CM who has arrived for a contrast-enhanced examination but has not been premedicated and whose examination cannot be easily rescheduled. 2. Emergency department patient or inpatient with a prior allergic-like or unknown-type contrast reaction to the same class of CM in whom the use of 12-or 13-hour premedication is anticipated to adversely delay care decisions or treatment.

CM: Contrast Medium

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Wang C, Ramsey A, Lang D, Maria Copaescu A, Krishnan P, Kuruvilla M, Mervak B, Newhouse J, Sumkin A, Saff R.
Management and Prevention of Hypersensitivity Reactions to Radiocontrast Media: A Consensus Statement from the American College of Radiology and the American Academy of Allergy, Asthma & Immunology. Radiology. 2025 May;315(2):e240100. doi: 10.1148/radiol.240100. PMID: 40326871.

Good Clinical Practice - Premedication

Specific Recommended Premedication Regimens by ACR 2025

Oral Premedication

Corticosteroids (Any of the following)	1) Prednisone-based: 50mg orally, at 13h, 7h and 1h before CM administration *Hydrocortisone: 200 mg IV for each dose of oral prednisone
+	2) Methylprednisolone-based: 32 mg orally, 12h and 2h before CM administration
Antihistamine (Optional)	Diphenhydramine: 50 mg intravenously/intramuscularly/orally 1h before CM administration

IV Premedication

(*in decreasing order of desirability*)

- Methylprednisolone sodium succinate 40 mg IV or hydrocortisone sodium succinate 200 mg IV immediately, and then every 4 hours until CM administration, plus diphenhydramine 50 mg IV 1 hour before CM administration.
  This regimen usually is 4-5 hours in duration.

- Dexamethasone sodium sulfate 7.5 mg IV immediately, and then every 4 hours until CM administration, plus diphenhydramine 50 mg IV 1 hour before CM administration.
  This regimen may be useful in patients with an allergy to methylprednisolone and is also usually 4-5 hours in duration.

- Methylprednisolone sodium succinate 40 mg IV or hydrocortisone sodium succinate 200 mg IV, plus diphenhydramine 50 mg IV, each 1 hour before CM administration.
  This regimen, and all other regimens with a duration less than 4-5 hours, has no evidence of efficacy. It may be considered in emergent situations when there are no alternatives.

Note: Premedication regimens less than 4-5 hours in duration (oral or IV) have not been shown to be effective.
CM: Contrast Medium

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ACR Manual on Contrast Media 2025

Good Clinical Practice - CM Extravasation

ESUR (V.10.0) & ACR 2025	
Technique-related risk factors	• Use of a power injector. • Less optimal injection sites including lower limb and small distal veins. • Large volume of CM. • Injections are made into more peripherally placed catheters [A] • High-osmolar CM. • More viscous contrast media.
Patient-related risk factors	• Inability to communicate. • Severely ill or debilitated patients [A] • Patients with abnormal circulation in the limb to be injected [A] • Fragile or damaged veins. • Arterial insufficiency. • Injection through indwelling peripheral intravenous lines (placed for more than 24 hours) and multiple punctures into the same vein[A] • Compromised lymphatic and/or venous drainage. • Obesity.
To reduce the risk	• Intravenous technique should always be meticulous using appropriate sized plastic cannula placed in a suitable vein to handle the flow rate used during the injection. • Consider use of cannulas with sideholes. • Test injection with normal saline. • Use non-ionic ICM.
Management	• Conservative management is adequate in most cases • Limb elevation (Elevation of the affected extremity above the level of the heart to decrease capillary hydrostatic pressure and thereby promote resorption of extravasated fluid is recommended) • Ice packs: Helpful for relieving pain at the injection site * many surgeons recommend initial use of cold compresses [A] • Warm compresses: Helpful in improving absorption of the extravasation as well as in improving blood flow, particularly distal to the site. [A] • Careful monitoring: If a serious injury is suspected, seek the advice of a surgeon. • Consider less viscous contrast media or pre-warm to human body temperature.
Update in ACR 2022 Chapter 7 Extravasation of Contrast Media	• Evidence based update on extravasation recommendations and strength of evidence. • The focus on the cause of extravasation in terms of choice of iodinated contrast media has shifted from osmolality to viscosity. • ACR 2022 covers various aspects of extravasation in a Q&A format with levels of evidence.

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Good Clinical Practice – Waiting time between contrast media injection for repeat scans

NEW

Patient Condition	Iodine-Based Contrast Media (ICM)	Gadolinium-Based Contrast Agents (GBCA)	Combined Imaging (ICM + GBCA)	Additional comments
Normal Renal Function (eGFR > 60)	12 hours (optimally)	12 hours (optimally)	6 hours (optimally)	The effects of ICM are longer-lived and more disturbing on subsequent contrast-enhanced MRI than the effects of GBCA in contrast-enhanced CT. Therefore, it is better to schedule MRI with GBCA before CT with ICM when combining studies. Only for renal imaging CT (including CT urography) is best performed before MRI because kidneys will concentrate GBCA, so that the enhancement of the renal collecting systems, ureters, and bladder may last considerably longer, with risk of misdiagnosis.
	4 hours (minimally)	4 hours (minimally)	2 hours (minimally)	
Moderately Reduced Renal Function (eGFR 30-60)	48 hours (optimally)	48 hours (optimally)	48 hours (optimally)	
	16 hours (minimally)	16 hours (minimally)	16 hours (minimally)	
Severely Reduced Renal Function (eGFR < 30)	7 days (optimally)	7 days (optimally)	7 days (optimally)	
	2.5 days (minimally)	2.5 days (minimally)	2.5 days (minimally)	

*In emergency or life-threatening situations, employ less waiting time between successive a) iodine-based contrast media administrations or b) gadolinium-based contrast agent administrations. Not enough evidence for combined scans

Van Der Molen, A. J., Dekkers, I. A., Geenen, R. W. F., Bellin, M., Bertolotto, M., Brismar, T. B., Correas, J., Heinz-Peer, G., Mahnken, A. H., Quattrocchi, C. C., Radbruch, A., Reimer, P., Roditi, G., Romanini, L., Sebastià, C., Stacul, F., & Clement, O. (2023). Waiting times between examinations with intravascularly administered contrast media: a review of contrast media pharmacokinetics and updated ESUR Contrast Media Safety Committee guidelines. European Radiology, 34(4), 2512–2523. https://doi.org/10.1007/s00330-023-10085-5

Good Clinical Practice - CM in Pregnancy and Lactation

NEW

ESUR (V.10.0) ACR 2025	ICM	GBCAs
Pregnancy	In exceptional circumstances, when radiographic examination is essential, **ICM may be given to the pregnant female.** [EA]	When there is a very strong indication for enhanced MR, the smallest possible dose of **a macro-cyclic GBCA** (Agents with lowest risk of NSF) **may be given to the pregnant female.** [EA] ACR 2022 Updated in Chapter 15: • Newly added **"Gadolinium Pregnancy Screening Statement"** • Recommends **avoidance of routine administration of GBCAs to pregnant patients**. • A decision to administer GBCAs to a pregnant woman should only be made when there is the **potential for significant clinical benefit that outweighs the unknown risk of fetal exposure** and should be the product of discussion that involves the referring provider and patient.[A]
Testing for the Neonates	Following administration of ICM to the mother during preg+ nancy, **thyroid function** should be **checked in the neonate during the first week.** [E]	Following administration of GBCAs to the mother during pregnancy, **no neonatal tests are necessary.** [E]
Lactation	• **Breast feeding may be continued normally** when ICMs are given to the mother. [EA] • If the mother remains concerned about breast feed the infant after ICM administration: she may abstain from breast-feeding from the time of contrast administration for a period of 12 to 24 hours. [A] • **The available data suggests that it is safe for the mother and infant to continue breast-feeding after receiving ICM, stopping breastfeeding for 24 hours after maternal IV or IA exposure to iodinated contrast material is not required and recommended patients make an informed decision on managing breastmilk after exposure to iodinated contrast material.** [A] • Routine thyroid function testing is not recommended due to no strong data exists in the literature. [A]	• **Breast feeding may be continued normally** when macrocyclic GBCAs are given to the mother. [EA] • If the mother remains concerned about breast feed the infant after ICM administration: she may abstain from breast-feeding from the time of contrast administration for a period of 12 to 24 hours. [A] • **The available data suggests that it is safe for the mother and infant to continue breast-feeding after receiving macrocyclic GBCAs, stopping breastfeeding for 24 hours after maternal IV or IA exposure to gadolinium-based contrast is not required.** [A]

ESUR (V.10.0) ACR 2025	ICM	GBCAs
Pregnant or lactating mother with renal impairment	• Mother- refers to renal adverse reactions • **No additional precautions** are necessary **for the fetus or neonate**	**Do not administer GBCAs** [E]

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media
*Please always consult local hospital/center guidelines to make informed decisions.

