Supplement 1: Nephrotoxic or renally eliminated medications that trigger inclusion*

Medications to Avoid in AKI		Medications to Adjust in AKI	Medications to Review in AKI
ACARBOSE†	METFORMIN†	ACYCLOVIR (>400mg Q12H)	ADEFOVIR†
ACETAZOLAMIDE†	METHOTREXATE†	ALLOPURINOL (>100mg Q24H)	AMOXICILLIN-CLAVULANATE
ACETOHEXAMIDE†	MOEXIPRIL†	AMANTADINE	AMPICILLIN
AMIKACIN	NABUMETONE†	AZTREONAM	BRETYLIUM
AMPHOTERICIN B†	NAPROXEN†	TRIMETHOPRIM/	CEFAZOLIN
BENAZEPRIL†	NITROFURANTOIN†	SULFAMETHOXAZOLE	CEFEPIME
CANDESARTAN†	NITROPRUSSIDE†	(>1 DS tablet BID)	CEFOTAXIME
CAPREOMYCIN†	OLMESARTAN†	CARBOPLATIN†	CEFOTETAN
CAPTOPRIL†	PANCURONIUM†	CISPLATIN†	CEFOXITIN
CELECOXIB†	PERINDOPRIL†	COLCHICINE (>0.6mg Q24H)	CEFTAZIDIME
CHLORPROPAMIDE†	PIROXICAM†	CYCLOSERINE	CEFUROXIME
CIDOFOVIR†	QUINAPRIL†	DAPTOMYCIN	CHLOROQUINE
CYCLOPHOSPHAMIDE†	RAMIPRIL†	DIDANOSINE	CIPROFLOXACIN
CYCLOSPORINE†	ROFECOXIB†	DIGITOXIN	CLOFIBRATE
CYTARABINE†	SITAGLIPTIN	DIGOXIN	DISOPYRAMIDE
DICLOFENAC SODIUM†	STREPTOMYCIN†	DOFETILIDE	DOXACURIUM INJ
DIFLUNISAL†	SULINDAC†	DORIPENEM	ETHAMBUTOL
ENALAPRIL†	TACROLIMUS†	EPTIFIBATIDE	FLECAINIDE
ENALAPRILAT†	TELMISARTAN†	ERTAPENEM	FLUCONAZOLE (>100mg Q24H)
ENOXAPARIN† (>30mg Q24H)	TETRACYCLINE†	ETOPOSIDE†	HYDROXYUREA†
ETODOLAC†	TOBRAMYCIN	FAMCICLOVIR	IDARUBICIN†
EXENATIDE†	TOLMETIN†	FLUCYTOSINE	INDINAVIR
FENOPROFEN†	TRANDOLAPRIL†	FOSCARNET	LAMIVUDINE
FLURBIPROFEN†	TRIMETREXATE†	GANCICLOVIR	LEVOFLOXACIN
FONDAPARINUX	VALDECOXIB†	IMIPENEM-CILASTATIN	MELPHALAN†
FOSINOPRIL†	VALSARTAN†	ITRACONAZOLE	METOCURINE
GALLAMINE†		LACOSAMIDE†	MIVACURIUM
GENTAMICIN INJ		MEROPENEM	MORPHINE†
GLYBURIDE†		METOCLOPRAMIDE†	NEOSTIGMINE†
IBUPROFEN†		MITOMYCIN†	NORFLOXACIN
IFOSFAMIDE†		PENICILLIN-VK	OFLOXACIN
IMMUNE GLOBULIN†		PENTOSTATIN†	PENICILLIN-G
INDOMETHACIN†		PRAMIPEXOLE†	PIPERACILLIN
IRBESARTAN†		PREGABALIN†	PYRAZINAMIDE
KETOPROFEN†		PROCAINAMIDE	QUINIDINE
KETOROLAC†		PYRIDOSTIGMINE	TEMOZOLOMIDE†
LISINOPRIL†		SOTALOL†	TENOFOVIR†
LITHIUM		STAVUDINE	TICARCILLIN
LOSARTAN†		TOPOTECAN†	TOCAINIDE
MELOXICAM†		VALACYCLOVIR	ZIDOVUDINE
MEPERIDINE†		VALGANCICLOVIR (>450mg Q24H)	
		VANCOMYCIN	
		VORICONAZOLE	

*Supplement 1's contents were determined by a committee of nephrologists, internists, and pharmacists using medication package inserts, textbooks (21, 22), and primary literature. We included medications that could contribute to AKI or have the potential for adverse effects with drug accumulation in AKI. Supplement 1 is limited to medications on VUH's formulary and is not intended to be reflective of all medications available.

