Suffolk Drug & Therapeutics Committee

Shared Care Guidelines for the Treatment of hyperphosphataemia in renal (haemodialysis) patients with sevelamer (Renagel)

What is a shared care document?

Suffolk D&T operates a traffic light system to clarify prescribing responsibility and improve consistency across Suffolk:

Double Red – Prescribing within hospital or general practice would not be supported.
Red – Hospital only
Amber – Hospital initiated but suitable for GP prescribing if a suitable shared care document is in place.
Green – Hospital initiated; GP prescribing
Double Green – GP prescribing

The basic principles of a shared care arrangement are:
1) The shared care document will include a clear statement of the hospital specialist/GPs responsibilities
2) Shared care documents must provide sufficient information such that after patient stabilisation under hospital supervision, prescribing responsibility could safely be transferred to primary care
3) Both hospital specialist and general practitioner have a duty of care for the overall management of the patient
4) Patient convenience may be a major factor for GPs taking on prescribing responsibility and not the cost of the therapy
5) The onus is on the hospital specialist to liaise with the GP, and if the GP does not wish to undertake the clinical and legal responsibility for the drug he does not have to do so. Responsibility to prescribe will therefore remain with the hospital
6) Agreement to accept prescribing responsibility should be obtained from the GP before the patient is informed

For more details please refer to the traffic light document on the Suffolk Extranet website.

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Date approved by the Local Medical Committee – September 2005

The document is available on the Suffolk Extranet website under County Wide & Core Documents □ Prescribing Guidelines

1. Background to shared care document:

Sevelamer was classified as a red drug (hospital only) by Suffolk D&T in July
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2003. Since then it has been widely used by the renal consultants at Ipswich hospital and new data on its use in renal patients has shown it to be of benefit in reducing serum phosphate levels whilst minimising some of the undesirable effects associated with calcium or aluminium based phosphate binders.
The role of Sevelamer in the treatment of Hyperphosphataemia.

Sevelamer (Renagel), an aluminium free, calcium free oral phosphate binder is licensed for the treatment of hyperphosphataemia in adult patients on haemodialysis. It reduces serum phosphate levels by reducing absorption of dietary phosphorus. Sevelamer is not absorbed from the gastrointestinal tract and so systemic side effects are minimal.

The UK Renal Association and the US National Kidney Federation (K/DOQI) recommends target phosphate levels of <1.8 mmol/l and serum calcium levels of <2.6 mmol/l. In addition K/DOQI also recommends target plasma parathyroid hormone (PTH) levels of 150 -300 pg/ml (15.8 - 31.6 pmol/l). ¹

Cardiovascular disease accounts for approximately half the deaths among adults undergoing regular dialysis. ² Risk factors for cardiovascular calcification include both hyperphosphataemia and excess calcium load. A study including 16 young adults aged between 20 – 30 showed that 14 had some evidence of coronary artery calcification, which illustrates the need for awareness of the calcification risk in all haemodialysis patients, not just older patients. ²

Some of the risk factors for calcification in dialysis are modifiable. Diet, dialysis and the appropriate dose of a phosphate binder can correct hyperphosphataemia. Excess calcium load can result from a number of factors, as patients are exposed to a variety of calcium sources including dialysate, vitamin D replacement therapy dietary calcium and some phosphate binders. Use of a non-calcium based phosphate binder is a simple way to reduce a patient’s calcium intake. Sevelamer is a non-absorbed, calcium and metal-free phosphate binder that has been found to effectively control serum phosphate levels.³ In a recent study of 99 patients taking sevelamer for 52 weeks at an average daily dose of eight 800mg tablets, serum phosphate levels were reduced to a mean end-of-study value of 1.64mmol/l (within the K/DOQI target range). In addition the study showed that treatment with sevelamer improved the control of PTH and is less likely to cause episodes of hypercalcaemia.³


2. Patient Selection for sevelamer

- Adult haemodialysis patients with hyperphosphataemia associated with chronic renal failure (sevelamer is not at present licensed for use in patients receiving peritoneal dialysis).
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3. Hospital Specialist Responsibilities

- Diagnosis of hyperphosphataemia and initiation of sevelamer treatment.
- Discuss benefits and side effect of treatment with the patient.
- Dose stabilisation: initial dosage adjustment until serum phosphate concentration is stable and within required limits. Thereafter, during maintenance treatment, provide advice to and discussion with the GP with regard to any further dosage adjustments required.
- Confirm with the GP that they are willing to participate in shared care of the patient.
- Monitor serum phosphate and calcium levels and any other parameters considered necessary.
- Prompt communication with the GP of any changes in treatment and assessment of adverse events.
- Have in place a mechanism to receive rapid referral of a patient from the GP in the event of a deteriorating clinical condition.
- Advise GP on stopping treatment if appropriate.
- Report any adverse events to the Committee on safety of medicines (CSM).
- Ensure clear arrangements in place for back up, advice and support.

4. GP responsibilities

- Reply to the request for shared care as soon as practicable.
- Prescribe sevelamer at the dosage recommended and adjust dose as advised by the specialist.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
- Use agreed mechanism for rapid referral of patient to the specialist in the event of deteriorating clinical condition.
- Stop treatment on the advice of the specialist or immediately if an urgent need arises.
- Report any adverse events to the specialist and the CSM.