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Recommedations from ESUR (V.10.0) & ACR 2025

To reduce the risk of contrast reactions	
For all patients	• Use a non-ionic CM.
For patients at increased risk of reaction	• Consider an altemative test not requiring an iodine-based contrast agent. • Use a different iodine-based agent for previous reactors to CM.
For patient with previous moderate or severe allergic-like reactions to a specific gadolinium based contrast media (GBCM)	• It may be prudent to use a different GBCM and premedicate for subsequent MR examinations
Methods of preventing contrast reactions	
Hydration	• Patients with impaired renal function. • Elderly patients, patients with reduced general conditions.
Warming CM	• Reduces their viscosity and may make the injection more comfortable for the patient. • GBCAs are administered at room temperature (15 to 30˚C) and according to package inserts, **should not** be externally warmed for routine clinical applications. [A]
Not Recommended	
Pretesting[A]	Intradermal skin testing with CM to predict the likelihood of adverse reactions has not been shown to be useful in minimizing reaction risk.
Fasting[E]	Fasting is not recommended before administration of low-or iso-osmolar non-ionic iodine-based CM or of gadolinium-based agents.

CM: Contrast Medium

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Gadolinium Retention in the Brain

ESUR (V.10.0) & ACR 2025	
Detection	• Seen as regions of increased signal intensity in the deep brain nuclei on unenhanced T1-weighed MR-images. • The association between these appearances and GBCAs was first noted in 2014.
Characteristics	• The signal intensity changes are not specific and may occur after manganese, iron, calcium etc. • MR is less sensitive for detecting gadolinium in the brain than tissue analysis after biopsy. • It is not known whether the deposited gadolinium is chelated. • No neurological symptoms have yet been reported. • The clinical significance of these changes is not yet known. • All studies have been retrospective. • Occurs independent of renal function.
Relation to gadolinium -based agents	• High signal intensity in the deep brain nuclei on MRI has been reported after all linear GBCAs, but not after macrocyclic agents. • Analysis of brain tissue has detected gadolinium after all GBCAs, with the highest levels of gadolinium in patients who had linear chelates and the lowest levels in those who had macrocyclic agents. • The greater the previous cumulative dose of the GBCAs, the more widespread are the areas of increased signal intensity. • Only occurs after multiple doses.

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

U.S. Food and Drug administration (FDA)

- On Sept 8, 2017, the U.S. FDA Medical Imaging Drugs Advisory Committee (MIDAC) met for a scientific discussion of the GBCA drug class and the presence of Gd in the brain and other organs.

- **Suggestions from MIDAC:**
  - class warning for potential risk of Gd presence in the prescribing information for all GBCAs
  - risk minimization steps for certain patient populations e.g. patients who receive multiple MRIs
  - collaboration with regulators and the academic community to design and conduct additional non-clinical and clinical studies
    - These studies would be used to inform the FDA's decisions about the need for further regulatory actions

FDA/EU Decision on MR Contrast Media

EMA - EC Final Decision

- Nov 23, 2017, EC Final Decision: Adoption of the CHMP Opinion with one minor amendment:
  - Option to defer the suspension of respective products for up to 12 months on the basis of potential unmet medical need & considering the availability of suitable alternatives.

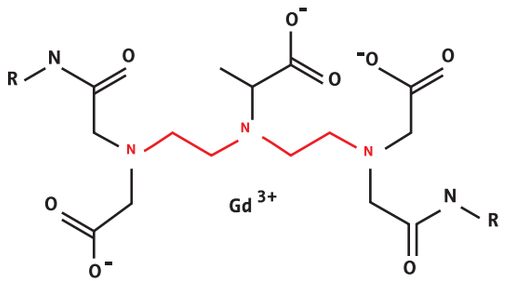
- **Suspend** the marketing authorizations of **multi-purpose linear GBCAs (Gadodiamide, Gadoversetamide, Magnevist, Gadobenate dimeglumine with limited indicatlon for liver imaging only)**

- **Continue to** use **macrocyclic (Gadovist, gadoteridol, gadoterate meglumine)** and special linear GBCAs (liver-specific Primovist, Magnevist 2 mmol/L intra-articular, gadobenate dimeglumine liver imaging only)

Linear GBCAs

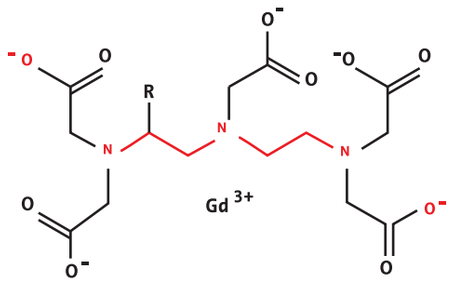
Non-ionic

(Gadodiamide, Gadoversetamide)



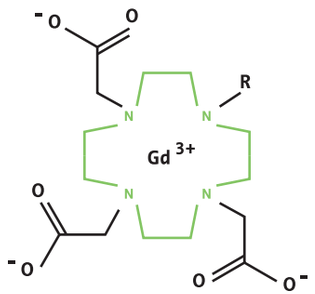
Ionic

(Magnevist®, Gadobenate dimeglumine, Primovist®)



Macrocyclic GBCAs

(Gadovist®, Gadoteridol, Gadoterate meglumine)



FDA/EU Decision on MR Contrast Media

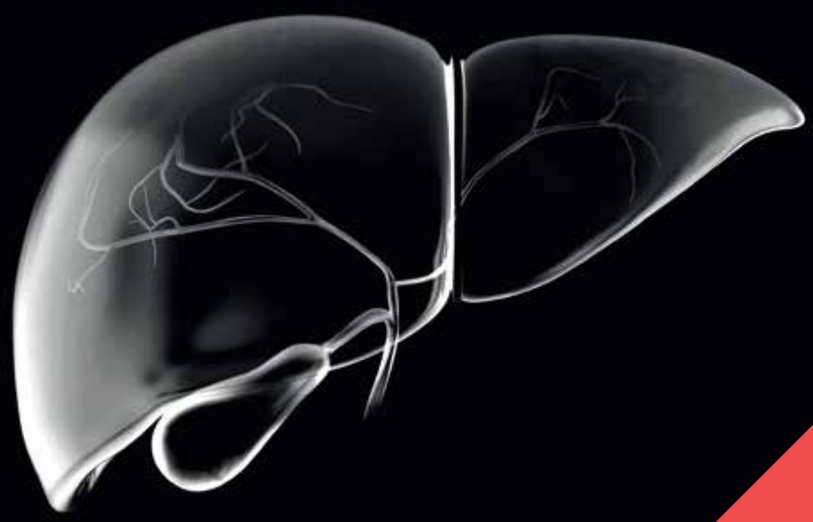
Primovist®

Gadoxetic Acid

Updated Gadoxetate disodium (Bayer Primovist® - Liver specific MRI contrast) from NSF Risk Group III to Group II

Liver-specific MRI contrast offers high sensitivity and specificity on early diagnosis of liver lesions

- Good detection, delineation and characterization, especially of small liver lesions (< 1 cm)[1]
- Good tolerability[2]
- Superior liver imaging as compared to CT[2]
- High rate of correct diagnosis[1]
- Recommended as 1st line diagnostic tools for Hepatocelluar Carcinoma (HCC) at APASL 2017 guideline[3]
- Has a low Gadolinium dose, high stability and relaxivity for patient safety and excellent image quality[4,5,6]



References:

1. Halavaara J. et al, Comput Assist Tomogr 2006; 30:345-354 **2.** Hammersting R. et al, Eur Radiol 2008; 18:457-467 **3.** Omata M, et al, Hepatol Int 2017 Jul; 11(4):317-370
4. Frenzel T et al. Invest Radiol 2008; 43:817-828 **5.** Rohrer M et al. Invest Radiol 2005; 40(11):715-24 **6.** Shen Y et al. Invest Radiol 2015; 50(5):330-338

For further details of products, please refer to the product's individual full prescribing information.

