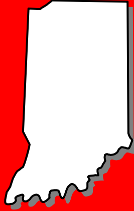

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Indiana Medicaid Drug Utilization Review Board Newsletter

Inside this Issue

1	Pharmacological Treatments For Secondary Hyperparathyroidism In Patients With Chronic Kidney
2	Top 25 Drugs for 2Q2005
3	MCO PA Process flow and MCO contact sheet

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Pharmacological Treatments For Secondary Hyperparathyroidism In Patients With Chronic Kidney Disease

Patients with chronic kidney disease have altered metabolism of calcium and phosphorus, which results in hyperphosphatemia and hypocalcemia. To correct these imbalances, the level of parathyroid hormone increases. Chronically elevated parathyroid hormone stimulates osteoclasts, which mobilize calcium from bones into blood. The results are decreased bone strength, increased risk of fracture, and increased vascular and soft tissue calcifications. Based on the recommendations from the Kidney Disease Outcomes Quality Initiative (K/DOQI)[1], serum levels of calcium, phosphorus and parathyroid hormone should be evaluated and treated in the early stage of the chronic kidney disease (see table 1). The treatment of secondary hyperparathyroidism in patients with chronic kidney disease has improved markedly in recent years. The pharmacological options include: phosphate binders, vitamin D therapies, and calcimimetics.

Phosphate Binders
In patients with chronic kidney disease, hyperphosphatemia is developed due to decreased renal elimination of phosphorus. Elevated phosphorus triggers parathyroid hormone secretion. Calcium serves as a binding agent for phosphorus. Administration of calcium with each meal reduces the absorption of phosphorus. Commonly used calcium-based phosphate binders are calcium acetate (PhosLo®) or calcium carbonate. Calcium acetate is more efficient than other calcium products. The goal of therapy is a serum phosphate concentration less than 6 mg/dl. The usual dosage is 3-4 tablets or gelcaps with each meal. Since hypercalcemia may develop with high doses, calcium levels should be monitored[2]. When parathyroid hormone reaches a level that is 2 to 3 times normal in patients with end-stage renal disease, there is a tendency to development hypercalcemia. When this occurs, calcium-based phosphate binders cannot be used. Other phosphate binders that do not increase calcium levels are required to control hyperphosphatemia. Aluminum-based phosphate binders (e.g., Amphojel) were commonly used before the resin-based phosphate binder (e.g. Renagel) became available. Sevelamer (Renagel®) binds with phosphate without increasing calcium absorption. The phosphate lowering effects of sevelamer were comparable to calcium acetate or aluminum phosphate binders. It is an alternative to calcium salts in hyperphosphatemic patients who also have high calcium levels. In addition, sevelamer has beneficial cholesterol-lowering effects, which may be useful in patients with renal disease and coexisting diabetes or atherosclerotic disease. The dose of sevelamer is 800 to 1600mg three times a day with meals. The common adverse events are gastrointestinal related, such as constipation and diarrhea[3]. Lanthanum carbonate (Fosrenol®) is a non-aluminum, non-calcium

phosphate-binding agent approved by FDA in 2004. The dose is 250 to 500 mg PO three times daily with meals and may be titrated to an acceptable serum phosphate level. The most commonly reported adverse events are nausea/vomiting, abdominal pain[4].

Vitamin D Therapy

Vitamin D ingested by diet or synthesized in the skin is transformed in the kidney to an active form of vitamin D. This form of active vitamin D increases intestinal absorption of calcium and helps regulate parathyroid hormone. The decreased production of active vitamin D in patients with chronic kidney disease often leads to hypocalcemia, which leads to increased secretion of parathyroid hormone. Supplementation with active vitamin D may correct this metabolic imbalance. Oral calcitriol (Rocaltrol®) can be administered as a capsule or solution from 0.25mcg every other day to 2mcg every day. The dose of injectable calcitriol (Calcijex®) ranges from 1mcg to 2mcg three times a week. The optimal dose must be carefully determined for each patient. The most common side effects are hypercalcemia and hyperphosphatemia[5]. Paricalcitol (Zemplar®) is another synthetic vitamin D analog. Paricalcitol has a lower incidence of hypercalcemia and hyperphosphatemia than calcitriol. Intravenous paricalcitol is indicated for patients requiring dialysis. Oral paricalcitol, which was recently approved by the FDA, is indicated for patients with moderate to severe reduction in glomerular filtration rate (GFR < 59ml/min to GFR>15ml/min). The dose of paricalcitol should be adjusted based on calcium, phosphate and parathyroid hormone concentrations[6].