5. Prescribing information for Sevelamer (Renagel\textsuperscript{1})
Summary prescribing information for guidance only; please refer to the full Summary of Product Characteristics (available at www.medicines.org.uk), local specialist or medicines information centre. The information is correct at the time of writing – April 04 but maybe subject to change.

Pharmacology
Sevelamer hydrochloride is a non-aluminium, non-calcium containing hydrogel of cross linked poly(allylamine hydrochloride). It is not absorbed from the gastrointestinal tract and is resistant to digestive degradation. Sevelamer binds dietary phosphate by ionic and hydrogen bonding which is believed to occur primarily in the proximal small intestine.

Preparations available
Renagel 800mg tablets.

Licensed indications
The control of hyperphosphataemia in adult patients on haemodialysis. Sevelamer should be used within the context of a multiple therapeutic approach, which could include calcium supplements, 1,25 – dihydroxy vitamin D3 or one of its analogues to control the development of renal bone disease.

Recommended dosage and administration – Adults and elderly (>65years)
For patients who are not on phosphate binders, dosage is determined individually based on serum phosphate concentration as indicated in the table below:

<table>
<thead>
<tr>
<th>Serum phosphate level inpatients not on phosphate binders</th>
<th>Starting dose of sevelamer 800mg tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.94 – 2.42 mmol/l</td>
<td>1 tablet x 3 times a day</td>
</tr>
<tr>
<td>2.42 – 2.91 mmol/l</td>
<td>2 tablets x 3 times a day</td>
</tr>
<tr>
<td>&gt;2.91 mmol/l</td>
<td>3 tablets x 3 times a day</td>
</tr>
</tbody>
</table>

If Sevelamer is prescribed as an alternative phosphate binder, it should be given in equivalent doses on a mg weight basis compared to the patient’s previous calcium based phosphate binder. Serum phosphate levels should be closely monitored and the dose of sevelamer adjusted accordingly with the goal of lowering serum phosphate to 1.8 mmol/l or less. Serum phosphate should be tested every two to three weeks until a stable level is reached and on a regular basis thereafter.

The dose range may vary between one and five 800mg tablets per meal. The average dose used in clinical trials was equivalent to two 800mg tablets per meal.

Patients should take sevelamer tablets with meals, adhering to any prescribed diet. The tablets should be swallowed whole and not chewed.

Contra-indications
- Hypophosphataemia.
- Bowel obstruction.
- Hypersensitivity to sevelamer or to any of the excipients in the product.

Cautions
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Efficacy and safety of sevelamer has not been studied in children, predialysis patients or peritoneal dialysis patients.

Careful assessment of benefits and risks should be carried out in patients with swallowing disorders, untreated or severe gastro paresis and retention of gastric contents as safety and efficacy of Sevelamer has not been studied in these groups. Similarly caution should be used in patients with active inflammatory bowel disease, gastrointestinal motility disorders, abnormal or irregular bowel motion and those with a history of major gastrointestinal surgery. During treatment with sevelamer rare cases of intestinal obstruction have been seen. Patients who are constipated should be carefully monitored during treatment with sevelamer and treatment should be re-evaluated if severe constipation develops.

Sevelamer alone is not indicated for the control of hyperparathyroidism. In patients with secondary hyperparathyroidism it should be used within the context of a multiple therapeutic approach, which could include calcium supplements, 1,25 – dihydroxy Vitamin D3 or one its analogues to lower the intact parathyroid hormone levels.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency of monitoring</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum phosphate concentration</td>
<td>Every 2 –3 weeks until a stable serum phosphate concentration is reached, then monthly Monthly</td>
<td>Adjustment of sevelamer dosage and communication of changes between the specialist and GP. Adjustment of calcium and/or vitamin D supplement and communication of changes between the specialist and GP</td>
</tr>
<tr>
<td>Serum calcium concentration</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Depending on dietary intake and the nature of end stage renal failure, dialysis patients may develop low levels of vitamin A, D, E and K. If patients are not taking these vitamins, levels of vitamin A, D, and E should be monitored and vitamin K status should be assessed, with supplementation initiated where necessary.

Treatment with sevelamer may lead to an increase in serum chloride levels and should be monitored as part of the routine follow up of dialysis patients.

Drug interactions
Interaction studies have not been conducted in patients on haemodialysis. However in studies performed on animals and on healthy volunteers, the pharmacokinetic profiles of drugs commonly used in the target patient population have not been found to be significantly affected by concurrent administration of sevelamer.

Adverse effects
The following undesirable effects have been reported in:

ε 10% of patients:
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Pain, diarrhoea, nausea, vomiting, dyspepsia, constipation, infection, headache, respiratory disorder, cough, hypotension, hypertension, dizziness, dyspnoea, thrombosis, peripheral oedema, accidental injury, chest pain, abdominal pain, fever, leg cramps, and pruritis.

≤10% of patients:
Flatulence, cardiovascular disorder, pharyngitis and rash.

As all of the above effects are commonly seen in patients with end stage renal failure they may not necessarily be attributable to sevelamer.

Prescribing costs
From MIMS April 2004.
Basic NHS price for 120 Renagel® (sevelamer) 800mg capsules is £132.00. With average dosing of two tablets per meal the average cost will be £4.40 per day or £123.20 for 28 days.

6. Hospital Department Contact Details
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7. References
Genzyme Ltd. Renagel 800mg tablets. Summary of Product Characteristics, 2003