Primovist® 0.25 mmol / mL, solution for injection, prefilled syringe (gadoxetate disodium). Prescribing Information (Refer to Full Summary of Product Characteristics (SmPC) before prescribing). Presentation: Each mL solution for injection contains 181.43 mg / mL gadoxetate disodium. Indication: Detection of focal liver lesions and providing information on the character of lesions in T1-weighted magnetic resonance imaging (MRI). Posology and method of administration: Primovist is a ready-to-use aqueous solution to be administered undiluted as an intravenous bolus injection at a flow rate of about 2 ml/sec. After the injection of the contrast medium, the intravenous cannula / line should be flushed using sterile 9 mg/ml (0.9 %) saline solution. Recommended doses are: The lowest dose that provides sufficient enhancement for diagnostic purposes should be used. The dose should be calculated based on the patient's body weight and should not exceed the recommended dose per kilogram of body weight detailed in this section. The recommended dose of Primovist is: Adults 0.1ml per kg body weight Primovist. Repeated use No clinical information is available about repeated use of Primovist. Additional information on special populations • Impaired renal function Use of Primovist should be avoided in patients with severe renal impairment (GFR < 30 ml/min/1.73m2) and in patients in the perioperative liver transplantation period unless the diagnostic information is essential and not available with non-contrast enhanced MRI. If use of Primovist cannot be avoided, the dose should not exceed 0.025 mmol/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, Primovist injections should not be repeated unless the interval between injections is at least 7 days. • Patients with hepatic impairment: No dosage adjustment is necessary. • Paediatric population: The safety and efficacy of Primovist have not been established in patients under 18 years old. Therefore, use of Primovist in this patient group cannot be recommended. • Elderly population (aged 65 years and above) No dosage adjustment is considered necessary. Caution should be exercised in elderly patients. Contraindications: Hypersensitivity to active substance or to any excipients. Warnings and precautions: It is recommended to screen all patients for renal dysfunction by obtaining laboratory tests, particularly patients over 65 years. Nephrogenic systemic fibrosis (NSF) has been reported with some gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment (GFR < 30 mL / min / 1.73 m2); Patients undergoing liver transplantation are at particular risk since incidence of acute renal failure is high in this group. Use should be avoided in patients with severe renal impairment and in patients in perioperative liver transplantation period unless diagnostic information is essential and not available with non-contrast enhanced MRI. Haemodialysis shortly after Primovist® administration may be useful at removing Primovist® from the body. There is no evidence to support initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis. Use with caution in patients: with severe cardiovascular problems; with, or with a family history of, congenital long QT syndrome; with drugs known to prolong cardiac repolarisation, particularly in patients with previous arrhythmias. Should not be used in patients with uncorrected hypokalaemia. Primovist® may cause transient QT prolongation. Allergy-like reactions, including shock, reported rarely. Patients with a history of allergic disorders or bronchial asthma or who have previously reacted to contrast media are at higher risk of hypersensitivity reactions. Most reactions occur within 30 minutes of administration but rarely delayed reactions may occur after hours to days. Appropriate drugs and instruments for treatment of hypersensitivity must be readily available. Hypersensitivity reactions can be more intense in patients on beta-blockers, particularly in patients with asthma. Patients taking beta-blockers who experience hypersensitivity may be resistant to treatment effects of beta-agonists. If hypersensitivity reactions occur, stop injection immediately. Do not administer intramuscularly due to risk of local intolerance reactions including focal necrosis. Consider the sodium content (11.7 mg / mL) for patients on controlled sodium diet. Interactions: As transport of gadoxetate to the liver may be mediated by OATP transporters, it cannot be excluded that potent OATP inhibitors could cause drug interactions reducing the hepatic contrast effect. However, no clinical data have been presented to support that theory. An interaction study in healthy subjects demonstrated that the co-administration of erythromycin did not influence efficacy and pharmacokinetics of Primovist. No further clinical interaction studies with other medicinal products have been performed. • Interference from elevated bilirubin or ferritin levels in patients Elevated levels of bilirubin or ferritin can reduce the hepatic contrast effect of Primovist.• Interference with diagnostic tests Serum iron determination using complexometric methods (e.g. Ferrocine complexation method) may result in false values for up to 24 hours after the examination with Primovist because of the free complexing agent contained in the contrast medium solution. Pregnancy,lactation and fertility • Pregnancy There are no data from the use of gadoxetate in pregnant women. Animal studies have shown reproductive toxicity at repeated high doses. Primovist should not be used during pregnancy unless the clinical condition of the woman requires use of gadoxetate. • Breast-feeding Gadolinium containing contrast agents are excreted into breast milk in very small amounts. At clinical doses, no effects on the infant are anticipated due to the small amount excreted in milk and poor absorption from the gut. Continuing or discontinuing breast feeding for a period of 24 hours after administration of Primovist, should be at the discretion of the doctor and lactating mother. • Fertility Animal studies did not indicate impairment of fertility. Undesirable effects: (please refer to the Contraindications and the Warnings and Precautions sections). Usually mild to moderate and transient. The most serious adverse reaction is anaphylactoid shock. Delayed allergoid reactions (hours later up to several days) are rare. Common: Headache, nausea. Uncommon: Vertigo, dizziness, dysgeusia, paraesthesia, parosmia, increased blood pressure, flushing, dyspnea*, respiratory distress, vomiting, dry mouth, rash, pruritus, back pain, chest pain, injection site reactions, feeling hot, chills, fatigue, feeling abnormal. Rare: Tremor, akathisia, bundle branch block, palpitation, maculopapular rash, hyperhidrosis, malaise. Additionally, altered laboratory tests and transient QT prolongation were reported. Frequency not known: Hypersensitivity/anaphylactoid reaction (including shock*, hypotension, pharyngolaryngeal edema, oedema, urticaria, face edema, rhinitis, conjunctivitis, abdominal pain, hypoesthesia, sneezing, cough, pallor), tachycardia and restlessness.*Life-threatening and / or fatal cases have been reported post marketing. Prescribers should consult the SmPC in relation to other side effects. Overdose No cases of overdose have been reported and no symptoms could be characterised. Single doses of Primovist as high as 0.4 ml/kg (0.1mmol/kg) body weight were tolerated well. In a limited number of patients, a dose of 2.0 ml/kg (0.5 mmol/kg) body weight was tested in clinical trials, more frequent occurrences of adverse events but no new undesirable effects were found in these patients. In the event of excessive inadvertent overdose, the patient should be carefully observed including cardiac monitoring. In this case induction of QT prolongations is possible (see section 5.3). Primovist can be removed by hemodialysis. However there is no evidence that haemodialysis is suitable for prevention of nephrogenic systemic fibrosis (NSF). Reporting of suspected adverse reactions: Adverse events can be reported to drugsafety.hk@bayer.com. Date of revision of text: June 2024. Please note: For current prescribing information refer to the package insert and / or contact Bayer HealthCare Limited. 14/F, Oxford House, Taikoo Place, 979 King's Road, Quarry Bay, Hong Kong.

Gadovist® 1.0

Gadobutrol

Whole Body MRI with Gadovist® Offers:

- Macrocyclic compound = Highest stability for safety[1]
- Highest T1-shortening resulting in excellent image quality = Highest Diagnostic efficacy[2,3]
- Approved for Whole Body Indication[4,5]
- Approved for All Age Group include pediatrics from Age 0[5]

References:

1. Balzer JO et al. Eur Radiol 2003; 13(9): 2067-2074 **2.** Rohrer M et al. Invest Radiol. 2005; 40(11):715-724
3. Port M, Corot C, Violas X. et al. 2005;40(9):565-573 **4.** Gadovist® Whole Body Brochure. BHC Hong Kong 2019.(PP-GAD-CN-0181-1)
5. Gadovist® Product Insert. BHC Hong Kong 2019. (Version July 2019)

For further details of products, please refer to the product's individual full prescribing information.

Gadovist® 1.0 mmol / mL solution for injection. Composition: 1 mL solution for injection contains 604.72 mg gadobutrol (equiv. 1.0 mmol gadobutrol containing 157.25 mg gadolinium) as active ingredient. Excipient with known effect: 1 mL contains 0.00056 mmol (equivalent to 0.013 mg) of sodium. Indications: For diagnostic use only. Gadovist® is indicated in adults and children of all ages (including term neonates) for: 1.) Contrast enhancement in cranial and spinal magnetic resonance imaging (MRI); 2.) Contrast-enhanced MRI of liver or kidneys in patients with high suspicion or evidence of having focal lesions to classify these lesions as benign or malignant; 3.) Contrast enhancement in MR angiography; 4.) MR imaging of pathologies of the whole body. Gadovist® facilitates visualisation of abnormal structures or lesions and helps in the differentiation between healthy and pathological tissue. Gadovist® should be used only when diagnostic information is essential and not available with unenhanced magnetic resonance imaging (MRI). Posology: Gadovist® should only be administered by healthcare professionals experienced in the field of clinical MRI practice. The lowest dose that provides sufficient enhancement for diagnostic purposes should be used. The dose should be calculated based on the patient's body weight, and should not exceed the recommended dose per kilogram of body weight detailed in this section. Gadovist® is for intravenous administration only. Contraindications: Hypersensitivity to the active substance or any of the excipients. Special warnings and precautions for use: While injecting Gadovist® into veins with a small lumen there is the possibility of adverse effects such as reddening and swelling. The usual safety requirements for MRI, especially the exclusion of ferromagnetic materials, also apply when using Gadovist®. Hypersensitivity reactions: As with other intravenous contrast agents, Gadovist® can be associated with anaphylactoid / hypersensitivity or other idiosyncratic reactions, characterized by cardiovascular, respiratory or cutaneous manifestations, and ranging to severe reactions including shock. In general, patients with cardiovascular disease are more susceptible to serious or even fatal outcomes of severe hypersensitivity reactions. The risk of hypersensitivity reactions may be higher in case of 1.) previous reaction to contrast media; 2.) history of bronchial asthma; 3.) history of allergic disorders. In patients with an allergic disposition the decision to use Gadovist® must be made after particularly careful evaluation of the risk-benefit ratio. Most of these reactions occur within half an hour of administration. Therefore, post-procedure observation of the patient is recommended. Medication for the treatment of hypersensitivity reactions as well as preparedness for institution of emergency measures are necessary. Delayed reactions (after hours up to several days) have been rarely observed. Impaired renal function: Prior to administration of Gadovist® it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests. There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of some gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment (GFR < 30 mL / min / 1.73 m²). Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. As there is a possibility that NSF may occur with Gadovist®, it should therefore only be used in patients with severe renal impairment and in patients in the perioperative liver transplantation period after careful risk / benefit assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI. Haemodialysis shortly after Gadovist® administration may be useful at removing Gadovist® from the body. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis. Neonates and infants: Due to immature renal function in neonates up to 4 weeks of age and infants up to 1 year of age, Gadovist® should only be used in these patients after careful consideration. Elderly: As the renal clearance of Gadovist® may be impaired in the elderly, it is particularly important to screen patients aged 65 years and older for renal dysfunction. Seizure disorders: Like with other gadolinium containing contrast agents special precaution is necessary in patients with a low threshold for seizures. Pregnancy and lactation: There are no data from the use of Gadovist® in pregnant women. Gadovist® should not be used during pregnancy unless the clinical condition of the woman requires use of Gadovist®. Continuing or discontinuing of breast feeding for a period of 24 hours after administration of Gadovist®, should be at the discretion of the doctor and lactating mother. Undesirable effects: The overall safety profile of Gadovist® is based on data from more than 6,300 patients in clinical trials and from post-marketing surveillance. The most frequently observed adverse drug reactions (≥ 0.5 %) in patients receiving Gadovist® are headache, nausea and dizziness. The most serious adverse drug reactions in patients receiving Gadovist® are cardiac arrest and severe anaphylactoid reactions (including respiratory arrest and anaphylactic shock). Delayed anaphylactoid reactions (hours later up to several days) have been rarely observed. Most of the undesirable effects were of mild to moderate intensity. Following adverse reactions have been observed: 1.) Common (≥ 1 / 100 to < 1 / 10) headache, nausea; 2.) Uncommon (≥ 1 / 1,000 to < 1 / 100) hypersensitivity anaphylactoid reaction, dizziness, dysgeusia, paresthesia, dyspnea, vomiting, erythema, pruritus, rash, injection site reaction, feeling hot; 3.) Rare (≥ 1 / 10,000 to < 1 / 1,000) loss of consciousness, convulsion, parosmia, tachycardia, palpitations, dry mouth, malaise, feeling cold; 4.) Not known: cardiac arrest, NSF. Patients with an allergic disposition suffer more frequently than others from hypersensitivity reactions. Isolated cases of NSF have been reported with Gadovist®. Paediatric population: Frequency, type and severity of adverse reactions in children of all ages (including term neonates) are consistent with the adverse drug reaction profile known in adults. Overdose: The maximum daily single dose tested in humans is 1.5 mmol gadobutrol / kg body weight. No signs of intoxication from an overdose have so far been reported during clinical use. In case of inadvertent overdosage, cardiovascular monitoring (including ECG) and control of renal function is recommended as a measure of precaution. In case of overdose in patients with renal insufficiency, Gadovist® can be removed by haemodialysis. After 3 haemodialysis sessions approx. 98 % of the agent are removed from the body. However, there is no evidence that haemodialysis is suitable for prevention of NSF. Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system or to drugsafety.hk@bayer.com. Date of revision of text: Jan 2020. Please note: For current prescribing information refer to the package insert and / or contact your local Bayer HealthCare Organization: Bayer HealthCare Limited. 14/F Oxford House, Taikoo Place, 979 King's Road, Quarry Bay, Hong Kong.