Calcimimetics

The only calcimimetic currently available is cinacalcet (Sensipar™), which was approved by FDA in March 2004. Cinacalcet increases the sensitivity of the calcium-sensing receptor on the surface of the chief cell in the parathyroid gland. This calcium-sensing receptor is thought to be the principal regulator of parathyroid hormone secretion. Cinacalcet, mimicking calcium, binds to the receptor and increases its sensitivity to extracellular calcium. In response, the release of parathyroid hormone is inhibited and parathyroid hormone level is decreased. The reduction in parathyroid hormone is associated with a concomitant decrease in serum calcium levels. Cinacalcet is indicated for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis and hypercalcemia in patients with parathyroid carcinoma. The starting dose of cinacalcet in chronic kidney disease is 30mg once daily and may be titrated up to 180mg once daily for secondary hyperparathyroidism. Higher doses are required for the treatment of parathyroid carcinoma. It is important to monitor serum calcium levels frequently during the titration. The seizure threshold may be lowered due to significant reduction in serum calcium, particularly in patients with a history of a seizure disorder. Cinacalcet can be used alone or in combination with vitamin D sterols and/or phosphate binders. In addition to hypocalcemia, other common side effects are nausea and vomiting[6].

The symptoms of hyperparathyroidism in patients with chronic kidney disease may not be clear or noticeable. However, if it is not treated, the consequences are bone loss and soft tissue calcification. In the early stage of hyperparathyroidism, calcium salts can supplement the deficiency of calcium and decrease phosphorus level. Vitamin D therapies also promote the absorption of calcium and lower phosphorus and parathyroid hormone. As the chronic kidney disease progresses, other options that do not increase calcium levels may be needed to suppress parathyroid hormone. Cinacalcet has a unique mechanism of action and is an ideal agent to help patients achieve the goal levels of parathyroid hormone, calcium and phosphorus recommended by K/DOQI. However, its effects on long term mortality and morbidity has not been determined.

References:

1. K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. http://www.kidney.org/professionals/kdoqi/guidelines_bone/index.htm accessed August 2005
2. Calcium acetate drug monograph. Clinical Pharmacology 2005
3. Renagel prescribing information. Genzyme Corp., Cambridge MA http://www.renagel.com/docs/renagel_pi.pdf accessed August 2005
4. Fosrenol prescribing information. Shire Pharmaceuticals, Wayne PA http://www.fosrenol.com/prescribingInfo.pdf accessed August 2005
5. Calcitriol drug monograph. Clinical Pharmacology 2005
6. Zemplar prescribing information. Abbott Laboratory, Chicago IL http://www.rxabbott.com/pdf/Zemplarcappi.pdf accessed August 2004
7. Sensipar prescribing information. Amgen Inc., Thousand Oaks CA http://www.sensipar.com/downloads/prescribingInfo.pdf accessed August 2005

Program Assistance

All prior authorization requests or questions regarding the PDL should be directed to the ACS Clinical Call Center at 1-866-879-0106.

PDL Listing

The fee-for-service PDL listing may be found at the following website:
http://www.indianapbm.com/

Table 1 The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI™) guidelines for the treatment of bone metabolism and disease in chronic kidney disease (goals for key laboratory measurements)

Laboratory measurements	K/DOQI goal
Parathyroid hormone	150 – 300/pg/ml
Calcium and Phosphorus product (Ca x P)	< $55mg^2/dl^2$
Calcium	8.4 – 9.5 mg/dl
Phosphorus	3.5 – 5.5 mg/dl

Top 25 Drugs 2nd Quarter 2005 By Total Amount Paid

Drug	Total Paid	Total Claims
Zyprexa	$9,878,748	28,604
Risperdal	$8,380,882	37,446
Seroquel	$6,496,067	29,238
Abilify	$4,312,585	13,101
Depakote	$4,229,221	30,494
Lipitor	$4,036,436	43,469
Zoloft	$3,306,489	34,344
Novoseven	$3,035,607	21
Plavix	$3,028,532	24,529
Protonix	$2,851,122	25,071
Topamax	$2,678,049	12,021
Gabapentin	$2,610,787	27,326
Zocor	$2,432,166	18,617
Fentanyl	$2,253,101	14,249
Lexapro	$2,239,890	31,168
Aricept	$2,202,788	16,507
Effexor	$2,143,157	16,702
Advair	$2,063,899	13,778
Geodon	$2,022,162	7,695
Oxycontin	$1,969,103	8,262
Advate	$1,950,546	71
Lamictal	$1,835,409	8,152
Trileptal	$1,601,664	9,579
Singulair	$1,563,215	18,098
Norvasc	$1,557,209	26,429

