Duke Radiology

Contrast Media Guidelines

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I. Introduction

Contrast media is used to improve medical imaging. Various forms of contrast media can be administered intravenously, intra-arterially, or intraluminally. Contrast media is considered a pharmaceutical agent and like all other pharmaceuticals, contrast media is not completely devoid of risk. The purpose of these guidelines is to assist the radiologist in managing the small but real risks inherent in the use of contrast media.

II. Patient selection

Before any administration of contrast media, the radiologist should consider the following:

1. Assessment of risk versus benefit of the contrast administration.
2. Alternate imaging that would provide the same or better diagnostic information without need for contrast media.
3. Valid clinical indication for contrast administration.

III. Intravenous iodinated contrast media

The following parameters will be used when assessing patients requiring IV iodinated contrast media:

1. All patients with a serum creatinine (regardless of age) which measures < 2.0 mg/dL (and/or eGFR > 40) are eligible for intravenous iodinated contrast administration.
2. All patients >60 years old require a serum creatinine (and/or eGFR) performed within the last 30 days.
3. Patients < 60 years old, scheduled for a routine intravascular study, and do not have one or more risk factors (listed below), do not require a baseline serum creatinine (and/or eGFR) determination before iodinated contrast medium administration.
4. Administration of intravenous contrast with serum creatinine ≥ 2.0 mg/dL (and/or eGFR ≤ 40) requires discussion with radiologist. The radiologist should consider discussing the risks of contrast-induced nephropathy (see page 12) with a member of the patients care team which may include the requesting physician or physician extender prior to approval of contrast administration.

Risk factors that may require serum creatinine determination:

1. **Chemotherapy**: All patients receiving nephrotoxic chemotherapy require a serum creatinine performed since the last dose.
2. **Metformin**: Patients on metformin require serum creatinine and estimated GFR. See page 11 for more information.
3. **Renal disease:** Patients with a history of significant renal disease (e.g. may result in impaired renal function), nephrectomy, kidney transplant, or recognized upward trend in creatinine may have a point of care creatinine performed at the discretion of the nurse, technologist, radiologist, or ordering provider.

4. **Hypertension requiring medical therapy, diabetes mellitus, or gout:** patients with one or more of these three conditions may have a point of care creatinine performed at the discretion of the nurse, technologist, radiologist, or ordering provider.

5. **Recent intravenous contrast:** All patients who have received IV iodinated contrast in the last 24 hours require approval by a radiologist for additional intravenous contrast media administration and may have a point of care creatinine performed at the discretion of the nurse, technologist, radiologist, or ordering provider.

**Emergency patients**
The ordering physician can choose to bypass screening in an emergency and have IV contrast administered without screening. This screening process bypass must be documented by the nurse, technologist or the ordering physician. The ordering physician’s name must be included in the documentation.

**IV. Gadolinium**
Eligibility criteria for administration of intravenous gadolinium are described in the section on Gadolinium guidelines (see page 13).

**V. Specific conditions**

1. **Allergic-like reactions and premedication protocols**—see pages 6-8.

2. **Renal insufficiency**—see page 12.

3. **Pregnancy or breast-feeding**—see page 17-18.

4. **Sickle cell disease/trait:** There is no evidence for any clinically significant risk, particularly after the injection of low-osmolality contrast media (1, 2).

5. **Myasthenia Gravis:** This condition may be a relative contraindication for intravenous administration of iodinated contrast media (1, 3).
6. **Thyroid Disease:**
   a. Hyperthyroidism: patients with hyperthyroidism or other thyroid disease can potentially experience iodine-provoked delayed hyperthyroidism. This effect may appear 4-6 weeks after IV administration of iodinated contrast media. This condition is usually self-limited. However, patients with history of hyperthyroidism should follow-up with their endocrinologists after receiving iodinated contrast media (1, 4).
   b. Thyroid carcinoma: Iodinated contrast media may interfere with both diagnostic scintigraphy and radio-iodine treatment. Therapeutic uptake of $\text{I}^{131}$ radioiodine therapy may be decreased substantially after iodinated contrast injection. Patients are required to wait a minimum of 4 weeks (preferably 6 weeks) after receiving intravenous iodinated contrast administration, before undergoing either $\text{I}^{123}$ diagnostic scintigraphy or $\text{I}^{131}$ radioiodine therapy (1, 4).

7. **Multiple myeloma:** Paraproteinemias, such as multiple myeloma, has previously been considered a risk factor for developing contrast-induced nephropathy after high-osmolality contrast media. However, there are no data predicting risk with the use of low-osmolality or iso-osmolality intravenous contrast media (1). Patients with multiple myeloma may receive iodinated IV low-osmolality or iso-osmolality contrast if they are adequately hydrated and not significantly hypercalcemic (5).

8. **Pheochromocytoma:** Previous investigations have shown no clinical effect from injection of low osmolality contrast media in patients with pheochromocytoma (6). However, direct injection of high or low osmolality contrast media into the adrenal or renal artery is to be avoided because of the risk of causing a hypertensive crisis (1).

9. **Dialysis:** Most low-osmolality iodinated contrast media are not protein-bound, have relatively low molecular weights, and are readily cleared by dialysis. Unless an unusually large volume of contrast medium is administered, or there is substantial underlying cardiac dysfunction, there is no need for urgent dialysis after IV contrast medium administration (1).
I. Allergic-like reactions to contrast media

A history of prior allergy-like reaction to contrast media is associated with up to a five-fold increased likelihood of the patient experiencing a subsequent reaction. Patients who describe an “allergy” to contrast media or other substances (food, medication) should be questioned further to clarify the type and severity of the “allergy” or reaction. A patient with a history of anaphylaxis or life-threatening reaction to contrast media should not receive contrast media, regardless of prep. The patient records should be reviewed to see that this allergy is appropriately documented.

Please see Appendix A for additional information regarding allergic-like reactions to contrast media.

II. Categorization:  Acute adverse events can be categorized as either allergic-like or physiologic, and classified into three categories: mild, moderate, or severe (1).