DOTAGRAF®

Gadoteric Acid

- *Gadoteric Acid*
- *Ionic Macrocyclic*
- *0.5 Molar*
- *10ml, 20ml, 60ml vials*

Same Formula

Therapeutic indications

Dotagraf® serves to intensify the contrast in Magnetic Resonance Imaging (MRI) Techniques for a better visualization/delineation:

- *Adult and paediatric population (0-18 years)*
- MRI of the CNS including lesions of the brain, spine, and surrounding tissues
- Whole body MRI including lesions of the liver, kidneys, pancreas, pelvis, lungs, heart, breast, and musculoskeletal system.
- *Adult population*
- MR angiography including lesions or stenosis of the non-coronary arteries.

Available Presentation

Presentation	Packing size	Content of gadoteric acid (meglumine salt)	Equivalent to
Vial	10 mL	2793.2 mg	5.0 mmol
	20 mL	5586.4 mg	10.0 mmol
Bottle	60 mL	16759.2 mg	30.0 mmol

Made in Austria

Dotagraf ®0.5 mmol/ml solution for injection. Active ingredient: gadoteric acid (as meglumine salt). Qualitative and quantitative composition: 1 ml solution for injection contains 279.32 mg gadoteric acid (as meglumine salt), equivalent to 0.5 mmol. Other excipients: meglumine, data, water for injections. Therapeutic indications: MRI of the CNS including lesions of the brain, spine, and surrounding tissues; whole body MRI including lesions of the liver, kidneys, pancreas, pelvis, lungs, heart, breast, and musculoskeletal system; MR angiography including lesions or stenoses of the non-coronary arteries. Contraindications: Hypersensitivity to gadoteric acid, to meglumine or to any medicinal products containing gadolinium. Undesirable effects: Uncommon: hypersensitivity, headache, dysgeusia, dizziness, somnolence, paraesthesia including burning sensation), hypotension, hypertension, nausea, abdominal pain, rash, feeling hot, feeling cold, asthenia, injection site reactions (extravasation, pain, discomfort, oedema, inflammation, coldness) Rare: anaphylactic reaction, anaphylactoid reaction, anxiety, presyncope, eyelid edema, palpitations, sneezing, vomiting, diarrhoea, salivary hypersecretion, urticaria, pruritus, hyperhidrosis, chest pain, chills Very rare: agitation, coma, convulsion, syncope, tremor, parosmia, conjunctivitis, ocular hyperaemia, vision blurred, lacrimation increased, cardiac arrest, taclhycardia, anrhythmia, bradycardia, pallor, vasodilatation, cough, dyspnoea, nasal congestion, respiratory arrest, bronchospasm, laryngospasm, pharyngeal oedema, dry throat, pulmonary oedema, erythema, angioedema, eczema, erythema, angioedema, eczema, muscle cramps, muscular weakness, baclk pain, malaise, chest discomfort, pyrexia, face oedema, injection stte necrosis On case of extravasation), phlebitis superficial, decreased oxygen saturation Not known:nephrogenic systemic fibrosis (NSF).Special precautions: There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of some gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment (GFR < 30 ml/min/1 .73m^2). Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. As there is a possibility that NSF may occur with Dotagraf ®, it should therefore not be used in patients with severe renal impairment and in patients in the perioperative liver transplanta-tion period after careful risk/benefit assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI. Haemodialysis shortly after gadoteric acid administration may be useful at removing gadoteric acid from the body. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis. Due to immature renal function in neonates up to 4 weeks of age and infants up to 1 year of age, Dotagraf ® should only be used in these patients after careful consideration at a dose not exceeding 0.1 mmol/kg body weight. The peel-off tracking label on the vials should be stuck onto the patient record to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded. If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record. Any unused medicinal product or waste material should be disposed of in accordance with local requirements. Reference: July 2019.

Our universe of devices and informatics

CT Portfolio

MEDRAD® Centargo
CT Injection System

MEDRAD® Stellant
CT Injection System

Angiography Portfolio

MEDRAD® Avanta
Fluid Management Injection System

MEDRAD® Mark 7 Arterion
Injection System

MR Portfolio

MEDRAD® MRXperion
MR Injection System

Mammography Portfolio

MEDRAD® Salient
Contrast Injection System

Nuclear Medicine

MEDRAD® Intego
PET Infusion System

Digital Solution

Radimetrics™
Radiation Dose Management

Certegra™
@ Point of Care

Clinical updates on

ESUR V.10.0 & ACR 2025

on Iodine -based contrast media

Latest ACR (2025) Guideline Version

Bayer HealthCare Limited
14/F Oxford House, Taikoo Place, 979 King's Road, Quarry Bay, Hong Kong
Tel: (852) 8100 2755 Fax: (852) 3526 4752 radiology.bayer.com.hk

Clinical updates on ESUR V.10.0 & ACR 2025

Iodine Contrast Media

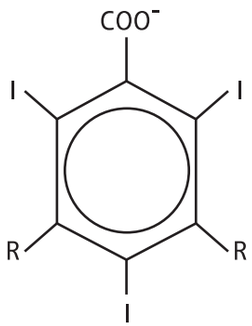
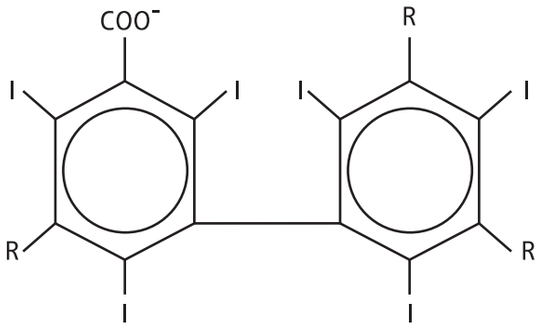
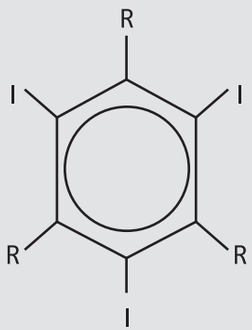
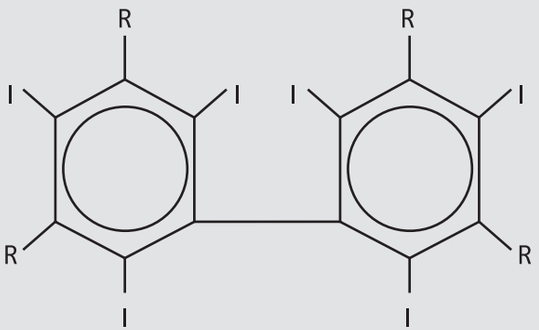
[E]ESUR Guidelines on Contrast Media Version 10.0; 2018 [A]ACR Manual Contrast Media 2025

