

Proton Pump Inhibitors: Intake Criteria

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The Basics

- Proton Pump Inhibitor Products
- The Injuries
- Intake Criteria

PPIs - Rx

Generic	Brand	FDA Approved	Manufacturer
Omeprazole	Prilosec	1989	AstraZeneca (London,UK / Delaware)
Lansoprazole	Prevacid	1995	Takeda Pharmaceuticals (Chuo-ku, Osaka - Japan)
Rabeprazole	AcipHex	1999	EISAI,Co.,Ltd. (Tokyo,Japan)
Pantoprazole	Protonix	2000	Pfizer (New York, NY)
Esomeprazole	Nexium	2001	AstraZeneca (London,UK/ Delaware)
Omeprazole/ Sodium Bicarbonate	Zegerid	2004	Salix Pharmaceuticals (Raleigh,NC)
Dexlansoprazole	Dexilant	2009	Takeda Pharmaceuticals (Chuo-ku, Osaka- Japan)
Esomeprazole/ Naproxen (NSAID)	Vimovo	2010	AstraZeneca (London,UK/ Delaware)

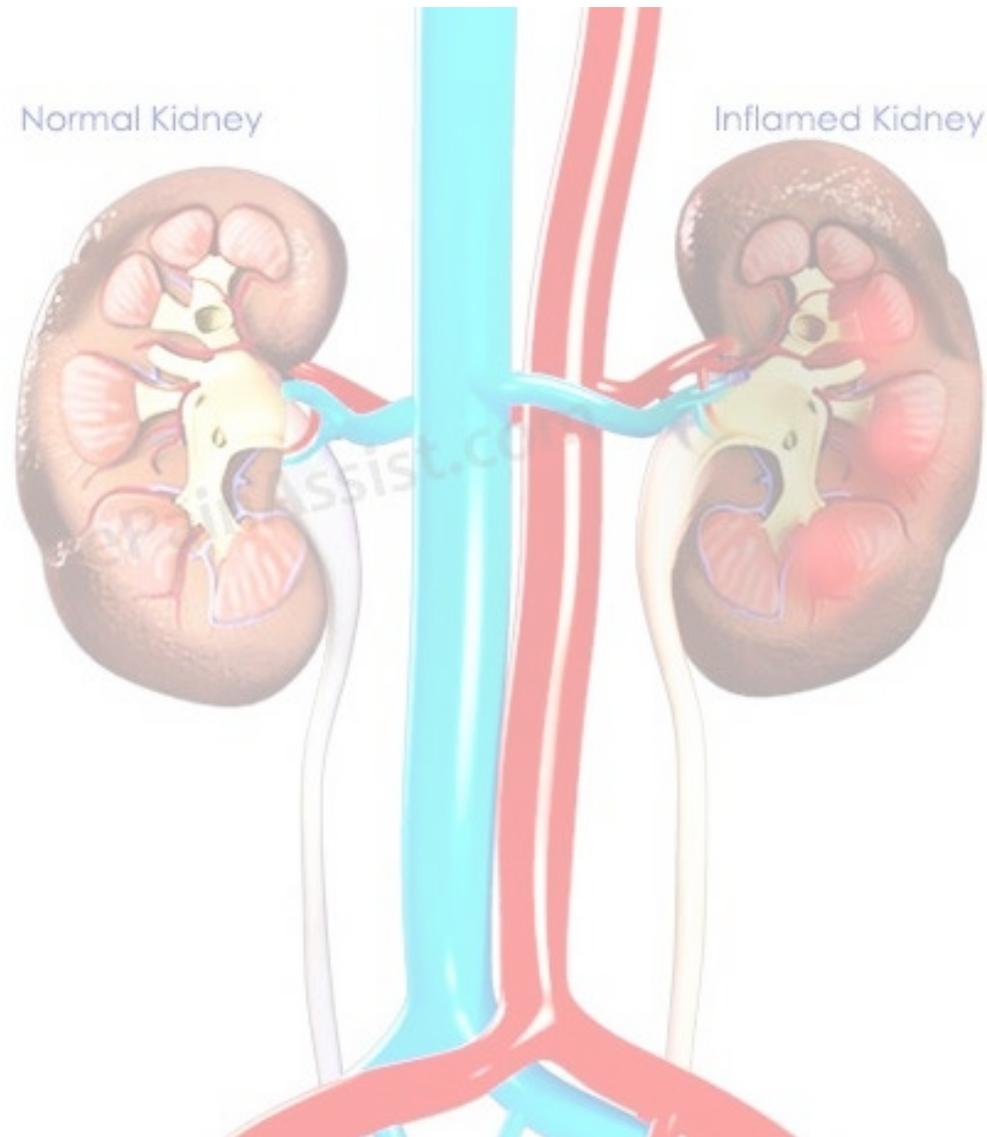
PPIs - OTC

Generic	OTC	FDA Approved	Manufacturer
Prilosec	Prilosec OTC	2003	Procter & Gamble (Cincinnati, OH)
Prevacid	Prevacid 24 Hour	2009	Novartis Consumer Health, Inc. (Parsippany, NJ)
Zegerid	Zegerid OTC	2010	Bayer (Leverkusen, Germany)
Nexium	Nexium 24 Hour	2014	Pfizer (New York, NY)

