**Association of Potentially Inappropriate Medication Classes with Mortality Risk Among Older Adults Initiating Hemodialysis**

**Potentially Inappropriate Medications in Dialysis**

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**Supplemental Table 1.** List of Medication within each Potentially Inappropriate Medication (PIM) Class

|  |  |
| --- | --- |
| **Drug Class** | **Generic Name** |
| Acetylcholinesterase Inhibitors | Echothiophate Iodide |
| Galantamine HBr |
| Pyridostigmine Bromide |
| Malathion |
| Rivastigmine |
| Rivastigmine Tartrate |
| Alpha-1 Blockers | Doxazosin Mesylate |
| Prazosin HCl |
| Terazosin HCl |
| Androgens | Methyltestosterone |
| Testosterone |
| Testosterone Cypionate |
| Testosterone Enanthate |
| Anticholinergics | Benztropine Mesylate |
| Chlorpromazine HCl |
| Darifnacin HBr |
| Dicyclomine HCl |
| Diphnoxylate HCl/Atropine |
| Fesoterodine Fumarate |
| Flavoxate HCl |
| Glycopyrrolate |
| Homatropine HBr |
| Hyoscyamine Sulfate |
| Methscopolamine Bromide |
| Opium/Belladonna Alkaloids |
| Orphenadrine Citrate |
| Orphenadrine/Aspirin/Caffeine |
| Oxybutynin |
| Oxybutynin Chloride |
| Propantheline Bromide |
| Scopolamine |
| Scopolamine HBr |
| Solifenacin Succinate |
| Tolterodine Tartrate |
| Trihexyphenidyl HCl |
| Tropsium Chloride |
| Antidepressants | Amitrip HCl/Chlordiazpoxide |
| Amitriptyline HCl |
| Amoxapine |
| Citalopram HBr |
| Clomipramine HCl |
| Desipramine HCl |
| Desvenlafaxine |
| Desvenlafaxine Succinate |
| Doxepin HCl |
| Duloxtine HCl |
| Escitalopram Oxalate |
| Fluoxetine HCl |
| Fluvoxamine Maleate |
| Imipramine HCl |
| Imipramine Pamoate |
| Levomilnacipran HCl |
| Milnacipran HCl |
| Nefazodone HCl |
| Nortriptyline HCl |
| Olanzapin/Fluoxetine HCl |
| Paroxetine HCl |
| Paroxetine/Amitriptyline HCl |
| Perphenazine/Amitriptyline HCl |
| Protriptyline HCl |
| Sertraline HCl |
| Trazodone HCl |
| Trimipramine Maleate |
| Venlafaxine HCl |
| Vilazodone HCl |
| Vortioxetine HBr |
| Antiemetics | Metoclopramide HCl |
| Prochlorperazine Edisylate |
| Prochlorperazine Maleate |
| Promethazine HCl |
| Promethazine HCl/Codeine |
| Promethazine/Phenyleph/Codeine |
| Antiepileptics | Acetozolamide |
| Carbamazepine |
| Clorazepate Dipotassium |
| Eslicarbazepine Acetate |
| Ethosuximide |
| Ezogabine |
| Felbamate |
| Fosphenytoin Sodium |
| Gabapentin |
| Gabapentin Enacarbil |
| Lacosamide |
| Lamotrigine |
| Levetiracetam |
| Magnesium Sulfate |
| Magnesium Sulfate in Water |
| Magnesium Sulfate/D5W |
| Oxcarbazepine |
| Perampanel |
| Phentermine/Topiramate |
| Phenytoin |
| Phenytoin Sodium |
| Phenytoin Sodium Extended |
| Pregabalin |
| Primidone |
| Rufinamide |
| Tiagabine HCl |
| Topiramate |
| Valproic Acid |
| Valproic Acid (Sodium Salt) |
| Vigabatrin |
| Zonisamide |
| Antihistamines | Acetaminophen/diphenhydramine |
| Carbinoxamine Maleate |
| Chlorpheniramine Maleate |
| Clemastine Fumarate |
| Cyproheptadine HCl |
| Dimnhydrinate |
| Diphenhydramine HCl |
| Diphenhydramine HCl/Zinc Acet |
| Doxylamine Succinate |
| Hydroxyzine HCl |
| Hydroxyzine Pamoate |
| Meclizine HCl |