CA: Contrast Agent; CM: Contrast Medium; GBCA: Gadolinium-Based Contrast Agent; ICM: Iodine-Based Contrast Media

Provided by

PP-PF-RAD-HK-0070-1

Iodinated Contrast Media - Chemical Structures

	MONOMER	DIMER
IONIC	 lothalamate Diatrizoate 'First generation' **HOCM** (1400-2016 mOsm/kg water)	 loxaglate **LOCM** (600 mOsm/kg water)
NON-IONIC	 lopromide (Ultravist®) lopamidol lohexol loversol loxilan **LOCM** (659-796 mOsm/kg water)	 Iodixanol **IOCM** (290 mOsm/kg water)

Acute Adverse Reactions - Classification

Definition: An adverse reaction which occurs within 1 hour of contrast agent injection.[E]

- The same acute adverse reactions are seen after ICM and GBCAs[E]
- The incidence is highest after ICM[E]

ESUR V.10.0

	Hypersensitivity / Allergy-like	Grade (Ring and Messmer classification	Chemotoxic
Mild	Mild urticaria Mild itching Erythema	Grade 1 Grade 1 Grade 1	Nausea/mild vomiting Warmth/chills Anxiety Vasovagal reaction which resolves spontaneously
Moderate	Marked urticaria Mild bronchospasm Facial / laryngeal edema	Grade 1 Grade 2 Grade 2	Vasovagal reaction
Severe	Hypotensive shock Respiratory arrest Cardiac arrest	Grade 3 Grade 4 Grade 4	Arrythmia Convulsion

ACR 2025

Allergic-like	Physiologic
Mild Signs and symptoms are self-limited without evidence of progression.	
Limited urticaria/pruritis Cutaneous edema Limited "itchy"/Scratchy" throat Nasal Congestion Sneezing/Conjunctivitis/rhinorrhea	Limited nausea / vomiting Transient flushing/ warmth / chills Headache / dizziness / anxiety / altered taste Mild hypertension Vasovagal reaction that resolves spontaneously
Moderate Signs and symptoms are more pronounced and commonly require medical management.	
Diffuse urticaria / pruritis Diffuse erythema, stable vital signs Facial edema without dyspnea Throat tightness or hoarseness without dyspnea Wheezing / bronchospasm, mild or no hypoxia	Protracted nausea/vomiting Hypertensive urgency Isolated chest pain Vasovagal reaction that requires and is responsive to treatement
Severe Signs and symptoms are often life-threatening and can result in permanent morbidity or death if not managed appropriately.	
Diffuse edema, or facial edema with dyspnea Diffuse erythema with hypotension Laryngeal edema with stridor and/or hypoxia Wheezing / bronchospasm, significant hypoxia Anaphylactic shock (hypotension + tachycardia)	Vasovagal reaction resistant to treatment Arrhythmia Convulsions, seizures Hypertensive emergency

GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Acute Adverse Reactions

Allergic-Like Reactions

Allergic-like reactions to ICM manifest similarly to true allergic reactions seen with other drugs and allergens, but because an antigen-antibody response cannot be always identified, allergic-like contrast reactions are classified as “anaphylactoid”, “allergic-like”, or “idiosyncratic”. Allergic-like contrast reactions are likely independent of dose and concentration above a certain unknown threshold.

Physiologic Reactions

Physiologic reactions to ICM likely relate to specific molecular attributes that lead to direct chemotoxicity, osmotoxicity (adverse effects due to hyperosmolality), or molecular binding to certain activators. Physiologic reactions are frequently dose and concentration dependent.

Incidence of Acute Adverse Reactions by ICM

ESUR (V.10.0)	ACR 2025
• High-osmolality ionic CM. • There is **no difference** in the incidence of acute reactions between the non-ionic low-osmolar contrast agents and the non-ionic iso-osmolar contrast agents. • There is **no difference** in the incidence of acute adverse events among the non-ionic low-osmolar agents.	• LOCM are associated with a **very low** incidence of acute adverse events, and the bulk of these are not life-threatening. • Nearly all life-threatening contrast reactions occur within the first 20 minutes after CM injection. • In patients with a prior allergic-like or unknown-type contrast reaction to a known contrast medium, changing contrast media within the same class (e.g. one iodinated medium for another) may help reduce the likelihood of a subsequent contrast reaction.

CM: Contrast Medium ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Late Adverse Reactions

Definition:
A late adverse reaction to intravascular ICM is defined as a reaction which occurs 1 h (30-60mins)[A] to 1 week after CM injection.[E]
- Majority occurring between 3 hours and 2 days[A]

ESUR (V.10.0) & ACR 2025

Reactions[E]	• Skin reactions similar in type to other drug induced eruptions occur. - Maculopapular rashes, erythema, swelling and pruritus are most common. - Most skin reactions are mild to moderate and self-limiting. • A variety of late symptoms (e.g., nausea, vomiting, headache, musculoskeletal pains, fever) have been described following CM, but many are not related to the CM.
Risk factors for skin reactions[E]	• Previous late CM reaction • Interleukin-2 treatment • Use of non-ionic dimers
Incidence[A]	• 0.5% to 14% (Delayed allergic-like reactions) • A prospective study of 258 individuals receiving intravenous **iohexol** demonstrated a delayed reaction rate of **14.3**% compared to **2.5**% in a control group undergoing imaging without intravascular contrast material. (Loh et al 2010)

Note: Late skin reactions of the type which occur after ICM have not been described after GBCA and ultrasound contrast media.

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Very Late Adverse Reactions

Definition:
An adverse reaction which usually occurs more than 1 week after contrast agent injection.[E]

ESUR (V.10.0)

Reaction (by ICM)[E]	• **Thyrotoxicosis** • ICM solutions contain small amounts of free iodide and excess free iodide in the blood (ingested or injected) may cause thyrotoxicosis in patients at risk.
Risk factors for thyrotoxicosis[E]	• Patients with untreated Graves' disease. • Patients with multinodular goiter and thyroid autonomy, especially if they are elderly and/or live in area of dietary iodine deficiency.
Recommedations	• ICM **should not** be given to patients with manifest hyperthyroidism. • In patients suspected of being at risk of thyrotoxicosis, TSH measurement may be helpful. • In selected high-risk patients, prophylactic treatment may be given by an endocrinologist. • Patients at risk should be closely monitored by endocrinologists after ICM injection. • Intravenous cholangiographic CM **should not** be given to patients at risk.
Clinical presentations of thyrotoxicosis	• Weight loss, nervousness, easy fatigability, intolerance to heat, hyperkinesia, palpitations and cardiac arrhythmias. • *Cardiovascular events*

CM: Contrast Medium

ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
J. van der Molen et al 2004 (by ESUR Contrast Media Safety Committee)

Renal Safety: PC-AKI vs CIN

Post-contrast acute kidney injury (PC-AKI) is a general term used to describe a sudden deterioration in renal function that occurs within 48 hours following the intravascular administration of iodinated contrast medium. PC-AKI may occur regardless of whether the contrast medium was the cause of the deterioration. *PC- AKI is a correlative diagnosis.*

Contrast-induced nephropathy (CIN) is a specific term used to describe a sudden deterioration in renal function that is caused by the intravascular administration of iodinated contrast medium; therefore, CIN is a subgroup of PC-AKI. *CIN is a causative diagnosis.*

Gadolinium-based contrast media either do not cause CIN when administered at FDA-approved doses, or this event is exceptionally rare.

Renal Safety - Post-Contrast Acute Kidney Injuiry (PC-AKI)

	ESUR (V.10.0)	ACR 2025
Definitions	• **PC-AKI:** An increase in serum creatinine ≥ 0.3 mg/dl (or ≥ 26.5 µmol/l), or ≥1.5 times baseline, within 48-72 hours of intravascular administration of a contrast agent. • **Intra-arterial injection with first pass renal exposure** indicates that contrast agent reaches the renal arteries in a relatively undiluted form, e.g. injection into the left heart, thoracic and suprarenal abdominal aorta or the renal arteries. • **Intra-arterial injection with second pass renal exposure** indicates that contrast agent reaches the renal arteries after dilution either in the pulmonary or peripheral circulation, e.g. injection into the right heart, pulmonary artery, carotid, subclavian, coronary, mesenteric or infra-renal arteries.	**Acute Kidney Injury Network (AKIN) criteria** Within 48 hours after a nephrotoxic event (e.g., intravascular ICM exposure) 1) Absolute serum creatinine increase ≥ 0.3mg/dL (≥26.4µmol/l). 2) A percentage increase in serum creatinine ≥50% (≥1.5-fold above baseline). 3) Urine output reduced to ≤0.5 mL/kg/hour for at least 6 hours. **KDIGO AKI Staging** (ACR & NKF Consensus Statements 2020) Stage — Serum Creatinine Criteria 1 — 1.5-1.9 times baseline serum creatinine *OR* Increase in serum Cr ≥ 0.3 mg/dL (≥26.5µmol/l) 2 — 2.0-2.9 times baseline serum creatinine 3 — 3.0 times baseline serum creatinine *OR* Increase in serum Cr to ≥ 4.0 mg/dL (≥353.6µmol/l) *OR* Initiation of kidney replacement therapy *OR* Decrease in eGFR to <35 mL/min/1.73m² (for patients <18 years old)
Patient related risk factors	• **eGFR < 45mL/min/1.73 m²** before intra-arterial CM administration with first pass renal exposure or in ICU patients. • **eGFR < 30mL/min/1.73 m²** before intravenous / intra-arterial CM administration with second pass renal exposure. • Known or suspected acute renal failure.	• Patients with **eGFR < 30mL/min/1.73m²** • Patients with pre-existing severe renal insufficiency (most important risk factor) • Other risk factors: diabetes mellitus, dehydration, cardiovascular disease, diuretic use, advanced age, multiple myeloma, hypertension, hyperuricemia, and multiple iodinated contrast medium doses in a short time interval (<24 hours)
Procedure related risk factors	• Intra-arterial CM administration with first pass renal exposure. • Large doses of CM given intra-arterially with first pass renal exposure. • High-osmolality CM. • Multiple CM injections within 48-72 hours.	