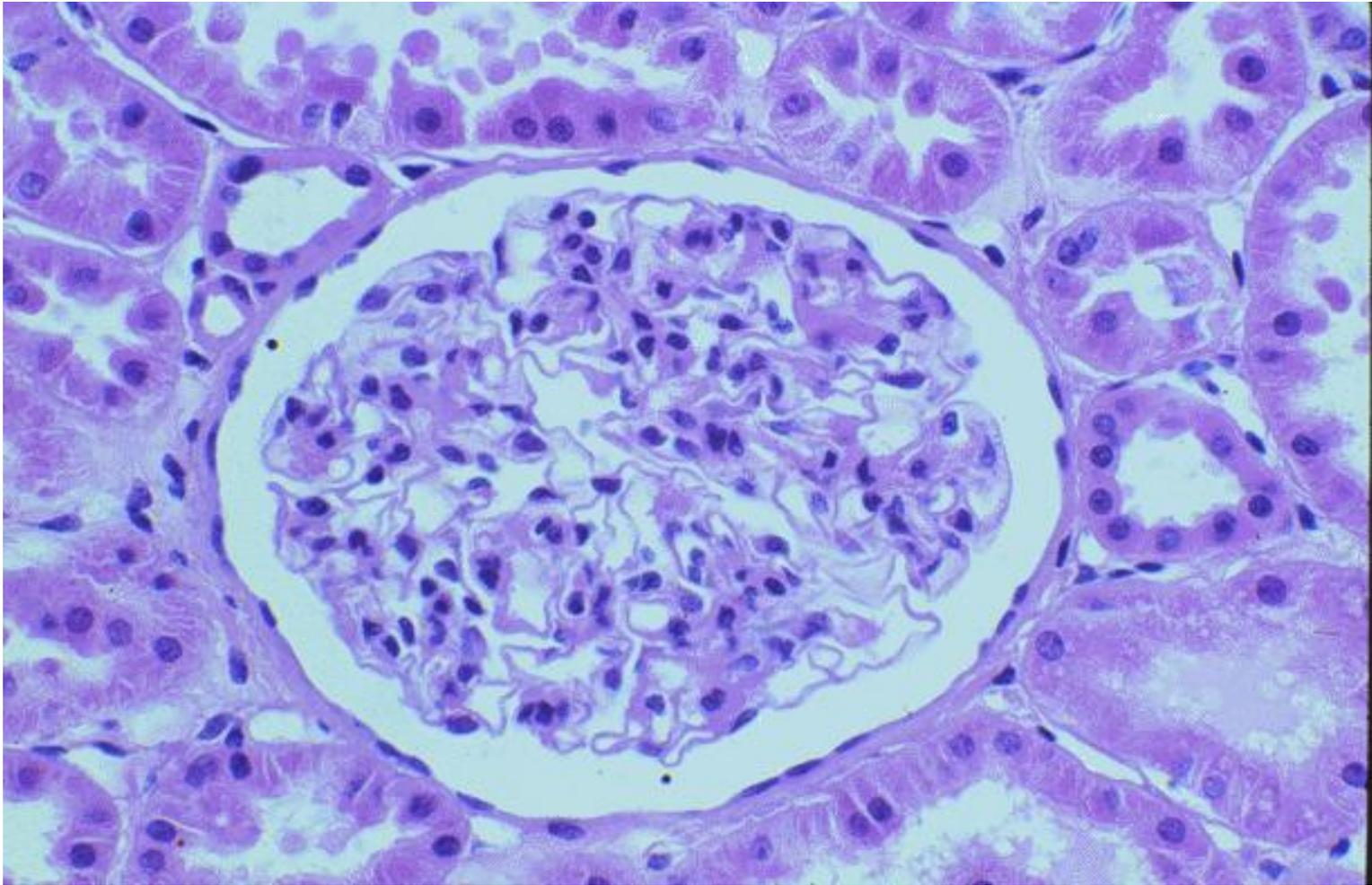
The Injuries - Kidneys

- **Acute Interstitial Nephritis** – An abrupt inflammation of the connective tissue inside the kidney, often causing acute kidney injury/acute renal failure. (see below) Allergic reactions and drug side effects are the usual causes.
- **Acute Kidney Injury (AKI)/Acute Renal Failure** – A sudden worsening in kidney function. Dehydration, a blockage in the urinary tract, or kidney damage can cause AKI, which may be reversible.
- **Chronic Kidney Disease (CKD) Stages 1-4/Chronic Renal Failure** – A permanent partial loss of kidney function. Diabetes and high blood pressure are the most common causes.
- **CKD Stage 5/End Stage Renal Disease (ESRD)** – Complete loss of kidney function, usually due to progressive CKD. People with CKD Stage 5/ESRD require regular dialysis for survival.
- **Diabetic Nephropathy** – High blood sugar from diabetes progressively damages the kidneys, eventually causing CKD. Protein in the urine (nephrotic syndrome) may also result.