Top 25 Drugs 2nd Quarter 2005 Ranked by Claims Paid

Drug	Total Claims	Total Paid
Hydrocodone/APAP	97,545	$726,827
Furosemide	60,356	$312,776
Lipitor	43,469	$4,036,436
Albuterol	42,817	$411,998
Lisinopril	41,944	$319,809
Ranitidine	38,270	$478,630
Risperdal	37,446	$8,380,882
Aspirin	36,019	$25,096
Alprazolam	34,544	$216,611
Zoloft	34,344	$3,306,489
Levothyroxine	32,966	$362,929
Lexapro	31,168	$2,239,890
Loratadine	30,703	$397,027
Depakote	30,494	$4,229,221
Potassium	30,238	$401,668
Seroquel	29,238	$6,496,067
Docusate	28,878	$62,726
Zyprexa	28,604	$9,878,748
Gabapentin	27,326	$2,610,787
Norvasc	26,429	$1,557,209
Propoxyphene N/APAP	26,094	$155,136
Protonix	25,071	$2,851,122
Amoxicillin	24,868	$210,342
Metformin	24,714	$342,354
Toprol	24,599	$864,294

MCO Process for Drugs Requiring Authorization

- Prescriber writes for drug that requires PA or is non-PDL
- Has Prescriber completed a PA Fax form or called MCO Medical Management?
  - Yes → MCO reviews request and approves?
  - No → Pharmacy gets reject for PA
    - After Hours?
      - No → Pharmacist contacts MCO provider or Med Mgmt → MCO reviews request and approves?
      - Yes → Is Rx urgent per pharmacist?
        - No → Pharmacist contacts MCO provider or Med Mgmt
        - Yes → Pharmacist calls for an override → Pharmacist fills 72 hour supply
- MCO reviews request and approves?
  - Yes → Authorization entered into system → Pharmacist fills prescription
  - No → Prescriber modifies prescription/ Provider can appeal the denial
    - Yes → Pharmacist fills prescription
    - No → Provider may appeal on behalf of member

Pharmacy Help Desk
1-800-558-1655

To Process Claim:
RxBIN: **600428**
RxPCN: **03210000**
Hoosier Healthwise Card #
Date of Birth
Prescriber DEA #

PDL and PA forms found at:
www.mdwise.org
(Clinical PAs should be submitted by the prescriber)

Pharmacy Help Desk
1-877-647-7473

To Process Claim:
RxBIN: **603286**
RxPCN: **01410000**
RxGroup: **476257**
Hoosier Healthwise Card #
Date of Birth
Prescriber DEA #

PDL and PA forms found at:
www.harmonyhmi.com
(Clinical PAs should be submitted by the prescriber)

Pharmacy Help Desk
1-800-213-5640

To Process Claim:
RxBIN: **900020**
RxPCN: **CLAIMWT**
RxGroup: **MHSINN**
MHSINC
MHSINS
MHSINTS
Hoosier Healthwise Card #
Date of Birth
Prescriber DEA #

PDL and PA forms
or Rx questions:
1-800-944-9661

Pharmacy Help Desk
1-800-642-4509
Fax: (219) 736-9140

To Process Claim:
RxBIN: **610473**
RxPCN: **Not required**
RxGroup: **Not required**
Hoosier Healthwise Card #
Date of Birth
Prescriber DEA #

PDL and PA forms found at:
www.molinahealthcare.com
(Clinical PAs should be submitted by the prescriber)

ESI Pharmacy Help Desk
1-800-417-8164
CareSource Pharmacy
PA and Help Desk
1-800-488-0134
PA Fax: 1-866-930-0019

To Process Claim:
RxBIN: **003858**
RxPCN: **A4**
RxGroup: **C4SA**
Hoosier Healthwise Card #
Date of Birth
Prescriber DEA #

PDL found at:
www.care-source.com