| Phenylephrine/Bromopheniramine |
| Phenylephrine/Diphenydramine |
| Promthazine HCl |
| Promethazine HCl/Codeine |
| Promthazine/Phenyleph/Codeine |
| Antiinfective | Nitrofurantoin |
| Nitrofurantoin Macrocrystal |
| Nitrofurantoin Monohyd/M-Cryst |
| Antiparkinsons | Amantadine HCl |
| Benztropine Mesylate |
| Trihexyphenidyl HCl |
| Antipsychotics | Asenapine Maleate |
| Chlorpromazine HCl |
| Clozapine |
| Fluphenazine Decanoate |
| Fluphenazine HCl |
| Haloperidol |
| Haloperidol Decanoate |
| Haloperidol Lactate |
| Iloperidone |
| Lamotrigine |
| Loxapine Succinate |
| Lurasidone HCl |
| Olanzapine |
| Olanzapine Pamoate |
| Olanzapine/Fluoxetine HCl |
| Paliperidone |
| Paliperidone Palmitate |
| Perphenazine |
| Perphenazine/Amitriptyline HCl |
| Pimozide |
| Prochlorperazine Edisylate |
| Prochlorperazine Maleate |
| Quetiapine Fumarate |
| Risperidone |
| Risperidone Microspheres |
| Tetrabenzapine |
| Thioridazine HCl |
| Thiothixene |
| Trifluoperazine HCl |
| Ziprasidone HCl |
| Ziprasidone Mesylate |
| Antispasmodics | Dicyclomine HCl |
| Diphenoxylate HCl/Atropine |
| Homatropine HBr |
| Hyoscyamine Sulfate |
| Methscopolamine Bromide |
| Propanthline Bromide |
| Scopolamine |
| Scopolamine HBr |
| Antithrombotics | Aspirin/Dipyridamole |
| Dipyridamole |
| Barbiturates | Butalb/Acetaminophen/Caffeine |
| Butalbital/Acetaminophen |
| Butalbital/Aspirin/Caffeine |
| Codeine/Butalbital/ASA/Caffeine |
| Phenobarbital |
| Phenobarbital Sodium |
| Benzodiazepines | Alprazolam |
| Chlordiazepoxide HCl |
| Clobazam |
| Clonazepam |
| Clorazepate Dipotassium |
| Diazepam |
| Estazolam |
| Flurazepam HCl |
| Lorazepam |
| Midazolam HCl |
| Midazolam HCl/PF |
| Oxazepam |
| Temazepam |
| Triazolam |
| Central Alpha-1 Agonists | Clonodine |
| Clonodine HCl |
| Clonodine HCl/Chlorthalidone |
| Guanfacine HCl |
| Methyldopa |
| Reserpine |
| Corticosteroids | Acetic Acid/Hydrocortisone |
| Acyclovir/Hydrocortisone |
| Alclometasone Dipropionate |
| Budsonide |
| Ciprofloxacin/Hydrocortisone |
| Cortisone Acetate |
| Dexamethasone |
| Dexamethasone SOD Phosphate |
| Dexamethasone SOD Phosphate/PF |
| Fludrocortisone Acetate |
| Flurandrenolide |
| Hydrocortisone |
| Hydrocortisone SOD Succ/PF |
| Hydrocortisonee SOD Succinate |
| Methylprednisolone |
| Methylprednisolone Acetate |
| Methylprednisolone SOD Succ |
| Methylprednisolone SOD Succ/PF |
| Prednisolone |
| Prednisolone Acetate |
| Prednisolone SOD Phosphate |
| Prednisone |
| Diuretics | Acetazolamide |
| Aliskiren/Hydrochlorothiazide |
| Amiloride HCl |
| Amiloride/Hydrochlorothiazide |
| Atenolol/Chlorthalidone |
| Azilsartan Med/Chlorthalidone |
| Benazepril/Hydrochlorothiazide |
| Bumetanide |
| Captopril/Hydrochlorothiazide |
| Chlorothiazide |
| Chlorthalidone |
| Clonidine HCl/Chlorthalidone |
| Drospirenon/Estradiol |
| Enalapril/Hydrochlorothiazide |
| Eplerenone |
| Ethacrynate Sodium |
| Ethacrinic Acid |
| Fosinopril/Hydrochlorothiazide |
| Furosemide |
| Hydrochlorothiazide |
| Indapamide |
| Irbesartan/Hydrochlorothiazide |
| Lisinopril/Hydrochlorothiazide |
| Losartan/Hydrochlorothiazide |
| Methyclothiazide |