1. Mild: Allergic-like: limited urticarial/pruritus, cutaneous edema, “itchy”/“scratchy” throat, nasal congestion, sneezing, rhinorrhea Physiologic: limited nausea/vomiting, transient flushing, headache, dizziness, mild hypertension, vasovagal reaction that resolves spontaneously

2. Moderate: Allergic-like: diffuse urticarial/pruritus; diffuse erythema (stable vital signs), facial edema or throat hoarseness without dyspnea, wheezing with no hypoxia Physiologic: protracted nausea/vomiting, isolated chest pain, vasovagal reaction requiring treatment

3. Severe: Allergic-like: diffuse or facial edema with dyspnea, diffuse erythema with hypotension, laryngeal edema with stridor and/or hypoxia, wheezing/bronchospasm with hypoxia, anaphylactic shock (hypotension + tachycardia) Physiologic: vasovagal resistant to treatment, arrhythmia, seizures, hypertensive emergency, cardiovascular collapse
I. Premedication guidelines

1. Steroid prep needed (if no prep given, consult radiologist; if prep given, do not consult radiologist):
   a. Prior allergic-like reaction (mild, moderate) to the same class of contrast media agent (iodinated / gadolinium)
   b. Actively asthmatic (e.g., in the ER with active asthma exacerbation)
   c. Prior mild breakthrough reaction. Note: an individual radiologist may elect to not perform the examination in this setting. This decision should be coordinated such as during ordering/scheduling process.

2. Steroid prep not needed (may scan patient without consulting radiologist):
   a. Physiologic reaction to contrast media such as nausea or vomiting
   b. Seafood or shellfish allergy (mild or moderate)
   c. Allergy to a different type of contrast agent (e.g., allergy to gadolinium if receiving iodinated contrast or allergy to iodinated contrast if receiving gadolinium)

3. Steroid prep possibly needed (consult radiologist if no prep given):
   a. One or more allergies to any substance(s) except for the same type of contrast material (which would necessitate a steroid prep, see 1a above) and also excluding seafood or shellfish (see 2b above)
   b. Asthma

4. Contrast media administration is relatively contraindicated (consult radiologist):
   a. Prior severe reaction to any substance (active angioedema, laryngeal edema, anaphylactic shock) including any type of contrast media agent (iodinated or gadolinium); if such a history is present, please consult a radiologist
   b. Prior moderate or severe breakthrough reaction. For prior mild breakthrough reaction, contrast media may be administered after a steroid prep (see 1c above)

5. Miscellaneous:
   a. If an alternate prep has been given, consult the radiologist. If all scheduled doses of a full steroid prep (12-13 hours) have been given but the timing is off by 2-3 hours, no consultation is required and the scan can be performed. The initial dose of steroids must precede contrast material administration by not less than 4 hours.
   b. Using Visipaque (iodixanol) may somewhat reduce the risk of a contrast reaction in patients with a history of allergic-like reaction to iodinated contrast, but the data supporting this is weak and the practice is not required. Substituting Visipaque is not considered a substitute for
premedication when premedication is indicated.

II. Elective Prep: 13-Hour Prep (Greenberger Protocol)

1. Adults:
   Prednisone 50 mg (oral) q 6 hours x 3 doses starting 13 hours prior to scan:
   13 hours + 7 hours + 1 hour prior to scan

   Optional: Benadryl 50 mg maximum dose 1 hr prior to exam

   Steroid Equivalences
   Decadron (dexamethasone) 8 mg X 3 doses, IV or oral
   OR
   Solu-Cortef (hydrocortisone) 200 mg X 3 doses, IV or oral (IV preferred)
   OR
   Solu-Medrol (Methylprednisolone) 40 mg x 3 doses, IV or oral (IV preferred)

   Total Doses required for full strength prep prior to contrast media
   
   50 x 3       = 150 mg Prednisone
   8 x 3        = 24 mg Decadron (Dexamethasone)
   200 x 3      = 600 mg Solu-Cortef (Hydrocortisone)
   40 x 3       = 120 mg Solu-Medrol (Methylprednisolone)

2. Pediatrics:
   Prednisone 0.5-0.7 mg/kg PO (up to 50 mg) q 6 hours x 3 doses starting 13 hours prior to scan:
   13 hours + 7 hours + 1 hour prior to scan
   Benadryl (optional) 1.25mg/kg PO 1 hour prior to scan (50 mg maximum dose)

III. Emergency Prep: 4-hour Prep

Use the following prep when you do not have 13 hours to follow the Greenberger protocol listed above.

1. Adults:
   Solu-Medrol (Methylprednisolone) 60 mg IV Q 4 hours x 2 doses prior to contrast administration (the first dose is given 4 hours prior to the scan and the second dose is given before the patient is put on the CT table)
   Benadryl (Diphenhydramine) 25-50 mg IV one-hour prior to scan (per Radiologist)

I. Contrast Extravasation

1. Risk Factors:
   - Non-communicative patients: infants, small children, non-English speaking and unconscious
   - Small peripheral veins (hands and feet)
   - Injection of an older IV line
   - Multiple attempts at IV access
   - Abnormality in limb to be injected (trauma, lymphedema, etc.)
   - Higher injection rates (4-5 mL/sec)

2. Sequela of Extravasations:
   Iodinated contrast media is toxic to surrounding tissues/skin resulting in an acute local inflammatory response. The vast majority of patients recover with no significant injury.

   Possible significant injuries include:
   1. Compartment syndrome: more likely to occur with large volumes or injection in a small tight space (i.e. ventral or dorsal surface of wrist)
   2. Skin ulceration/blister/tissue necrosis

3. Actions/Treatment:

   1. Call referring physician to notify of event and severity.

   2. Evaluate and observe patient in the Department of Radiology as appropriate depending on amount and severity of extravasation.

   3. Physical Exam:
   - Confirm pulses in affected limb
   - Assess skin color/sensation and monitor for change (compared to unaffected limb)
   - Elevate affected extremity
   - Apply cold compress

   4. Indications for Surgical Consult (“Hand Service” on call)
   - Increasing pain over 1-2 hours
   - Increasing pain on passive stretch of flexor or extensor tendons
   - Skin blistering
   - Altered tissue perfusion (↓ capillary refill)
   - Change in sensation (or ↓ sensation) distal to site of extravasation

   5. Give patient Radiology phone number when sending home.

   6. Tell patient to call if he/she develops:
- Significant residual pain or increasing pain
- Skin changes (including blistering)
- Hardness or ↓ temperature sensation at site of extravasation
- Change in sensation distal to site of extravasation

I. Metformin Guidelines (1)

Metformin (see Appendix C for brand names) is an oral anti-hyperglycemic agent used primarily to treat insulin resistant diabetes mellitus. The most significant adverse effect of metformin therapy is the potential for the development of metformin-associated lactic acidosis. Iodinated contrast media is not an independent risk factor for patients taking metformin but is a concern only if post-contrast acute kidney injury should develop.