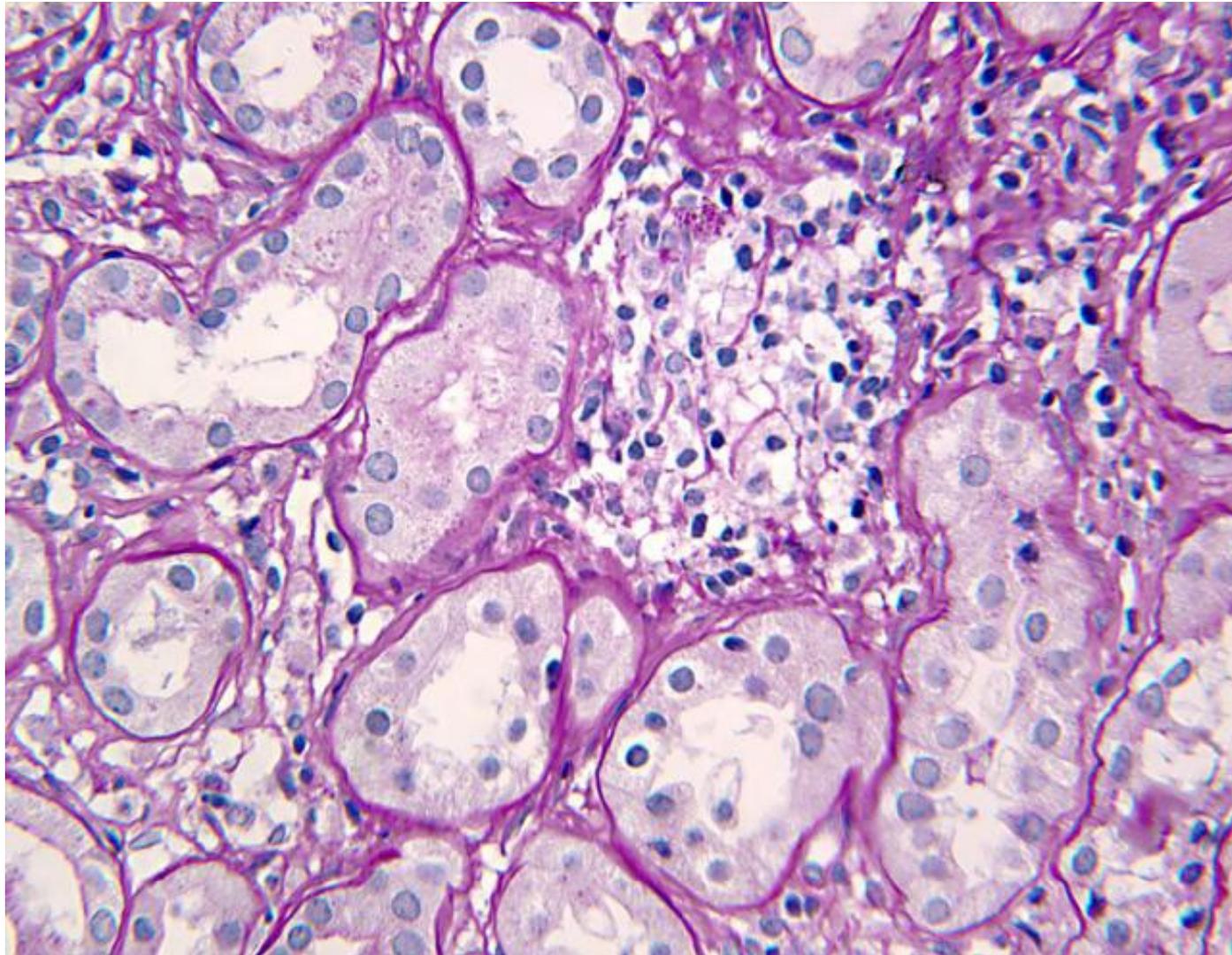
AIN



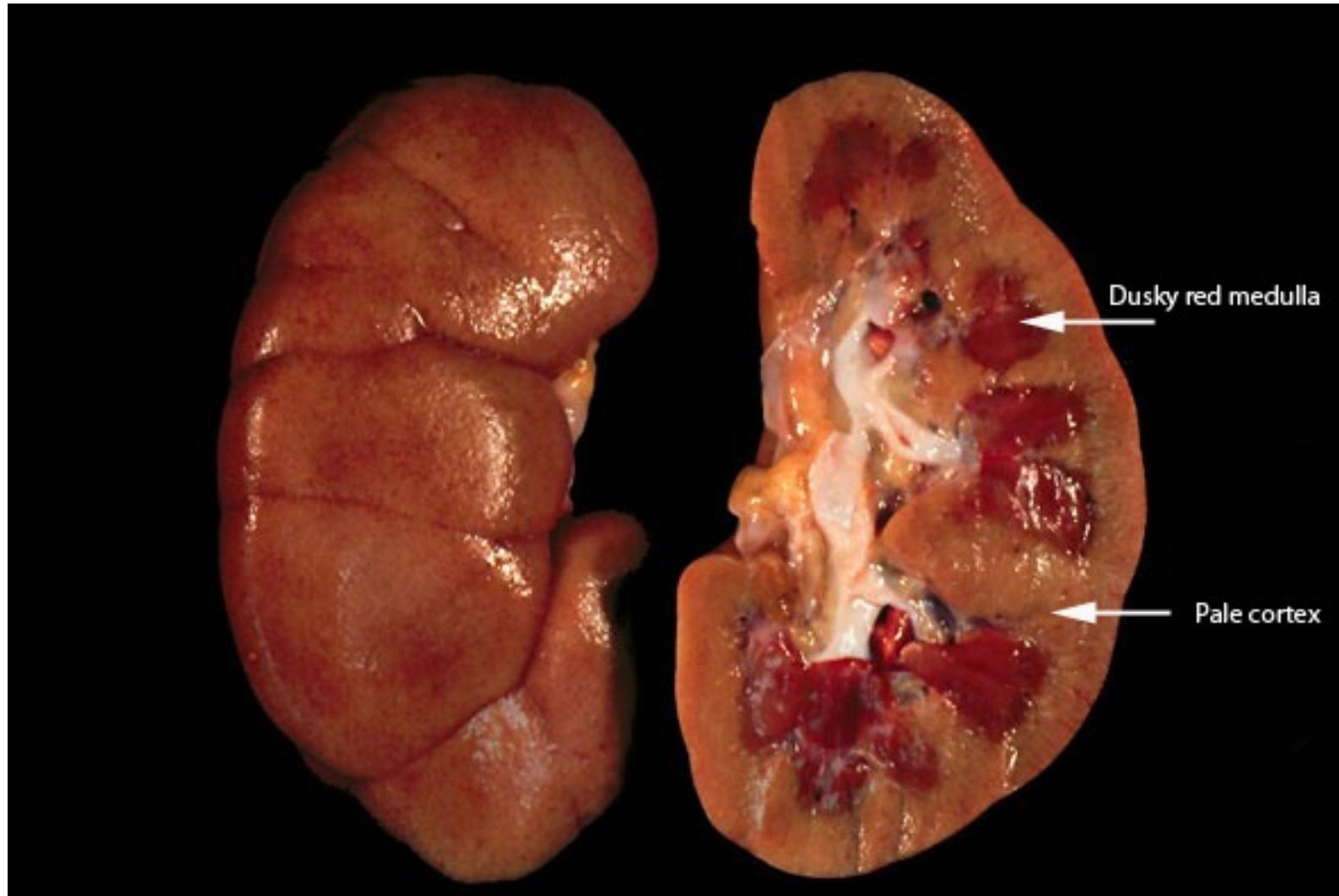
Normal Kidney Biopsy



AIN Biopsy



AKI



NOT the Injuries (1/2)

- **Glomerulonephritis** – Overactive immune system attacks the kidney, causing inflammation and some damage. Blood and protein in the urine are common problems that occur with glomerulonephritis. It can also result in kidney failure.
- **Hypertensive Nephrology** – Kidney damage caused by high blood pressure. CKD may eventually result.
- **Kidney Cancer** – Renal cell carcinoma is the most common cancer affecting the kidney. Smoking is the most common cause of kidney cancer.