| Metolazone |
| Metoprolol/Hydrochlorothiazide |
| Moexipril/Hydrochlorothiazide |
| Olmesartan/Hydrochlorothiazide |
| Quinapril/Hydrochlorothiazide |
| Spironolactone |
| Torsemide |
| Triamterene |
| Triamterene/Hydrochlorothiazide |
| Valsartan/Hydrochlorothiazide |
| Estrogens | Desog-E.estradiol/E.Estradiol |
| Desogestrel-Ethinyl Estradiol |
| Drospirenone/Estradiol |
| Estradiol |
| Estradiol Acetate |
| Estradiol Cypionate |
| Estradiol Valerate |
| Estradiol Valerate/Dienogest |
| Estradiol/Levonorgestrel |
| Estradiol/Norethindrone Acetate |
| Estramustine Phosphate Sodium |
| Estrogens,Conj/Bazdoxifene |
| Estropipate |
| Ethinyl Estradiol/Drospirenone |
| Ethynodiol D-Ethinyl Estradiol |
| Etonogestrel/Ethinyl Estradiol |
| Levonorgestrel-Eth Estradiol |
| Levonorgestrel-Ethin Estradiol |
| Norelgestromin/Ethin.Estradiol |
| Noreth-Ethinyl Estradiol/Iron |
| Norethind Ac/Ethinyl Estradiol |
| Norethindrone A-E Estradiol |
| Norethindrone Ac-Eth Estradiol |
| Norethindrone-E.Estradiol-Iron |
| Norethindrone-Mestranol |
| Norgestimate-Ethinyl Estradiol |
| Norgestrel-Ethinyl Estradiol |
| H2 Receptor Blockers | Cimetidine |
| Cimetidine HCl |
| Famotidine |
| Famotidine in NaCl, Iso-Osm/PF |
| Famotidine/PF |
| Ibuprofen/Famotidine |
| Nizatidine |
| Ranitidine HCl |
| Ranitidine in 0.45% NaCl |
| Insulin | Hum Insulin NPH/Reg Insulin HM |
| Insulin Aspart |
| Insulin Detemir |
| Insulin Glargin,Hum.Rec.Anlog |
| Insulin Glulisine |
| Insulin Lispro |
| Insulin NPH Hum/Reg Insulin HM |
| Insulin NPH Hum Isophane |
| Insulin NPL/Insulin Lispro |
| Insulin Reg, Hum |
| Insulin Asp PRT/Insulin ASPART |
| NPH, Hum Insulin Isophane |
| Muscle Relaxants | Baclofen |
| Carisoprodol |
| Carisoprodol/Aspirin |
| Chlorzoxazone |
| Codeine/Carisopordol/Aspirin |
| Cyclobnzaprine HCl |
| Dantrolene Sodium |
| Metaxalone |
| Methocarbamol |
| Orphenadrine Citrate |
| Orphenadrine/Aspirin/Caffeine |
| Tizanidine HCl |
| Nonbenzodiazepines | Zaleplon |
| Zolpidem Tartrate |
| Non DHP CCB | Diltiazem HCl |
| Trandolapril/Verpamil HCl |
| Verapamil HCl |
| NSAID | Apremilast |
| Aspirin |
| Aspirin/Dipyridamole |
| Balsalazid Disodium |
| Bromfenac Sodium |
| Butalbital/Aspirin/Caffeine |
| Carisoprodol/Aspirin |
| Celecoxib |
| Codeine/Carisopordol/Aspirin |
| Diclofenac Epolamine |
| Diclofenac Potassium |
| Diclofenac Sodium |
| Diclofenac Sodium/Misoprostol |
| Diclofenac Submicronized |
| Diflunisal |
| Etanercept |
| Etodolac |
| Fenoprofen Calcium |
| Flurbiprofen |
| Flurbiprofen Sodium |
| Hydrocodone/Ibuprofen |
| Ibuprofen |
| Ibuprofen/Famotidine |
| Ibuprofen/Oxycodone HCl |
| Icatibant Acetate |
| Indomethacin |
| Ketoprofen |
| Leflunomide |
| Meclofenamate Sodium |
| Mefenamic Acid |
| Meloxicam |
| Mesalamine |
| Mesalamine w/ Cleansing Wipes |
| Methotrexate Sodium |
| Methotrexate Sodium/PF |
| Nabumetone |
| Naproxen |
| Naproxen Sodium |
| Naproxen/Esomprazole Mag |
| Nepafenac |
| Olsalazine Sodium |
| Orphenadrine/Aspirin/Caffeine |
| Oxaprozin |
| Oxycodone HCl/Aspirin |
| Pimecrolimus |
| Piroxicam |
| Salsalate |
| Sulfasalazine |
| Sulindac |