1. Metformin and Iodine-based Contrast Agents:

   **Category 1:** In patients with no evidence of acute kidney injury and with eGFR ≥ 45 mL/min/1.73m², there is no need to discontinue metformin either prior to or following the intravenous administration of iodinated contrast media, nor is there an obligatory need to reassess the patient’s renal function following the test or procedure.

   **Category 2:** In patients taking metformin who are known to have acute kidney injury or chronic kidney disease (eGFR < 45), 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 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal. Patients should be given written information to contact their PCP (primary care provider).

2. Metformin and IV Gadolinium: It is not necessary to discontinue metformin prior to contrast medium administration when the amount of gadolinium-based contrast material administered is in the usual dose range of 0.1 to 0.3 mmol per kg of body weight.
I. Renal Insufficiency and Contrast Induced Nephropathy

Contrast-induced nephropathy (CIN) is a specific term to which is used describe a type of post-contrast acute kidney injury (PC-AKI) where the deterioration in renal function is directly attributed to the administration of contrast media.

The most important risk factor for CIN is pre-existing severe renal insufficiency. A threshold of eGFR of < 30 mL/min/1.73m² has been proposed as the limit below which intravenous contrast administration becomes a risk factor for developing PC-AKI and CIN(1).

II. Acute Kidney Injury Network (AKIN) definition of acute kidney injury:

1. Absolute serum creatinine increase $\geq 0.3$ mg/dL.
2. A percentage increase in serum creatinine $\geq 50\%$ ($\geq 1.5$-fold above baseline).
3. Urine output reduced to $\leq 0.5$ mL/kg/hour for at least 6 hours.

III. Clinical course: The clinical course of CIN or PC-AKI depends on the baseline renal function, coexisting risk factors, degree of hydration, and other factors. However, the usual course consists of a transient asymptomatic elevation in serum creatinine. Serum creatinine usually begins to rise within 24 hours of IV iodinated contrast administration, peaks at 4 days, and often returns to baseline within 7 to 10 days. It is unusual for patients to develop permanent renal dysfunction.

IV. Treatment: The treatment of CIN or PC-AKI is largely supportive. The major preventative action to mitigate the risk of CIN is to provide intravenous volume expansion (see hydration protocol, page 21). One possible protocol would be 0.9% saline at 100 mL/hr, beginning 6-12 hours before and continuing 4-12 hours after iodinated contrast administration. This protocol is only practical in the inpatient setting.
I. Gadolinium Contrast Use and Nephrogenic Sclerosing Fibrosis

The association of nephrogenic sclerosing fibrosis (NSF) and gadolinium is well documented. However, the precise mechanism of the relationship is controversial and incompletely understood. One hypothesis is that the development of NSF is related to the release of gadolinium ions from the chelates in gadolinium based contrast agents (GBCA), in patients with decreased renal function and prolonged clearance time of GBCA from the bloodstream. Our gadolinium guidelines are therefore directed at identifying patients who are at risk for NSF.

II. Gadolinium Guidelines

Policy: Intravenous contrast agents in MRI
Last revised: 7/5/16

Background

This document is a guideline for administration of intravenous (IV) contrast agents during MRI in particular patient populations (particularly individuals with compromised renal function) for the Department of Radiology, Duke University Medical Center. The choices of whether to administer a contrast agent and the type of agent should ultimately be guided by patient clinical needs. Any MRI area in which IV contrast agents (or other medications) may be administered must have a supervising physician who is prepared for the evaluation and treatment of idiosyncratic and allergic reactions. Such measures and policies are not described in detail in this document.

Note that the following guidelines assume stable renal function over a period of several months. If there is any suggestion that the patient may have sustained an acute kidney injury, a point of care (POC) estimated glomerular filtration rate (eGFR) should be measured within 24 hours of the scan, and the decision regarding contrast media administration made in light of the most recent eGFR value and its trend over time. The presence of an acute kidney injury in and of itself, regardless of the eGFR, may represent a relative contraindication to the administration of gadolinium-based contrast agents (GBCA).

MRI contrast agents available at Duke

Gadolinium-based agents (GBCAs):
- Eovist (gadoxetate disodium)
- Gadavist (gadobutrol)
- Magnevist (gadopentetate dimeglumine)
- MultiHance (gadobenate dimeglumine)
- ProHance (gadoteridol)

Non-Gadolinium-based agent (off-label use as contrast agent):
- Feraheme (ferumoxytol)
Patients Requiring a Serum eGFR Measurement
1) All patients >60 years old; eGFR within last 30 days.
2) All patients receiving nephrotoxic chemotherapy; eGFR since the last dose of nephrotoxic chemotherapy.
3) Any patient with a history of renal disease, nephrectomy (complete or partial), kidney transplant, recognized downward trend in eGFR or upward trend in creatinine; eGFR within last 30 days or since last kidney-related intervention/event.

Categorization of patient renal function*
- eGFR > 60 mL/min/1.73m²: Normal function (category 0)
- eGFR 40-59 mL/min/1.73m²: Normal to mildly impaired (category I)
- eGFR 30-39 mL/min/1.73m²: Moderately impaired, borderline (category II)
- eGFR < 30 mL/min/1.73m²: Severely impaired (category III)
  (note: patients on chronic dialysis are also considered to fall within category III regardless of eGFR)

*Note that the above categorization system is for internal use only, and does not correspond to the National Kidney Foundation system for staging chronic kidney disease.

Guidelines
- **Category 0 (eGFR ≥ 60 mL/min/1.73m², measured within 3 months):** Normal renal function. GBCAs may be administered up to standard dosages.

- **Category I (eGFR between 40 and 59 mL/min/1.73m², measured within 1 month):** Normal to mildly impaired renal function. Risk of developing nephrogenic systemic fibrosis (NSF) from GBCA administration in this patient population is extremely low. GBCAs may be administered up to standard dosages.