CM: Contrast Medium

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025
Davenport et al.,2020

Renal Safety - Choice of Iodinated Contrast Medium

Scientific association	Recommendations
American College of Radiology (2025)	"Studies have **failed to establish a clear advantage of IV iso-osmolality iodixanol over IV LOCM with regard to PC-AKI or CIN.** A 2009 meta-analysis using data pooled from 25 trials found no difference in the rate of PC-AKI between iodixanol and low osmolality agents after intravenous administration." "There are **no clinically relevant differences in CI-AKI risk** between **iso-osmolality** and **low-osmolality** iodinated contrast media." by ACR & NKF Consensus Statements (2020) on the use of intravenous ICM in patients with kidney disease
ESUR Contrast Media Safety Committee (ESUR V10.0)	"**All patients**, use **low- or iso-osmolar contrast media**."
Canadian Association of Radiologists (Owen RJ et al. 2014)	"Larger studies and meta-analyses revealed **no significant difference between iodixanol and most low-osmolar contrast media.** [...] Currently, the Canadian Association of Radiologists recommends the **use of iso- or low-osmolar contrast media in patients** with GFR <45mL/ min in intravenous administration and **GFR <60 mL/min** at intraarterial administration"
The Renal Association, British Cardiovascular and Intervention Society and The Royal College of Radiologists (2013 update)	"Currently there is only one type of iso-osmolar media which has **failed to demonstrate any clear benefit compared to different low-osmolar media in preventing CI-AKI**"
American College of Cardiology Foundation /Society for Cardiovascular Angiography and Interventions (Bashore TM et al. 2012)	"[The volume of] contrast media should be minimized, and **low-osmolar or iso-osmolar contrast media should be used**"
European Society of Cardiology (2018 update)	"Use of low-osmolar or iso-osmolar contrast media is recommended for patients with moderate or severe CKD"

CM: Contrast Medium ICM: Iodine-Based Contrast Media

Renal Safety - Suggested Indications for Renal Function Assessment before Intravascular Administration of CM

ESUR (V.10.0)	ACR 2025
Risk Factors	
(a) In all patients or	
(b) In patients who have a history of - Renal disease (eGFR < 60 ml/min/1.73 m^2) - Kidney surgery - Proteinuria - Hypertension - Hyperuricemia - Diabetes mellitus	Personal history of renal disease, including: Known chronic kidney disease (CKD) Remote history of AKI Dialysis Kidney surgery Kidney ablation Albuminuria • History of diabetes mellitus (optional) • Metformin or metformin-containing drug combinations[1]
Timing of Renal Function Assessment	
• Within **7 days** before CM administration in patients with an acute disease, an acute deterioration of a chronic disease or who are hospital inpatients. • Within **3 months** before CM administration in all other patients.	> No agreed-upon acceptable maximum interval between baseline renal function assessment and CM administration in at-risk patients. • **30-day** interval in outpatients. • A **shorter interval** for inpatients.

#Metformin does not confer an increased risk of CIN. However, patients who develop AKI while taking metformin may be susceptible to the development of lactic acidosis.

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Renal Safety - ACR & NKF recommendations on Patients with High Risk Factor of Contrast-Induced AKI

Summary of Major ACR-NKF Consensus Statements on Use of Intravenous Iodinated Contrast Media in Patients with High Risk Factor of CI-AKI

- CI-AKI risk should be determined primarily by using CKD stage and AKI.
- High-risk patient include those with recent AKI and those with eGFR less than 30 mL/min/1.73m^2 , including nonanuric patients undergoing maintenance dialysis.

- CI-AKI risk from IV ICM is lower than previously thought. Necessary contrast material-enhanced CT without a suitable alternative **should not** be avoided solely on the basis of CI-AKI risk.

- Radiologist-clinician discussions about risks and benefits of contrast-enhanced imaging can be helpful in patients at high risk for CI-AKI.

- The presence of a solitary kidney **should not** independently influence decision making regarding the risk of CI-AKI.

- Kidney replacement therapy **should not** be initiated or have the schedule adjusted solely on the basis on CM administration.

- In patients at high risk of CI-AKI, **ad hoc lowering of CM** dose below a known diagnostic threshold **should be avoided.** Rather, the minimum routine clinical diagnostic dose should be used.

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

Davenport et al.,2020

Renal Safety - Patients with Diabetes Mellitus taking METFORMIN

ESUR (V.10.0)	ACR 2025
ICM	
Patients with eGFR > 30mL/min/1.73m^2 and no evidence of AKI, by either IV or IA with second pass renal exposure →continue taking metformin normally.	In patients with no evidence of AKI and with eGFR ≥ 30mL/min/1.73m^2 →no need to discontinue metformin either prior to or following the IV administration of ICM, nor is there an obligatory need to reassess the patient's renal function following the test or procedure.
Patients (a) with eGFR < 30mL/min/1.73m^2 by IV or IA with second pass renal exposure. (b) Receiving IA with first pass renal exposure. (c) With AKI. →stop taking metformin from the time of CM administration. Measure eGFR within 48 h and restart metformin if renal function has not changed significantly.	In patients taking metformin who are known to have acute kidney injury or severe chronic kidney disease (stage IV or stage V; i.e., eGFR< 30), or are undergoing arterial catheter studies that might result in emboli (atheromatous or other) to the renal arteries →metformin should be temporarily discontinued at the time of or prior to the procedure, and withheld for 48 h subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal.
GBCA	
No special precautions are necessary when diabetic patients on metformin are given GBCAs as the risk of PC-AKI is very low.	It is not necessary to discontinue metformin prior to CM administration when the amount of GBCAs administered is in the usual dose range of 0.1 to 0.3 mmol per kg of body weight.

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
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Renal Safety - Hydration

	At-risk patients	Hydration protocols
ESUR (V.10.0)	• For **IV** and **IA** CM administration with second pass renal exposure	(a) intravenous sodium bicarbonate 1.4 % (or 154 mmol/l in dextrose 5 % water): 3 ml/kg/h for 1 hour before CM **or** (b) intravenous saline 0.9 % 1 ml/kg/hr for 3-4 hours before and 4-6 hours after CM.
	• For **IA** CM administration with first pass renal exposure	(a) intravenous sodium bicarbonate 1.4 % (or 154 mmol/l in dextrose 5 % water): 3 ml/kg/h for 1 hour before followed by 1 ml/kg/hr for 4-6 hours after CM **or** (b) intravenous saline 0.9 % 1 ml/kg/hr for 3-4 hours before and 4-6 hours after CM.

- Intravenous saline and bicarbonate protocols have similar efficacy for preventive hydration.
- The responsible clinician should individualize preventive hydration in **patients with severe congestive heart failure** (NYHA grade 3-4) or **patients with end-stage renal failure** (eGFR < 15mL/min/1.73m^2).
- Oral hydration is not recommended as the sole method of preventive hydration.

Post examination
- Continue preventive hydration if appropriate (see protocols above).
- Determine eGFR 48 hours after CM administration.
- If at 48 hours there is a diagnosis of PC-AKI, monitor the patient clinically for at least 30 days and determine eGFR at regular intervals.

ACR 2025

Besides patients at risk of PC-AKI/CI-AKI,

In individual high-risk circumstances, prophylaxis may be considered in patients with eGFR of 30-44 mL/min/1.73m^2 at the discretion of the ordering clinician. – *ACR & NKF Consensus Statements (2020) on Use of Intravenous ICM in Patients with Kidney Disease.*

- The ideal infusion rate and volume is unknown, but isotonic fluids are preferred (0.9% normal saline).

Possible protocols:
- Typical prophylaxis regiments begin 1 hour prior to the exam and continue 3-12 hours after with longer regiments (approximately 12 hours) shown to lower the risk of CA-AKI compared with shorter regiments[61,95].
- Typical doses may be fixed volume (e.g., 500 mL NS) before and after or weight-based volumes (1-3mL/kg per hour)[61,79].
- Oral hydration has not been well studied for patients with eGFR less than 30 mL/min/1.73 m^2 or in patients with AKI
- Sodium bicarbonate – Bicarbonate is likely similar to normal saline for the prevention of CA-AKI, but it is not preferred due to the additional requirement for pharmacist compounding.
- N-acetylcysteine - Recent randomized trial showed that N-acetylcysteine was no more effective than placebo at preventing CA-AKI for intra-arterial iodinated contrast media administration and is therefore not recommended for intravenous contrast media prophylaxis[99].
- Oral hydration has also been utilized, but with less demonstrated effectiveness.