- **Kidney Stones (nephrolithiasis)** – Minerals in urine form crystals (stones), which may grow large enough to block urine flow. It's considered one of the most painful conditions. Most kidney stones pass on their own but some are too large and need to be treated.
- **Minimal Change Disease** – A form of nephrotic syndrome in which kidney cells look almost normal under the microscope. The disease can cause significant leg swelling (edema). Steroids are used to treat minimal change disease.
- **Nephrogenic Diabetes Insipidus** – The kidneys lose the ability to concentrate the urine, usually due to a drug reaction. Although it's rarely dangerous, diabetes insipidus causes constant thirst and frequent urination.

NOT the Injuries (2/2)

- **Nephrotic Syndrome** – Damage to the kidneys causes them to spill large amounts of protein in the urine. Leg swelling (edema) may be a symptom.
- **Papillary Necrosis** – Severe damage to the kidneys can cause chunks of kidney tissue to break off internally and clog the kidneys. If untreated, the resulting damage can lead to total kidney failure.
- **Polycystic Kidney Disease** – A generic condition resulting in large cysts in both kidneys that impair their function.
- **Pyelonephritis** (infection of kidney pelvis) – Bacteria may infect the kidney, usually causing back pain and fever. A spread of bacteria from an untreated bladder infection is the most common cause of pyelonephritis.
- **Renal Cyst** – A benign hollowed-out space in the kidney.