- **Category II (eGFR between 30 and 39 mL/min/1.73m²):** Borderline renal function. Importantly, it has been shown that eGFR measurements can fluctuate from day to day. As a result, these patients must have an eGFR rechecked within 24 hours of potential GBCA administration; this will be done via POC iSTAT test when the patient arrives in MRI for their scan if no other qualifying eGFR measurement is available. Those with an eGFR ≥ 30 mL/min/1.73m² within 24 hours of GBCA administration are managed as category I renal function. Those with eGFR < 30 mL/min/1.73m² are managed as category III. If it is not possible to check the eGFR within 24 hours of MRI, then these patients are considered category III for purposes of potential GBCA administration.

- **Category III (eGFR < 30 mL/min/1.73m²):** Severely impaired renal function. Note that since such severe renal insufficiency is typically chronic, a recent (within 3 months) eGFR measurement is only required if a provider has reason to believe that the patient’s renal function may have improved. Administration of ANY GBCA is relatively contraindicated in this patient population. Alternative techniques, such as non-MRI investigations, non-contrast MRI, or administration of an iron-based agent (ferumoxytol)
should be considered. In certain scenarios, where the future risk of development of NSF is outweighed by the need for GBCA administration, it may be reasonable to administer a GBCA. The following precautions must be observed:

1) A discussion of the risks and benefits must be undertaken with the referring attending physician, and a note must be placed in the medical record by the referring attending physician to document that the benefits of the examination are believed to outweigh the risks.

2) **For patients with eGFR < 15 mL/min/1.73 m²**: A discussion of the risks and benefits must be undertaken with the patient (or designee) by a physician member of the Radiology department or the referring clinical team. The patient (or designee) must provide written informed consent, and the scanned into PACS or MaestroCare. If the consent document is obtained by the referring team but documentation cannot be verified at the time of MRI examination, written consent must be re-obtained in MRI prior to GBCA administration.

3) Prior to GBCA administration, the non-contrast portion of the examination must be evaluated by a Radiologist to determine whether GBCA administration is necessary.

4) Following the above, if deemed necessary, GBCA may be administered at the lowest reasonable dose that is expected to yield a diagnostic examination and answer the clinical question, as determined by the supervising Radiologist. The choice of GBCA will depend upon the clinical situation, however agents with favorable safety profiles (MultiHance, ProHance, or Gadavist) should be used whenever possible. Magnevist is contraindicated for patients in this category of renal function, in concordance with the Food and Drug Administration’s guidelines.

5) The Radiologist reporting the MRI result must clearly summarize the steps taken above in their report, including verification of informed consent (if applicable) and the note from the referring physician.

While dialysis following GBCA administration has not shown clear benefit, the risks and benefits of dialysis should be considered following GBCA administration to patients who receive dialysis.

<table>
<thead>
<tr>
<th>eGFR Quick Reference</th>
<th>Category 0</th>
<th>Category I</th>
<th>Category II</th>
<th>Category III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior eGFR</td>
<td>eGFR ≥ 60</td>
<td>40 ≤ eGFR &lt; 59</td>
<td>30 ≤ eGFR &lt; 39</td>
<td>eGFR &lt; 30 or chronic dialysis</td>
</tr>
<tr>
<td>Time eGFR is valid</td>
<td>3 months</td>
<td>1 month</td>
<td>≤ 24 hours</td>
<td>Any time (most recent eGFR)</td>
</tr>
<tr>
<td>Action</td>
<td>Normal dose GBCA</td>
<td>Normal dose GBCA</td>
<td>eGFR must be within 24 hours; if most recent eGFR ≥ 30, manage as category I; otherwise manage as category III</td>
<td>GBCA relatively contraindicated; if GBCA is needed, follow steps 1-4 above</td>
</tr>
</tbody>
</table>
**Ferumoxytol**

Ferumoxytol is an iron-based agent with no theoretical increased risk of NSF. It is a bloodpool agent and has shown utility in vascular MRI. Use of ferumoxytol for non-vascular indications should be avoided due to its high cost and the uncertainty of incremental benefit from its use. The final determination regarding its suitability for use as a contrast agent is the responsibility of the individual divisions/protocoling physicians.

**Pregnancy**

Gadolinium chelates may accumulate in the amniotic fluid, and the potential effects on the pregnancy are unknown. As a result, GBCA administration is contraindicated in pregnant or potentially pregnant patients. If it is felt necessary to administer a GBCA to such a patient, this process is managed identically to that described for patients with category III renal dysfunction, as above.

**Breast-feeding mothers**

Given the tiny amount of GBCA excreted in breast milk, the even smaller amount expected to be absorbed by a breast-feeding infant’s GI tract, and the absence of any evidence of toxicity to breast-feeding infants in the literature, administration of GBCA at typical doses is considered safe in breast-feeding mothers. If a breast-feeding mother remains concerned about potential ill effects, she may express and discard breast milk (“pump and dump”) for 24 hours following GBCA administration to further reduce the already small risks associated with GBCA administration.

**Reference**

ACR Manual on Contrast Media v10.1
I. Pregnant or Breast Feeding patient

1. Pregnant or Potentially Pregnant patients (1)

Iodinated contrast agents

Diagnostic iodinated contrast media have been shown to cross the human placenta and enter the fetus when given in the usual clinical doses. In-vivo tests in animals have shown no evidence of either mutagenic or teratogenic effects with low-osmolar contrast media. However, no well-controlled studies of the teratogenic effects of these media in pregnant women have been performed.

For those patients who are known to be pregnant or may be pregnant and for whom iodinated IV or (or internal) contrast enhancement is most appropriate for performance of the CT examination, there is no need to get signed, informed consent to use contrast media. The data does not demonstrate mutagenic effects, fetal thyroid dysfunction or other biological effects, including renal insufficiency. According to the ACR manual on contrast media, Version 10.1 (2015), “given that there are no available data to suggest any potential harm to the fetus from exposure to iodinated contrast medium by maternal IV or intra-arterial injection, we cannot recommend routine screening for pregnancy prior to contrast media use.” This recommendation is also supported by the FDA classification of most iodinated contrast as Category B medications. Please also see departmental policy on use of ionizing radiation in pregnant or potentially pregnant patients.

