



## Therapeutic Class Review<sup>SM</sup>

### Phosphate Binders

May 2005

#### New Product for Review

sevelamer hydrochloride (Renagel<sup>®</sup>) [Genezyme]

lanthanum carbonate (Fosrenol<sup>™</sup>) [Shire]

Dossier Provided by Manufacturer: yes

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#### Available Therapeutic Alternative(s)

Preferred/Formulary	Non-Preferred/Non-Formulary
calcium acetate (PhosLo <sup>®</sup> )	

#### Executive Summary

- The National Kidney Foundation Kidney Disease Outcome and Quality Initiative (K/DOQI) guidelines recommend maintaining serum phosphorus (P) and calcium x phosphate (Ca x P) product in End-stage Renal Disease (ESRD) patients below 5.5 mg/dL and 55 mg<sup>2</sup>/dL<sup>2</sup>, respectively. ESRD patients are at increased risk for vascular calcification when recommended serum P and Ca x P goals are not maintained.
- Calcium acetate (PhosLo), sevelamer hydrochloride (Renagel) and lanthanum carbonate (Fosrenol) lower serum phosphorus in ESRD patients.
- The mean serum P and Ca x P values, discontinuation rates, advantages and disadvantages of the three dietary phosphate binders are shown below:

Parameters	calcium acetate (PhosLo)	sevelamer HCl (Renagel)	lanthanum carbonate (Fosrenol)
Serum P <i>Goal &lt;5.5mg/dL</i>	5.2 mg/dL <sup>A</sup>	6.1 mg/dL <sup>A</sup>	Insufficient data <sup>B</sup>
Serum Ca x P <i>Goal &lt;55 mg<sup>2</sup>/dL<sup>2</sup></i>	51 mg <sup>2</sup> /dL <sup>2A</sup>	58mg <sup>2</sup> /dL <sup>2A</sup>	Insufficient data <sup>B</sup>
Discontinuation	10-13%	<10%	60-80%
Advantages	<b><i>More likely to reach goals</i></b>	Modest LDL-C lowering	None
Disadvantages	1. Transient hypercalcemia 2. Gastrointestinal discomforts	1. Transient hypocalcemia 2. Gastrointestinal discomforts <b><i>3. Less likely to reach goals</i></b>	1. Severe nausea/vomiting, NNH=19 2. Patient stop therapy due to an adverse event, NNH= 8 3. Prolong QTc >30 ms, NNH= 40. 4. All cause mortality, NNH= 29. <b><i>5. Not likely to reach goals</i></b>

<sup>A</sup> Average values from 7 randomized controlled trials. <sup>B</sup> Data reported in a small single clinical trial; the reported serum P and Ca x P values were unreliable due to insufficient length of total drug exposure, and high discontinuation rates due to nausea and vomiting.

### Conclusion:

Sevelamer hydrochloride (Renagel) and lanthanum carbonate (Fosrenol) are non-formulary/non-preferred medications because these products provide inferior value at a higher cost in lowering serum P and Ca x P product in ESRD patients.

## Products

Drug Product	Date of FDA Approval	FDA Approved Indication(s)	Dose Route	AWP Cost*	Potential Off-Label Use(s)
calcium acetate (PhosLo) 667 mg (169 mg or 8.45 mEq elemental calcium) capsules	12/1990	Control of hyperphosphatemia in end stage renal failure	3-4 capsules by mouth three times daily with meals	\$42.12	No significant off label uses
sevelamer hydrochloride (Renagel) 400 mg or 800 mg tablets or capsules	7/2000	Reduction in serum phosphate in patients with end-stage renal disease (ESRD) who are on hemodialysis	1-3 tablets or capsules by mouth three times daily with meals	\$226.4	Reduction in valvular calcification. <sup>[1]</sup>  Treatment of secondary hyperparathyroidism in uremic patients. <sup>[2]</sup>  As a phosphate binder in pediatric patients on dialysis. <sup>[3]</sup>  Lowering of LDL-cholesterol in dialysis patients. <sup>[4,5]</sup>
lanthanum carbonate (Fosrenol)  250 and 500 mg chewable tablets	10/2004	Control of hyperphosphatemia in end stage renal failure	750-3750 mg by mouth 3 times daily with meals  Usual total dose 2250 mg/day	\$110	No off label uses are anticipated

\*AWP (average wholesale price) based on First Data Bank as of February 22, 2005, for 1 month of therapy.

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