† Medication only triggered inclusion for increasing serum creatinine.

Supplement 2: Definitions of pADES and ADEs attributable to Renal Medications*

A) Preventable Adverse Drug Events

Medication to Avoid administered for > 24 hours after AKI onset
Medication to Adjust or Review's dose or interval not adjusted for >24 hours if deemed clinically appropriate for renal function
Medication ineffective in low GFR continued for > 24 hours
SCr or serum drug levels not monitored if deemed clinically necessary

B) Lab Only Adverse Drug Events

Electrolytes	**Supratherapeutic drug levels**
Hypernatremia: Na > 145 mEq/L	Amikacin: EID Trough > 2mcg/ml
Hyponatremia: Na < 135 mEq/L	TD Trough > 10mcg/ml
Hyperkalemia: K > 5.3 mEq/L	Gentamicin/Tobramycin: EID Trough > 0.5mcg/ml
Hypokalemia: K < 3.5 mEq/L	TD Trough > 2mcg/ml
Hypoglycemia: Glucose <70mg/dl	Vancomycin: Trough >25mg/L
Severe: Glucose < 40mg/dl	Digoxin: Level > 1.7ng/ml
	Lithium: Level >1.2 mmol/L
	Procainamide: Level > 12mcg/ml

C) Adverse Drug Events

Bradyarrhythmia
HR < 60 bpm or Atropine for bradycardia

Hypotension
SBP < 90mmHg or
DPB < 60mmHg or
MAP < 65mmHg or
IV vasopressor use

QT Prolongation
QTc interval > 440msec

Cognitive changes/ somnolence
RASS $\leq$ -3 or documentation

Delirium
CAM-ICU + or documentation

Oversedation
Opiate antagonist for sedation or documentation

Symptomatic hypoglycemia
Glucose < 70mg/dl & administration of glucose source for documented symptoms

Pancreatitis
Amylase or Lipase > ULN & documentation

Anemia
Males: Hgb <13 g/dl
Females: Hgb < 12 g/dl

Lactic acidosis
Lactate > 4mmol/L

Major bleed
Hgb decrease $\geq$ 5g/dl with suspected site

Minor bleed
Hgb decrease 3- 4.9g/dl with suspected site

Neutropenia
ANC < 500 cells/mm^3

Thrombocytopenia
Plts < 150,000 cells/mm^3

Acute kidney injury
SCr change $\geq$ 0.5mg/dl in 48 hrs

Crystalurea
Urinary analysis

EPS/movement disorders: Documentation

Vision changes: Documentation

Hearing loss: Documentation

Tinnitus: Documentation

Renal replacement therapy: Documentation

Volume overload: Documentation

Respiratory depression: Documentation

Death: Documentation

Seizure: Documentation

Rash: Documentation

Diarrhea: Documentation

D) Therapeutic Failures

Subtherapeutic Drug Levels **Vancomycin** -Level drawn immediately prior to next ≤ 10mg/L -Level drawn early and calculated to be ≤ 10mg/L prior to the next dose -Level >3mg/dl below stated goal of 15mg/dl **Aminoglycosides** (Non-Extended Interval Dosing) -Peak or trough drawn correctly and > 10% below stated goal
Adverse patient outcome linked by adjudication committee to underdosing of drug in patients following AKI Recovery

* A committee of nephrologists, internists, and pharmacists compiled a list of possible adverse events using previous ADE literature, medication package inserts, and textbooks [21-26], using previously reported definitions, [11,23-27] when possible. Lab-only ADEs, a subcategory of ADEs, included critical value laboratory values attributable to an Supplement 1 medication that are associated with morbidity. [25] Thresholds for antibiotic supratherapeutic and subtherapeutic concentrations were selected based on prior publications. [28-30]