Gadolinium based contrast agents

Gadolinium chelates may accumulate in the amniotic fluid, and the potential effects on the pregnancy are unknown. As a result, GBCA administration is contraindicated in pregnant or potentially pregnant patients. If it is felt necessary to administer a GBCA to such a patient, this process is managed identically to that described for patients with category III renal dysfunction, as above, in the previous section on Gadolinium Contrast Use.

2. Breast Feeding Patients(1)

Iodinated contrast agents

The available literature on the excretion into breast milk of iodinated contrast media and the gastrointestinal absorption of these agents from breast milk is very limited. However, several studies have shown that the expected dose of contrast medium absorbed by an infant from ingested breast milk is extremely low. Therefore, it is safe for the mother and infant to continue breast-feeding after receiving iodinated contrast agents.
informed decision to temporarily stop breast-feeding should be left up to the mother after these facts are communicated. If the mother remains concerned about any potential ill effects to the infant, she may abstain from breast-feeding from the time of contrast administration for a period of 12-24 hours. There is no value to stop breast-feeding beyond 24 hours. The mother should be told to express and discard breast milk from both breasts during that period.

**Gadolinium based contrast agents**

Given the tiny amount of GBCA excreted in breast milk, the even smaller amount expected to be absorbed by a breast-feeding infant's GI tract, and the absence of any evidence of toxicity to breast-feeding infants in the literature, administration of GBCA at typical doses is considered safe in breast-feeding mothers. If a breast-feeding mother remains concerned about potential ill effects, she may express and discard breast milk ("pump and dump") for 24 hours following GBCA administration to further reduce the already small risks associated with GBCA administration.
I. Pediatric Considerations

IV Iodinated Contrast Kidney Screening Pediatric CT (in general applies to patients ≤16 years)

General Procedures
1. Check the computer for prior SCr value for all patients.
2. Administer the CT screening questionnaire.
3. If the history of significant kidney disease question is answered “no” and/or e-GFR is normal, then administer Isovue 300 (unless radiologists requests Isovue 370) per standard protocol weight-based protocol.
4. If the history of kidney disease question is answered “yes”, a Cr POC must be ordered unless there is a SCr result available within the last 6 months. Draw SCr and calculate e-GFR using the appropriate formula for age.
   a. SCr within 6 months of contrast administration is suitable for any outpatient without an acute history needing e-GFR calculation.
5. If e-GFR >60 ml/min/1.73 m2, administer Isovue per standard protocol.

Positive response to the history of kidney disease question and/or reduced e-GFR
1. If e-GFR <60 and >30 ml/min/1.73 m2
   a. Contact radiologist to review
   b. Administer Isovue at standard dose (2ml/kg) - 50% reduced dose (1ml/kg) based on the scan indication
   c. Nursing or MD will notify the ordering provider of e-GFR <60 ml/min/1.73 m2 and suggest consultation with nephrologist/urologist. Radiologist should be available to speak to ordering provider as well if needed.
   d. Document action in a nursing note.
   e. If contrast is warranted administer Isovue at standard dose (≤2ml/kg) per the scan indication
2. If e-GFR <30 ml/min/1.73 m2, or patients with acute kidney failure
   a. Notify radiologist.
   b. Consider non-contrast CT
   c. Nursing or MD will contact the ordering provider to request consult with nephrologist/urologist. A formal consult must be completed prior to any IV iodinated contrast administration. Rescheduling may be necessary. Radiologist will be available to speak to ordering provider if needed.
   d. Document action taken in a nursing note.

Special Populations
1. All ICU patients must have a SCr drawn and e-GFR calculated within 24 hours of IV contrast administration.
2. Patients on long-term hemodialysis do not require a SCr to be drawn. Standard dose of Isovue will be given per standard protocol. Referring service should be notified prior to administration.
Emergency patients
The ordering physician can choose to bypass screening in an emergency and have IV contrast administered without screening. This screening process bypass must be documented by the nurse, technologist or the ordering physician. The ordering physician’s name must be included in the documentation.

Use of Serum Creatinine to evaluate renal function
1. Glomerular Filtration Rate (GFR) or Creatinine Clearance (CrCl) is calculated using the appropriate calculation equation depending upon serum creatinine testing method:

   a. Serum Creatinine use:
      i. No calculation for patients less than 1 year of age.

      ii. Use serum creatinine to evaluation renal function; should be < 0.54mg/dL.

   ii. For patients 1 to 16 years old
      Use the “Bedside Schwartz Equation”:
      \[(0.413 \times \text{Height}) / \text{SCr}\]

Age = age in years
SCr = serum creatinine concentration in mg/dL
Height = height/length in centimeters
I. Hydration protocol

The major preventive action to mitigate the risk of contrast-induced nephropathy is to provide intravenous volume expansion prior to contrast medium administration. The ideal infusion rate and volume is unknown, but isotonic fluids are preferred (Lactated Ringer’s or 0.9% normal saline).

1. Protocols:
   a. Inpatients (1):
      1. 0.9% saline at 100 mL/hr, beginning 6-12 hours before and continuing 4-12 hours after iodinated contrast administration
      OR
      2. 15 mL/kg of 0.9% saline IV per hour for 6 hours prior to iodinated contrast administration
   b. Outpatients:
      Outpatients who need hydration prior to and after contrast administration should make arrangements to have this performed by the referring physician in his/her clinic. We cannot provide intravenous or oral hydration to patients in the radiology department.
   c. Oral Hydration:
      Oral hydration can be utilized but it is considered less effective than intravenous hydration.
I. Non-vascular Contrast Media

Contrast media may be administered into the body through the gastrointestinal tract, genitourinary tract, cutaneous fistulae, lymphatics, and intrathecal space. Adverse reactions to non-vascular contrast agents are rare; however, the appropriate management of contrast media in this setting is described in this section.

II. Barium sulfate: Barium contrast agents are frequently used for outpatient conventional fluoroscopic gastrointestinal studies and as an oral agent for some abdominal/pelvic CT and MRI scans (Redicat, Volumen).