Intake Criteria

- Use of (at least) one of PPIs:
 - Note that Nexium, Prilosec and Prevacid are the most prevalently used PPIs (see highlighted drugs in prior slides)
 - Brand Name vs. Generic considerations (discussed next)
- **During** usage of PPI, or **within 90 days** of stopping use, diagnosed with:
 - acute interstitial nephritis (AIN)
 - acute kidney injury (AKI)/kidney failure
 - chronic kidney disease
 - See prior slide re: definitions of injuries
- No prior history of kidney disease

Brand Name vs. Generic (1/2)

- Many Generics available, including ‘supermarket’ and ‘big box’ brands of OTCs
 - January 26, 2015 was first FDA approval of Nexium generic made by Ivax Pharmaceuticals, Inc., a subsidiary of Teva Pharmaceuticals
 - CostCo Prilosec OTC Generic:

KIRKLAND Signature
COMPARE TO **PRILOSEC® RX**
active ingredient

New smaller package size!

KIRKLAND Signature
OMEPRAZOLE
Delayed Release Tablets 20 mg

KIRKLAND Signature
OMEPRAZOLE
Delayed Release
Acid Reducer
Treats Frequent Heartburn!
Occurring 2 or More Days a Week

KIRKLAND Signature
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ONE TABLET EVERY 24 HOURS

Three 14-Day Courses of Treatment

Brand Name vs. Generic (2/2)

- Need to make state-by-state determination
 - Over-arching cases:
 - *PLIVA v. Mensing*, 131 S. Ct. 2567 (2011)
 - *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466 (2013)
 - A few example exceptions for consideration ...
 - Warning “Sameness” Requirement
 - *Fulgenzi v. PLIVA, Inc.*, 711 F.3d 578 (6th Cir. 2013)
 - PA
 - *Hassett v. Dafoe*, 2013 Pa. Super. Lexis 1683, slip op. (Pa. Super. July 29, 2013) & *In re Reglan Metoclopramide Litigation*, 2013 Pa. Super. Lexis 1688, slip op. (Pa. Super. July 29, 2013)
 - Cal.
 - *Conte v. Wyeth, Inc.*, 85 Cal. Rptr. 3d (Cal. App. 2009)

Kidney Tests in Med Recs to Find Injury

- **Urinalysis** – A routine test of the urine by a machine and often by a person looking through a microscope. Urinalysis can help detect infections, inflammation, microscopic bleeding, and kidney damage.
- **Kidney Ultrasound** – A probe placed on the skin reflects sound waves off the kidneys, creating images on a screen. Ultrasound can reveal blockages in urine flow, stones, cysts, or suspicious masses in the kidneys.
- **Computed Tomography (CT scan)** – A CT scanner takes a series of X-rays and a computer creates detailed images of the kidneys.
- **Urine and Blood Cultures** – If an infection is suspected, cultures of the blood and urine may identify the bacteria responsible. This can help target antibiotic therapy.
- **Ureteroscopy** – An endoscope (flexible tube with a camera on its end) is passed through the urethra into the bladder and ureters. Ureteroscopy generally cannot reach the kidneys themselves, but can help treat conditions that also affect the ureters.
- **Kidney Biopsy** – Using a needle inserted into the back, a small piece of kidney tissue is removed.

Specific OTC Issues

- Often Mixed Use (both Rx/OTC and different OTCs)
- OTC Proof of Use
 - OTC use noted in medical records?
 - Receipts
 - Purchase on credit card?
 - Member of pharmacy loyalty club?
 - Look for any way to verify regular use of OTC

Other Considerations

- SOL Considerations
 - Label Change Date: 12/19/14
 - **Only** adds AIN warning (not Acute Kidney Injury/Acute Renal Failure or Chronic Kidney Disease)
 - Do not let this date be your sole SOL guidance
 - Many states the SOL trigger = date of injury (or later linking of injury to product)
 - Linking of injury to product trigger date?: many January 2016 news stories linking PPIs with Chronic Kidney Disease (published as a result of JAMA Internal Medicine journal article)
- AIN occurring at the same time as taking Rx antibiotics (including penicillin, ampicillin, methicillin, sulfonamide medicines) -- Likely reject because specific causation; antibiotics as likely cause of AIN

Questions?