| Sumatriptan Succ/Naproxen SOD |
| Teriflunomide |
| Tolmetin Sodium |
| Zileuton |
| Opioids | Acetominophen with Codeine |
| Buprenorphine |
| Buprenorphine HCl |
| Buprenorphine HCl/Naloxone HCl |
| Butalbit/Actamin/Caffeine/Codeine |
| Butorphanol Tartrate |
| Codeine Sulfate |
| Codeine/Butalbital/ASA/Caffeine |
| Codeine/Carisopordol/Aspirin |
| DH Codeine BT/Acetaminophen/Caffeine |
| Diphnoxylate HCl/Atropine |
| Fentanyl |
| Fentanyl Citrate |
| Fentanyl Citrate/PF |
| Guaifenesin/Codeine Phosphate |
| Hydrocodone Bit/Homatrop ME-Br |
| Hydrocodone Bitartrate |
| Hydrocodone/Acetaminophen |
| Hydrocodone/Chlorphen P-Stirex |
| Hydrocodone/Chlorphen Polis |
| Hydrocodone/Ibuprofen |
| Hydromorphone HCl |
| Hydromorphone HCl/PF |
| Ibuprofen/Oxycodone HCl |
| Levorphanol Tartrate |
| Meperidine HCl |
| Meperidine HCl/PF |
| Methadone HCl |
| Morphine Sulfate |
| Nalbuphine HCl |
| Opium Tincture |
| Opium/Belladonna Alkaloids |
| Oxycodone HCl |
| Oxycodone HCl/Acetaminophen |
| Oxycodone HCl/Aspirin |
| Oxymorphone HCl |
| P-Ephed HCl/Hydrocodone |
| Pentazocine HCl/Acetaminophen |
| Pentazocine HCl/Naloxone HCl |
| Promethazine HCl/Codeine |
| Promethazine/Phenyleph/Codeine |
| Pseudophed/Hydrocodone/CPM |
| Tapentadol HCl |
| Tramadol HCl |
| Tramadol HCl/Acetaminophen |
| Proton Pump Inhibitors | Dexlansoprazole |
| Esomeprazole Mg |
| Esomeprazole Mg |
| Esomeprazole Sr |
| Lansoprazole |
| Lansoprazole/Amoxicilin/Clarith |
| Naproxen/Esomprazole Mg |
| Omeprazole |
| Omeprazole Mg |
| Omeprazole/Clarith/Amoxicillin |
| Omeprazole/Sodium Bicarbonate |
| Pantoprazole Na |
| Rabeprazole Na |
| RAS Inhibitors | Amlopidine Bes/Olmesartan Med |
| Amlopidine Besylate/Benazepril |
| Amlopidine/Valsartan |
| Amlopidine/Valsartan/Hydrochlorothiazide |
| Azilsartan Med/Chlorthalidone |
| Azilsartan Medoxomil |
| Benazepril HCl |
| Benazpril Hydrochlorothiazide |
| Candesartan Cilexetil |
| Candesartan/Hydrochlorothiazide |
| Captopril |
| Captopril/Hydrochlorothiazide |
| Enalapril Maleate |
| Enalapril/Hydrochlorothiazide |
| Enalaprilat Dihydrate |
| Eprosartan Mesylate |
| Fosinopril Sodium |
| Fosinopril/Hydrochlorothiazide |
| Irbesartan |
| Irbesartan/Hydrochlorothiazide |
| Lisinopril |
| Lisinopril/Hydrochlorothiazide |
| Losartan Potassium |
| Losartan/Hydrochlorothiazide |
| Moexipril HCl |
| Moexipril/Hydrochlorothiazide |
| Olmesartan Medoxomil |
| Olmesartan/Amlodipin/Hydrochlorothiazide |
| Olmesartan/Hydrochlorothiazide |
| Perindopril Erbumine |
| Quinapril HCl |
| Quinapril/Hydrochlorothiazide |
| Ramipril |
| Telmisartan |
| Telmisartan/Amlodipine |
| Telmisartan/Hydrochlorothiazide |
| Trandolapril |
| Trandolapril/Verapamil HCl |
| Valsartan |
| Valsartan/Hydrochlorothiazide |
| Sulfonylureas | Chlorpropamide |
| Glimepiride |
| Glyburide |
| Glyburide, Micronized |
| Glyburide/Metformin HCl |
| Pioglitazon HCl/Glimepiride |
| Rosiglitazone/Glimepiride |
| Thiazolidinediones | Alogliptin Benz/Pioglitazone |
| Pioglitazone HCl/Glimepiride |
| Pioglitazone HCl/Glimepiride |
| Pioglitazone HCl/Metformin HCl |
| Rosiglitazone/Maleate |
| Rosiglitazone/Glimepiride |