1. **Complications:**
   a. Allergic-like reactions to Barium are exceedingly rare. If a patient reports a history of allergic-like reaction to Barium, then an alternate intraluminal agent (Isovue or Gastrografin) may be substituted. Alternatively, if the reported reaction is mild, the patient may undergo a standard steroid pre-medication (see pages 6-8).
   b. Leakage into the pleural space, mediastinum, or peritoneal cavity: Barium leakage can lead to mediastinitis or peritonitis and is contraindicated in situations where extraluminal leakage is possible.
   c. Aspiration: While Barium is generally inert when aspirated, large volume aspiration can lead to inflammation or pneumonia and therefore should be avoided in patients at risk for aspiration.

III. Iodinated contrast media: Water-soluble iodinated contrast media agents which are specifically designed for enteric opacification can be used for certain indications. These include, but not limited to, suspected bowel perforation, leak, or to confirm feeding tube position.

1. **Complications:**
   a. High-osmolar contrast media agents, e.g. Gastrografin: these agents are hypertonic and if aspirated can cause a life-threatening pulmonary edema and pneumonitis. These agents are contraindicated in patients at risk for aspiration. In these patients, low-osmolar contrast media agents, e.g. Isovue, should be substituted.
   b. Allergic-like reactions to luminal administration of iodinated contrast media are rare. Nonetheless, the potential for systemic absorption of iodinated contrast media exists. Therefore, patients with a history of allergic like reaction to contrast media should be treated the same as if receiving intravenous dosing and undergo steroid pre-medication if appropriate (see pages 6-8).
References

Appendix A

Frequently Asked Questions Regarding Pretreatment in Pediatric and Adult Patients with a History of Allergy-like Reactions to Iodinated Contrast

1. If a patient has a prior reaction (mild/moderate) to contrast media, should we generally begin a pre-treatment regimen?
   Yes, a pretreatment regimen with steroids should be prescribed.

2. If a patient has a mild or moderate allergy to shellfish, should we begin a pretreatment regimen?
   No.

3. If a patient has multiple allergies but no documented reaction to iodinated contrast media, should we begin a pretreatment regimen?
   This is a controversial area. In general, no, but a strong history of allergies should increase awareness of the risk for reaction. In most cases, there is no need to avoid injection of contrast media in a patient with multiple mild or moderate allergies.

4. If a patient has well-controlled asthma but no documented reaction to iodinated contrast media, should we begin a pretreatment regimen?
   No, patients with a history of well-controlled asthma do not require premedication. Patients who are actively symptomatic (i.e., currently using their inhaler) from their asthma should be premedicated or an alternate test should be considered.

5. If a patient has a remote history of an allergic reaction to contrast media, but has had intervening, uneventful, contrast enhanced scans without a prep, should they receive a pretreatment regimen with steroids?
   No, in general, but these patients remain at risk for an adverse reaction. This is a controversial area.

6. If a patient with a prior contrast media reaction has undergone a steroid prep, what is their risk for a reaction?
   The risk is lowered but a breakthrough reaction may occur.

7. If a patient has had a severe and life-threatening reaction to contrast media (such as anaphylaxis) should we pretreat them?
   We should avoid administration of iodinated contrast media to such patients. An alternative imaging procedure should be considered. If a contrast enhanced scan is deemed absolutely necessary, a steroid prep should be given.
8. If a patient has had a steroid prep that differs from the Duke steroid prep, should we cancel the study and reschedule with a Duke prep?
No. There are several appropriate steroid preps that have been recommended. It is not clear whether one prep is advantageous over another. In these scenarios, consult the radiologist.
If all scheduled doses of a full steroid prep (12-13 hours) have been given but the timing is off by 2-3 hours, no consultation is required and the scan can be performed.

9. If a patient has had a prior breakthrough reaction, should they be prevented from having another contrast-enhanced exam?
The answer depends on the severity of the reaction.
Prior moderate or severe breakthrough reaction (anaphylaxis, laryngeal edema, hypotension): The patient should in general not be exposed to the same class of contrast (iodinated / gadolinium), regardless of premedication
Prior mild breakthrough reaction (itching, rash, hives): The patient can safely receive contrast if pre-medicated. An individual radiologist may elect to not perform the examination in this setting. This decision should be coordinated such as during ordering/scheduling process.

10. What is the likelihood that a patient will have a severe contrast reaction?
Patients with no risk factors have a risk of 4 in 10,000
Patients with a history of a prior contrast reaction have a risk of 18 in 10,000
Patients with a history of asthma have a reported risk of 23 in 10,000, but this data is likely somewhat skewed.
Patients with a history of a prior contrast reaction that are pre-medicated have a theoretical risk that is similar to someone with no risk factors. This has not been confirmed experimentally.

11. If someone has a reaction history to iodinated contrast, should they be pre-medicated before gadolinium contrast exposure (or vice versa)?
No.

12. What is the definition of a mild, moderate, and severe reaction? Are all adverse events considered contrast media reactions?
The definitions are not set in stone, but these are the most commonly published categories:
a. Mild (prep needed) – Rash, scattered hives, mild facial swelling, sneezing, cough, nasal stuffiness
b. Moderate (prep needed) – Mild laryngeal edema (“scratchy throat”, hoarseness), without dyspnea, wheezing without hypoxia, diffuse urticaria, significant facial swelling
c. Severe (avoid test altogether; if no other option, prep needed) – Severe respiratory distress, moderate or severe laryngeal edema, cardiopulmonary arrest, anaphylactic shock (hypotension and tachycardia)
d. Not an allergic-like reaction (no prep needed) – Nausea, flushing, vomiting, sensation of warmth
13. **What is the minimum length of an effective emergency prep?**
At least four hours are required for efficacy. The data supporting this are scant, but it is known that 1 and 2 hour steroid preps are ineffective. In cases where the clinical urgency demands it (e.g., trauma, aortic dissection, etc.), emergency preps shorter than 4 hours may be used at the Radiologist’s discretion.