CM: Contrast Medium

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025
Davenport et al.,2020

Renal Safety - Patients on Dialysis

	ESUR (V.10.0)	ACR 2025
Patients on hemodialysis	**ICM** • Correlation of time of the CM injection with the hemodialysis session is **unnecessary.** • Extra hemodialysis session to remove CM is **unnecessary.** **GBCA** • Correlation of time of the CA injection with the hemodialysis session is recommended. • **Extra hemodialysis** session to remove CA **as soon as possible** after it has been administered is recommended.	**ICM** • Patients with anuric end-stage chronic kidney disease who do not have a functioning transplant can receive intravascular iodinated contrast medium without risk of further renal damage because their kidneys are no longer functioning. • However, there is a theoretical risk of converting an oliguric patient on dialysis to an anuric patient on dialysis by exposing him or her to intravascular iodinated contrast medium. (Inconclusive) • Therefore, patients undergoing dialysis who make more than 1-2 cups of urine/day (100 mL) should be considered nonanuric and treated as high-risk patients similar to patients with AKI or eGFR less than 30 mL/min/1.73m^2 who are not undergoing hemodialysis. • Patients should not have acute dialysis nor continuous renal replacement therapy initiated or alter their schedule solely based on iodinated contrast media administration regardless of renal function due to the risks, costs and lack of benefit **GBCA** • In patients with end-stage renal disease on chronic dialysis, injection of Group I agents is contraindicated. **Group II agent is recommended.** • Elective GBCA-enhanced MRI examinations be performed before regularly scheduled dialysis. • Due to the risks of catheter placement and infection, the possibility of worsening kidney function in patients with AKI and CKD, and the perceived very low risk of NSF from group II and III GBCM agents, dialysis should not be initiated or altered in patients receiving a group II GBCM (i.e. daily dialysis or multiple per-day dialysis sessions) # Peritoneal dialysis may provide less NSF risk reduction compared to hemodialysis, but this has not been adequately studied
Patients on continuous ambulatory peritoneal dialysis	**ICM** • Hemodialysis to remove the CM is **unnecessary.** **GBCA** • The need for hemodialysis should be discussed with the referring physician.	

Group I: Gadodiamide, Gadopentetate dimeglumine (Magnevist®), Gadoversetamide
Group II: Gadobenate dimeglumine, Gadobutrol (Gadovist®), Gadoterate acid, Gadoteridol

CA: Contrast Agent CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Pulmonary Safety: ESUR Guidelines (V10.0)

Pulmonary Effects of Iodine-based Contrast Media

Pulmonary adverse effects

- Bronchospasm.
- Increased pulmonary vascular resistance.
- Pulmonary edema.

Patients at high risk

- History of asthma.
- History of pulmonary hypertension.
- Incipient cardiac failure

To reduce the risk of pulmonary adverse effects

- Use low- or iso-osmolar contrast media.
- Avoid large doses of contrast media.

Patient Selection & Preparation Strategies Before CM Administration

Primary Considerations

Allergy [P]	• Patients with **a history of previous allergic-like/ unknown-type reaction** to CM → 8 times higher risk of developing acute adverse reactions for GBCAs → An approximately 5-fold increased risk of developing a future allergic-like reaction if exposed to the same class of CM again. → Greatest risk factor for predicting future adverse events • Patients with **unrelated allergies** are at a 2- to 3-fold increased risk of an allergic-like contrast reaction. → Patients with shellfish or povidone-iodine allergies are at no greater risk from ICM than are patients with other allergies. • **No cross-reactivity** between different classes of CM. (e.g GBCA v.s ICM)
Asthma [P]	• A history of **asthma increases the likelihood** of an allergic-like contrast reaction. → Patients with asthma may be more prone to develop **bronchospasm**. Due to the modest increased risk, restricting contrast medium use or premedicating solely on the basis of a history of asthma is not recommended.
Renal Insufficiency	• **Renal Function Assessment** should be available/ obtained before the injection of CM in all patients considered at risk for CIN and NSF.
Cardiac Status [P]	• **Patients with severe cardiac disease** may be at increased risk of a **non-allergic cardiac event** if a contrast reaction occurs. → These include symptomatic patients and also patients with severe aortic stenosis, cardiac arrhythmias, primary pulmonary hypertension, or severe but compensated cardiomyopathy.
Anxiety	• Contrast reactions are **more common in anxious patients**. → Reassuring an anxious patient before CM injection may mitigate the likelihood of a mild contrast reaction.

[P] Due to the modest increased risk, restricting contrast medium use or premedicating solely on the basis of a medical history is not recommended.
CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

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Good Clinical Practice

Patient Selection & Preparation Strategies Before CM Administration

Other Historical and Pre-Procedure Considerations

Age and Gender [P]	• Infants, neonates, children, and the elderly < middle-aged patients; Females > males [A]
Beta-Blockers [P]	• The use of ß-blockers **lowers the threshold for contrast reactions, increases the severity of contrast reactions**, and **reduces the responsiveness of treatment with epinephrine**. [A] → Patients on ß-blocker therapy **do not need to discontinue** their medication(s) prior to CM administration.[A] • ß-blockers may impair the management of bronchospasm and the response to adrenaline.[E]
Sickle-Cell Trait/Disease [P]	• CM exposure to patients with sickle cell trait /disease might **increase the risk of an acute sickle crisis**. → No evidence this occurs with modern ICM (LOCM/IOCM) or GBCAs. [A] → Hydrate patients before CM administration [E]
Pheochromocytoma [P]	• **No evidence** that IV administration of modern ICM or GBCA increases the risk of hypertensive crisis in patients with pheochromocytoma.[A]
Myasthenia Gravis [P]	• There is **a questionable relationship** between IV ICM and exacerbations of myasthenic symptoms in patients with myasthenia gravis.[A] → It is **controversial** if ICM should be considered a relative contraindication in patients with myasthenia gravis[A]
Hyperthyroidism [P]	• Patients with a history of **hyperthyroidism can develop thyrotoxicosis** after exposure to ICM, but this complication is rare. [A] Two special situations may affect this: → In patients with **acute thyroid storm**, ICM exposure can potentiate thyrotoxicosis - **ICM should be avoided.** → In patients considering **radioactive iodine therapy / undergoing radioactive iodine imaging of the thyroid gland**, administration of ICM can interfere with uptake of the treatment and diagnostic dose. √ If ICM was administrated, **a washout period** is suggested to minimize this interaction: Hyperthyroidism: 3-4 weeks v.s Hypothyroidism: 6 weeks

[P] Due to the modest increased risk, restricting contrast medium use or premedicating solely on the basis of a medical history is not recommended.
CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media

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Good Clinical Practice

Good Clinical Practice - Premedication

NEW

ESUR (V.10.0) & ACR 2025

ESUR:

Premedication is not recommended because there is not good evidence of its effectiveness.

ACR:

- For patients with mild immediate ICM hypersensitivity, premedication is not recommended; switching the contrast agent is advised if the inciting agent is known and feasible.
- For patients with severe immediate ICM hypersensitivity, consider alternative imaging first. If none are acceptable, premedication and switching the contrast agent are recommended.
- No premedication is necessary for patients with prior chemotoxic reactions or isolated shellfish or iodine allergies, including topical povidone-iodine.

Indications for Premedication by ACR 2025

12- or 13-hour oral premedication	1. Outpatient with a prior allergic-like or unknown-type contrast reaction to the same class of CM (e.g Iodinated – iodinated). 2. Emergency department patient or inpatient with a prior allergic-like or unknown-type contrast reaction to the same class of CM in whom the use of premedication is not anticipated to adversely delay care decisions or treatment.
Accelerated IV premedication	1. Outpatient with a prior allergic-like or unknown-type contrast reaction to the same class of CM who has arrived for a contrast-enhanced examination but has not been premedicated and whose examination cannot be easily rescheduled. 2. Emergency department patient or inpatient with a prior allergic-like or unknown-type contrast reaction to the same class of CM in whom the use of 12-or 13-hour premedication is anticipated to adversely delay care decisions or treatment.

CM: Contrast Medium

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Wang C, Ramsey A, Lang D, Maria Copaescu A, Krishnan P, Kuruvilla M, Mervak B, Newhouse J, Sumkin A, Saff R.
Management and Prevention of Hypersensitivity Reactions to Radiocontrast Media: A Consensus Statement from the American College of Radiology and the American Academy of Allergy, Asthma & Immunology. Radiology. 2025 May;315(2):e240100. doi: 10.1148/radiol.240100. PMID: 40326871.

Good Clinical Practice

Good Clinical Practice - Premedication

Specific Recommended Premedication Regimens by ACR 2025

Oral Premedication

Corticosteroids (Any of the following)	1) Prednisone-based: 50mg orally, at 13h, 7h and 1h before CM administration *Hydrocortisone: 200 mg IV for each dose of oral prednisone
+	2) Methylprednisolone-based: 32 mg orally, 12h and 2h before CM administration
Antihistamine (Optional)	Diphenhydramine: 50 mg intravenously/intramuscularly/orally 1h before CM administration

IV Premedication

(*in decreasing order of desirability*)

- Methylprednisolone sodium succinate 40 mg IV or hydrocortisone sodium succinate 200 mg IV immediately, and then every 4 hours until CM administration, plus diphenhydramine 50 mg IV 1 hour before CM administration.
  This regimen usually is 4-5 hours in duration.