Ergoloid mesylates and growth hormones are also PIM classes not listed here. These classes were not dispensed sufficiently to conduct our analyses.

**Supplemental Table 2.** Baseline Characteristics of the Validation Cohort by Potentially Inappropriate Medication (PIM) counta

|  |  |  |  |
| --- | --- | --- | --- |
|  | **0 PIMs** | **1 PIM** | **≥2 PIMs** |
|  | **(N=7,313)** | **(N=12,108)** | **(N=4,148)** |
| **Age, median years [IQR]** | 74.4 [69.5-80.1] | 74.4 [69.5-80.1] | 73.7 [68.9-79.1] |
| **Male, %** | 43.2 | 49.3 | 56.3 |
| **Race, %** |  |  |  |
| **White** | 70.9 | 72.7 | 79.5 |
| **Black** | 22.3 | 22.2 | 17.9 |
| **Otherb** | 6.8 | 5.1 | 2.6 |
| **Hispanic Ethnicity, %** | 12.2 | 11.9 | 10.1 |
| **Comorbid Conditionsc, %** |  |  |  |
| **Diabetes** | 57.5 | 58.7 | 56.3 |
| **Cardiovascular Disease** | 58.7 | 60.1 | 61.5 |
| **Peripheral Vascular Disease** | 12 | 13.3 | 15.5 |
| **Hypertension** | 89.1 | 89.0 | 87.7 |
| **COPD** | 10.9 | 12.7 | 18.2 |
| **Cancer** | 9.2 | 9.5 | 11.5 |
| **Drug Dependence** | 0.9 | 0.8 | 0.9 |
| **Tobacco Use** | 3.4 | 3.3 | 4.8 |
| **Inability to Ambulate** | 17 | 18.8 | 23.4 |
| **Institutionalized** | 11.9 | 11.6 | 16.5 |
| **ESRD Cause, %** |  |  |  |
| **Diabetes** | 46.5 | 46.2 | 42.8 |
| **Hypertension** | 35.8 | 35.3 | 34.5 |
| **Glomerulonephritis** | 4.5 | 4.6 | 6.1 |
| **Other** | 13.3 | 13.9 | 16.7 |
| **Geographic Region, %** |  |  |  |
| **New England** | 4.1 | 3.5 | 3.8 |
| **Mideast** | 22.1 | 16.4 | 14.9 |
| **Great Lakes** | 16.8 | 18.1 | 19.1 |
| **Plains** | 4.6 | 5.6 | 5.3 |
| **Southeast** | 24.8 | 29.0 | 31.9 |
| **Southwest** | 10.4 | 11.3 | 11.3 |
| **Rocky Mountain** | 1.4 | 1.5 | 1.1 |
| **Farwest** | 15.7 | 14.7 | 12.5 |