14. **What do we do for a patient on chronic steroids?**
There is no data on this. We recommend the following: If a patient is getting more than the equivalent of 150 mg prednisone daily, no additional steroids are needed; they may be managed as though they had received a standard steroid prep. If the patient is getting less than 150 mg prednisone equivalents daily, supplement the daily dose with enough additional steroids to reach 150 mg. When doing this, discuss the situation with the clinical service so they understand our recommendation, consent to the altered steroid dose, and avoid overdosing the patient.
Appendix B

Basic Management of Adverse Reactions to Contrast Media

Adults:

**ALL ADVERSE EVENTS**
1. Stay calm
2. Obtain vital signs
3. Get help
4. Communicate with the patient (before and after treatment)
5. At conclusion, call referring physician
6. At conclusion, document in the medical record

**URTICARIA:**
1. No treatment needed in most cases
2. If severe: Diphenhydramine (Benadryl) 25-50 mg PO, IM, or IV
3. Patients receiving Benadryl need a driver

**LARYNGEAL EDEMA:**
1. Call a code (115)
2. Oxygen 10L/min by facemask
3. ADULT Epi Kit: 0.3 mL IM (1:1000 sol) repeat every 5-15 min up to 3 times. Available on Omnicell medication cart. IM is the preferred initial treatment route.
4. Epinephrine 1-3 mL IV (1:10,000 sol); inject slowly up to 10 mL
5. Do not intubate. Use bag-mask ventilation if needed.

**ANGIOEDEMA (DIFFUSE ERYTHEMA AND HYPOTENSION)**
1. Call a code (115)
2. Oxygen 10L/min by facemask
3. ADULT Epi Kit: 0.3 mL IM (1:1000 sol) repeat every 5-15 min up to 3 times. Available on Omnicell medication cart. IM is the preferred initial treatment route. Note that with profound hypotension, decreased peripheral perfusion may limit IM absorption.
4. Epinephrine 1-3 mL IV (1:10,000 sol); inject slowly up to 10 mL
5. Do not intubate. Use bag-mask ventilation if needed.
6. Isotonic IV fluids (normal saline or Lactated Ringer’s)
   - One or more liters wide open
7. Raise legs 60 degrees
8. Remove compression if present

**MILD / MODERATE BRONCHOSPASM**
1. Oxygen 10L/min by facemask
2. Albuterol 2-3 puffs with spacer (If spacer available)
3. Do not intubate. Use bag-mask ventilation if needed.
4. See below if condition worsens
MODERATE/SEVERE BRONCHOSPASM:
1. Call a code (115)
2. Oxygen 10L/min by facemask
3. ADULT Epi Kit: 0.3 mL IM (1:1000 sol) repeat every 5-15 min up to 3 times. Available on Omnicell medication cart. IM is the preferred initial treatment route.
4. Epinephrine 1-3 mL IV (1:10,000 sol); inject slowly up to 10 mL
5. Do not intubate. Use bag-mask ventilation if needed

HYPOTENSION WITH TACHYCARDIA (ANAPHYLACTIC SHOCK):
1. Call a code (115)
2. Oxygen 10L/min by facemask
3. ADULT Epi Kit: 0.3 mL IM (1:1000 sol) repeat every 5-15 min up to 3 times. Available on Omnicell medication cart. IM is the preferred initial treatment route. Note that with profound hypotension, decreased peripheral perfusion may limit IM absorption
4. Epinephrine 1-3 mL IV (1:10,000 sol); inject slowly up to 10 mL
5. Do not intubate. Use bag-mask ventilation if needed
6. Isotonic IV fluids (normal saline or Lactated Ringer’s)
   • One or more liters wide open
7. Raise legs 60 degrees
8. Remove compression if present

HYPOTENSION WITH BRADYCARDIA • VASOVAGAL REACTION
1. Oxygen 10L/min by facemask
2. Raise legs 60 degrees
3. Remove compression
4. Medications not normally needed
5. If persistent:
   Isotonic IV fluids (normal saline or Lactated Ringer’s)
   One or more liters wide open
6. Atropine 0.6-1.0 mg IV slowly into running fluids, repeat up to 3 mg total
7. Call a code if persistent hypotension (115)

HYPERTENSION, SEVERE (Diastolic BP > 12 mmHg; systolic BP > 200 mm Hg):
1. Oxygen 10L/min by facemask
2. Labetalol 20 mg IV; administer slowly over 2 mins; double dose every 10 min (e.g. 40 mg 10 min later, 80 mg 10 min after that)
3. Watch for iatrogenic bradycardia or heart block
4. If labetalol is not available:
   1. Furosemide (Lasix) 20-40 mg IV slowly over 2 min
   2. Nitroglycerine 0.4 mg SL; repeat every 5-10 min

PULMONARY EDEMA:
1. Oxygen 10L/min by facemask
2. Elevate head
3. Stop IV fluids
4. Furosemide (Lasix) 20-40 mg IV slowly over 2 min
Pediatrics:

ALL ADVERSE EVENTS
1. Stay calm
2. Obtain vital signs
3. Get help
4. Communicate with the patient (before and after treatment)
5. At conclusion, call referring physician
6. At conclusion, document in the medical record

URTICARIA:
1. No treatment needed in most cases
2. If severe: Diphenhydramine (Benadryl) 1 mg/kg (max 50 mg) PO, IM, or IV slowly over 1-2 min
3. Patients receiving Benadryl need a driver

LARYNGEAL EDEMA:
1. Call a code (115)
2. Oxygen 6-10L/min by facemask
3. 15 - 30 kg: PEDIATRIC Epi Kit--0.15 mL IM (1:1000 sol) repeat every 5-15 min up to 3 times. Available on Omnicell medication cart. IM is the preferred initial treatment route.
   < 15 kg: Epinephrine 0.01 mL/kg IM (1:1000 sol); max single dose of 0.30 mL (0.3 mg); can repeat every 5-15 min up to 1 mL total dose
   > 30 kg: use ADULT Epi Kit, as above
4. Epinephrine 0.1 mL/kg IV (1:10,000 sol); inject slowly, max single dose of 1 mL (0.1 mg); can repeat every 5-15 min up to 1 mg total dose
5. Do not intubate. Use bag-mask ventilation if needed.