- Dexamethasone sodium sulfate 7.5 mg IV immediately, and then every 4 hours until CM administration, plus diphenhydramine 50 mg IV 1 hour before CM administration.
  This regimen may be useful in patients with an allergy to methylprednisolone and is also usually 4-5 hours in duration.

- Methylprednisolone sodium succinate 40 mg IV or hydrocortisone sodium succinate 200 mg IV, plus diphenhydramine 50 mg IV, each 1 hour before CM administration.
  This regimen, and all other regimens with a duration less than 4-5 hours, has no evidence of efficacy. It may be considered in emergent situations when there are no alternatives.

Note: Premedication regimens less than 4-5 hours in duration (oral or IV) have not been shown to be effective.
CM: Contrast Medium

ACR Manual on Contrast Media 2025

Good Clinical Practice - CM Extravasation

ESUR (V.10.0) & ACR 2025	
Technique-related risk factors	• Use of a power injector. • Less optimal injection sites including lower limb and small distal veins. • Large volume of CM. • Injections are made into more peripherally placed catheters [A] • High-osmolar CM. • More viscous contrast media.
Patient-related risk factors	• Inability to communicate. • Severely ill or debilitated patients [A] • Patients with abnormal circulation in the limb to be injected [A] • Fragile or damaged veins. • Arterial insufficiency. • Injection through indwelling peripheral intravenous lines (placed for more than 24 hours) and multiple punctures into the same vein[A] • Compromised lymphatic and/or venous drainage. • Obesity.
To reduce the risk	• Intravenous technique should always be meticulous using appropriate sized plastic cannula placed in a suitable vein to handle the flow rate used during the injection. • Consider use of cannulas with sideholes. • Test injection with normal saline. • Use non-ionic ICM.
Management	• Conservative management is adequate in most cases • Limb elevation (Elevation of the affected extremity above the level of the heart to decrease capillary hydrostatic pressure and thereby promote resorption of extravasated fluid is recommended) • Ice packs: Helpful for relieving pain at the injection site * many surgeons recommend initial use of cold compresses [A] • Warm compresses: Helpful in improving absorption of the extravasation as well as in improving blood flow, particularly distal to the site. [A] • Careful monitoring: If a serious injury is suspected, seek the advice of a surgeon. • Consider less viscous contrast media or pre-warm to human body temperature.
Update in ACR 2022 Chapter 7 Extravasation of Contrast Media	• Evidence based update on extravasation recommendations and strength of evidence. • The focus on the cause of extravasation in terms of choice of iodinated contrast media has shifted from osmolality to viscosity. • ACR 2022 covers various aspects of extravasation in a Q&A format with levels of evidence.

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ESUR Guidelines on Contrast Media Version 10.0; 2018
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Good Clinical Practice – Waiting time between contrast media injection for repeat scans

NEW

Patient Condition	Iodine-Based Contrast Media (ICM)	Gadolinium-Based Contrast Agents (GBCA)	Combined Imaging (ICM + GBCA)	Additional comments
Normal Renal Function (eGFR > 60)	12 hours (optimally)	12 hours (optimally)	6 hours (optimally)	The effects of ICM are longer-lived and more disturbing on subsequent contrast-enhanced MRI than the effects of GBCA in contrast-enhanced CT. Therefore, it is better to schedule MRI with GBCA before CT with ICM when combining studies. Only for renal imaging CT (including CT urography) is best performed before MRI because kidneys will concentrate GBCA, so that the enhancement of the renal collecting systems, ureters, and bladder may last considerably longer, with risk of misdiagnosis.
	4 hours (minimally)	4 hours (minimally)	2 hours (minimally)	
Moderately Reduced Renal Function (eGFR 30-60)	48 hours (optimally)	48 hours (optimally)	48 hours (optimally)	
	16 hours (minimally)	16 hours (minimally)	16 hours (minimally)	
Severely Reduced Renal Function (eGFR < 30)	7 days (optimally)	7 days (optimally)	7 days (optimally)	
	2.5 days (minimally)	2.5 days (minimally)	2.5 days (minimally)	

*In emergency or life-threatening situations, employ less waiting time between successive a) iodine-based contrast media administrations or b) gadolinium-based contrast agent administrations. Not enough evidence for combined scans

Van Der Molen, A. J., Dekkers, I. A., Geenen, R. W. F., Bellin, M., Bertolotto, M., Brismar, T. B., Correas, J., Heinz-Peer, G., Mahnken, A. H., Quattrocchi, C. C., Radbruch, A., Reimer, P., Roditi, G., Romanini, L., Sebastià, C., Stacul, F., & Clement, O. (2023). Waiting times between examinations with intravascularly administered contrast media: a review of contrast media pharmacokinetics and updated ESUR Contrast Media Safety Committee guidelines. European Radiology, 34(4), 2512–2523. https://doi.org/10.1007/s00330-023-10085-5

NEW

Good Clinical Practice - CM in Pregnancy and Lactation

ESUR (V.10.0) ACR 2025	ICM	GBCAs
Pregnancy	In exceptional circumstances, when radiographic examination is essential, **ICM may be given to the pregnant female.** [EA]	When there is a very strong indication for enhanced MR, the smallest possible dose of **a macro-cyclic GBCA** (Agents with lowest risk of NSF) **may be given to the pregnant female.** [EA] ACR 2022 Updated in Chapter 15: • Newly added **"Gadolinium Pregnancy Screening Statement"** • Recommends **avoidance of routine administration of GBCAs to pregnant patients**. • A decision to administer GBCAs to a pregnant woman should only be made when there is the **potential for significant clinical benefit that outweighs the unknown risk of fetal exposure** and should be the product of discussion that involves the referring provider and patient.[A]
Testing for the Neonates	Following administration of ICM to the mother during pregnancy, **thyroid function** should be **checked in the neonate during the first week.** [E]	Following administration of GBCAs to the mother during pregnancy, **no neonatal tests are necessary.** [E]
Lactation	• **Breast feeding may be continued normally** when ICMs are given to the mother. [EA] • If the mother remains concerned about breast feed the infant after ICM administration: she may abstain from breast-feeding from the time of contrast administration for a period of 12 to 24 hours. [A] • **The available data suggests that it is safe for the mother and infant to continue breast-feeding after receiving ICM, stopping breastfeeding for 24 hours after maternal IV or IA exposure to iodinated contrast material is not required and recommended patients make an informed decision on managing breastmilk after exposure to iodinated contrast material.** [A] • Routine thyroid function testing is not recommended due to no strong data exists in the literature. [A]	• **Breast feeding may be continued normally** when macrocyclic GBCAs are given to the mother. [EA] • If the mother remains concerned about breast feed the infant after ICM administration: she may abstain from breast-feeding from the time of contrast administration for a period of 12 to 24 hours. [A] • **The available data suggests that it is safe for the mother and infant to continue breast-feeding after receiving macrocyclic GBCAs, stopping breastfeeding for 24 hours after maternal IV or IA exposure to gadolinium-based contrast is not required.** [A]

ESUR (V.10.0) ACR 2025	ICM	GBCAs
Pregnant or lactating mother with renal impairment	• Mother- refers to renal adverse reactions • **No additional precautions** are necessary **for the fetus or neonate**	**Do not administer GBCAs** [E]

CM: Contrast Medium GBCA: Gadolinium-Based Contrast Agent ICM: Iodine-Based Contrast Media
*Please always consult local hospital/center guidelines to make informed decisions.

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

NEW

Recommendations from ESUR (V10.0) & ACR 2025

To reduce the risk of contrast reactions	
For all patients	• Use a non-ionic CM.
For patients at increased risk of reaction	• Consider an altemative test not requiring an iodine-based contrast agent. • Use a different iodine-based agent for previous reactors to CM.
For patient with previous moderate or severe allergic-like reactions to a specific gadolinium based contrast media (GBCM)	• It may be prudent to use a different GBCM and premedicate for subsequent MR examinations
For patients on Gastrointestinal (GI) Contrast Media	• Updated contents for indications, contraindications, and adverse reactions primarily in Barium, iodinated, and negative GI contrast media.[A] • Premedication does not prevent all repeat allergy contrast reactions. Another mitigation strategy is to change a different agent in the same class or selecting a different class of contrast media.[A]
Methods of preventing contrast reactions	
Hydration	• Patients with impaired renal function. • Elderly patients, patients with reduced general conditions.
Warming CM	• Reduces their viscosity and may make the injection more comfortable for the patient. • GBCAs are administered at room temperature (15 to 30˚C) and according to package inserts, **should not** be externally warmed for routine clinical applications. [A]
Not Recommended	
Pretesting[A]	Intradermal skin testing with CM to predict the likelihood of adverse reactions has not been shown to be useful in minimizing reaction risk.
Fasting[E]	Fasting is not recommended before administration of low-or iso-osmolar non-ionic iodine-based CM or of gadolinium-based agents.

CM: Contrast Medium

ESUR Guidelines on Contrast Media Version 10.0; 2018
ACR Manual on Contrast Media 2025

Good Clinical Practice

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