aNumber of “High Risk” PIMs in any given month.

bOther includes Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, Other or Multiracial, and Unknown

cRefers to comorbidities, substance use and functional status reported on CMS 2728 form.

**Supplemental Table 3.** Hazards of Mortality for each PIM Class in the Validation Cohort

|  |  |  |
| --- | --- | --- |
| **PIM Class** | **HR (95% CI)** | **Proportion (%) in Cohort** |
| Antispasmodics | 2.04 (1.35 - 3.07) | 1.1 |
| Antiparkinsons | 1.92 (0.86 - 4.28) | 0.2 |
| Antithrombotics | 1.62 (0.4 - 6.48) | 0.1 |
| Antipsychotics | 1.45 (1.23 - 1.71) | 6.2 |
| Barbiturates | 1.39 (0.66 - 2.93) | 0.3 |
| Antiemetics | 1.27 (1.02 - 1.59) | 6.0 |
| Opioids | 1.26 (1.18 - 1.35) | 55.1 |
| Corticosteroids | 1.18 (1.05 - 1.34) | 20.9 |
| Antiinfectives | 1.18 (0.78 - 1.8) | 2.6 |
| Benzodiazepines | 1.15 (1.03 - 1.28) | 18.0 |
| Acetylcholinesterase Inhibitors | 1.06 (0.67 - 1.69) | 0.8 |
| Muscle Relaxants | 0.98 (0.72 - 1.31) | 4.1 |
| Estrogens | 0.97 (0.36 - 2.59) | 0.3 |
| Proton Pump Inhibitors | 0.93 (0.86 - 1.01) | 40.5 |
| Non-dihydropyridine Calcium Channel Blockers | 0.93 (0.78 - 1.13) | 6.8 |
| Anticholinergics | 0.9 (0.68 - 1.20) | 4.1 |
| Antidepressants | 0.89 (0.8 - 0.98) | 25.7 |
| H2 Receptor Blockers | 0.87 (0.73 - 1.04) | 8.7 |
| Antiepileptics | 0.86 (0.77 - 0.96) | 20.4 |
| Antihistamines | 0.84 (0.64 - 1.12) | 5.2 |
| Insulin | 0.83 (0.76 - 0.92) | 31.4 |
| NSAIDS | 0.82 (0.66 - 1.02) | 9.0 |
| Nonbenzodiazepines | 0.81 (0.66 - 0.99) | 7.9 |
| Diuretics | 0.8 (0.72 - 0.89) | 34.4 |
| Central Alpha-1 Agonists | 0.72 (0.6 - 0.85) | 13.2 |
| RAS Inhibitors | 0.64 (0.58 - 0.71) | 31.8 |
| Sulfonylureas | 0.63 (0.45 - 0.88) | 3.9 |
| Alpha-1 Blockers | 0.55 (0.42 - 0.71) | 7.0 |
| Thiazolidinediones | 0.4 (0.19 - 0.84) | 0.9 |
| Androgens | 0.34 (0.05 - 2.4) | 0.3 |

The mortality risk was obtained from a Cox proportional regression model adjusting for age, sex, race, ethnicity, diabetes, cardiovascular disease, peripheral vascular disease, hypertension, chronic obstructive pulmonary disease, history of cancer, drug dependence, tobacco use, inability to ambulate, institutionalization, ESRD cause, and geographic region.