Supplement 3: Examples of Adverse Drug Events and Therapeutic Failures

Description of Adverse Drug Events during Acute Kidney Injury	Preventable
Significant ADE (n=2) An error that can cause patient symptoms that, while harmful to the patient, pose little or no threat to the patient's life function	
A patient was treated for restless leg syndrome with pramipexole 2mg daily. During AKI, involuntary myoclonic arm "jerks" were noted which resolved with improving renal function.	Y
A patient with pneumonia requiring intubation was treated with piperacillin/tazobactam during AKI. The patient developed a rash during treatment.	N
Serious ADE (n=47) An error that can cause signs/symptoms that are associated with a serious level of risk that is not high enough to be life-threatening but can cause persistent alteration of daily function	
A patient with a history of a pulmonary emboli was admitted for pneumonia and bridged with enoxaparin 1mg/kg every 12 hours. Enoxaparin was not adjusted during AKI, resulting in a gastrointestinal bleed from documented duodenal ulcers (hemoglobin decreased 3g/dl in 72 hours) requiring blood transfusion.	Y
A patient with a history of human immunodeficiency virus was admitted for herpes simplex virus groin lesions and treated with acyclovir 1g intravenously every eight hours. Acyclovir was dosed on actual, instead of ideal body weight (102kg vs 64kg), causing AKI secondary to crystaluria.	Y
Life-threatening ADE (n=18) An error that can cause signs/symptoms that if not treated would put the patient at risk of death	

A patient was admitted with a small bowel obstruction requiring bowel resection. During AKI, morphine PCA pump (no basal rate and 2mg every 15 minutes demand rate) caused oversedation and respiratory depression requiring intensive care unit transfer and non-invasive mechanical ventilation.	Y
A patient was admitted for a lower extremity wound from a motorcycle crash and treated with vancomycin 1500mg (15mg/kg) intravenously every eight hours without serum creatinine monitoring, resulting in a level of 72mg/dl thirty hours after the dose on day 3. The patient required hemodialysis, which was continued as an outpatient.	Y
Fatal ADE (n=1) An error that caused the patient's death	
A patient admitted for sickle cell pain crisis was treated with ketorolac 30mg intravenously every 6 hours and hydromorphone PCA. The patient experienced a major upper gastrointestinal bleed (hemoglobin decreased 4.3g/dl with source documented on endoscopy), acute chest syndrome requiring intubation, and AKI requiring continuous veno-venous hemodialysis. The patient died less than 48 hours after the gastrointestinal bleed of a pulseless electrical activity arrest.	Y

Description of Adverse Drug Events & Therapeutic Failures during Recovering Acute Kidney Injury	Preventable
Serious (n=9) An error that can cause signs/symptoms that are associated with a serious level of risk that is not high enough to be life-threatening but can cause persistent alteration of daily function	
A patient with penicillin allergy treated for staphylococcal endocarditis with vancomycin. Over adjustment of vancomycin during AKI recovery resulted in a trough of 35mg/dl and the dose was promptly held.	N
A patient with fungal endocarditis was treated with amphotericin B and flucytosine 1500mg orally every six hours. Abdominal pain and a computerized topography scan indicated colitis attributed to flucytosine's elevated peak because it was improperly adjusted for AKI.	Y
Life-threatening (n=5) An error that can cause signs/symptoms that if not treated would put the patient at risk of death	
A patient with heart failure was admitted for sotalol (80 mg orally every twelve hours) initiation to reduce implantable cardiac defibrillator shocks. During AKI, sotalol was not adjusted and caused hypotension (systolic blood pressure of 80mmHg) and QTc prolongation (531msec).	Y
A patient admitted for sepsis and AKI was empirically treated with an	Y

antibiotic regimen including vancomycin. Vancomycin was not adjusted during AKI recovery over the next 72 hours, resulting in a level of 6mg/dl four hours before the next scheduled dose.	
Fatal (n=1) An error that caused the patient's death	
A patient treated with levofloxacin monotherapy (750mg every 48 hours) for a sensitive *Stenotrophomonas* ventilator associated pneumonia during AKI. Levofloxacin was not adjusted during AKI recovery. After 4 days of sub-therapeutic antibiotic concentrations, the patient died of hypoxic respiratory failure on maximal ventilator support.	Y