ANGIOEDEMA (DIFFUSE ERYTHEMA AND HYPOTENSION)
1. Call a code (115)
2. Oxygen 6-10L/min by facemask
3. 15 - 30 kg: PEDIATRIC Epi Kit--0.15 mL IM (1:1000 sol) repeat every 5-15 min up to 3 times. Available on Omnicell medication cart. IM is the preferred initial treatment route.
   < 15 kg: Epinephrine 0.01 mL/kg IM (1:1000 sol); max single dose of 0.30 mL (0.3 mg); can repeat every 5-15 min up to 1 mL total dose
   > 30 kg: use Adult Epi Kit, as above
   Note that with profound hypotension, decreased peripheral perfusion may limit IM absorption
4. Epinephrine 0.1 mL/kg IV (1:10,000 sol); inject slowly, max single dose of 1 mL (0.1 mg); can repeat every 5-15 min up to 1 mg total dose
5. Do not intubate. Use bag-mask ventilation if needed.
6. Isotonic IV fluids (normal saline or Lactated Ringer’s)
   • One or more liters wide open
7. Raise legs 60 degrees
8. Remove compression if present

MILD BRONCHOSPASM
1. Oxygen 6-10L/min by facemask
2. Albuterol 2-3 puffs with spacer (If spacer available)
3. Do not intubate. Use bag-mask ventilation if needed
4. See below if condition worsens

MODERATE/SEVERE BRONCHOSPASM:
1. Call a code (115)
2. Oxygen 6-10L/min by facemask
3. 15 - 30 kg: PEDIATRIC Epi Kit--0.15 mL IM (1:1000 sol) repeat every 5-15 min up to 3 times. Available on Omnicell medication cart. IM is the preferred initial treatment route. 
   < 15 kg: Epinephrine 0.01 mL/kg IM (1:1000 sol); max single dose of 0.30 mL (0.3 mg); can repeat every 5-15 min up to 1 mL total dose
   > 30 kg: use Adult Epi Kit, as above
4. Epinephrine 0.1 mL/kg IV (1:10,000 sol); inject slowly, max single dose of 1 mL (0.1 mg); can repeat every 5-15 min up to 1 mg total dose
5. Do not intubate. Use bag-mask ventilation if needed.

HYPOTENSION WITH TACHYCARDIA (ANAPHYLACTIC SHOCK):
1. Call a code (115)
2. Oxygen 6-10L/min by facemask
3. 15 - 30 kg: PEDIATRIC Epi Kit--0.15 mL IM (1:1000 sol) repeat every 5-15 min up to 3 times. Available on Omnicell medication cart. IM is the preferred initial treatment route. 
   < 15 kg: Epinephrine 0.01 mL/kg IM (1:1000 sol); max single dose of 0.30 mL (0.3 mg); can repeat every 5-15 min up to 1 mL total dose
   > 30 kg: use Adult Epi Kit, as above
   Note that with profound hypotension, decreased peripheral perfusion may limit IM absorption
4. Epinephrine 0.1 mL/kg IV (1:10,000 sol); inject slowly, max single dose of 1 mL (0.1 mg); can repeat every 5-15 min up to 1 mg total dose
5. Do not intubate. Use bag-mask ventilation if needed.
6. Isotonic IV fluids (normal saline or Lactated Ringer’s)
   • One or more liters wide open
7. Raise legs 60 degrees
8. Remove compression if present
HYPOTENSION WITH BRADYCARDIA • VASOVAGAL REACTION

1. Oxygen 6-10L/min by facemask
2. Raise legs 60 degrees
3. Remove compression if present
4. If mild, medications not normally needed
5. If persistent: Call a code (115)
6. Isotonic IV fluids (normal saline or Lactated Ringer’s)
7. Atropine 0.2 mL/kg of 0.1 mg/mL solution IV slowly in running fluids; minimum single dose 0.1 mg; maximum single dose 0.6-1.0 mg; maximum total dose 1 mg for infants and children, 2 mg for adolescents

PULMONARY EDEMA:

1. Oxygen 6-10L/min by facemask
2. Elevate head
3. Stop IV fluids
4. Furosemide (Lasix) 0.5-1.0 mg/kg; over 2 min; maximum 40 mg
EPI-KIT Guidelines

The new policy is that **IM administration will be given as the first option for all patients (even with existing lines) with anaphylactic or potentially anaphylactic reactions**. All department Omnicells now contain epi-pen equivalent kits for IM administration with instructions on each kit (see picture). There is an adult kit and a pediatric kit; the weight appropriate for the peds kit is on the kit.

There are Omnicell cabinets in every area of radiology where contrast is administered, except the offsite locations. They have drug boxes. The residents, fellows, and faculty do not have Omnicell access, so retrieving the kits will require nursing staff.

**Anaphylaxis Epinephrine Kits in Radiology**

- Kits will be added to all radiology Omnicells
- Other epinephrine formulations will be removed from the Omnicells *except* for Vascular Radiology which will keep 1:10,000
- Include everything needed for an IM epinephrine injection
- Intramuscular injection will be the standard route for treatment of anaphylaxis following contrast administration in radiology
- The code cart will remain as is; code dose epinephrine (1:10,000) should be pulled from the code cart
Pediatric Anaphylaxis Kit

Epinephrine Anaphylaxis Kit (PEDIATRIC)
Kit Contains: 1 vial Epinephrine (1mg/1mL); 1 syringe (1mL); 1 needle (25 G)

For Anaphylactic Reaction:
16-30 kg: Administer 0.15mg (0.15mL) epinephrine intramuscularly
DISCARD THE REMAINDER OF THE VIAL.
Appendix C

I. Oral Hypoglycemic Agents with Metformin

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic</th>
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<tr>
<td>Glucophage (XR); Glumetza; Riomet; Fortamet</td>
<td>Metformin</td>
</tr>
<tr>
<td>Glucovance</td>
<td>Metformin; Glyburide</td>
</tr>
<tr>
<td>Metaglip</td>
<td>Metformin; Glipizide</td>
</tr>
<tr>
<td>Actoplus Met</td>
<td>Metformin; Pioglitazone</td>
</tr>
<tr>
<td>Avandamet</td>
<td>Metformin; Rosiglitazone</td>
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<tr>
<td>Janumet</td>
<td>Metformin; Sitagliptin</td>
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II. Oral Hypoglycemic Agents without Metformin

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic</th>
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<td>Tolinase</td>
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<td>Tolbutamide</td>
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<tr>
<td>Diabinese</td>
<td>Chlorpropamide</td>
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<td>Glucotrol (XL)</td>
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<td>Amaryl</td>
<td>Glimepiride</td>
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<td>Miglitol</td>
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<tr>
<td>Januvia</td>
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