NEW ZEALAND DATA SHEET

1 RENAGEL 800 MG FILM COATED TABLETS

Renagel 800 mg film coated tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Renagel 800 mg tablets contain 800 mg sevelamer hydrochloride.

For the full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablets.

Renagel tablets are oval film coated tablets imprinted with "Renagel 800" for the 800 mg tablet on one side and blank on the other side.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Renagel is indicated for the management of hyperphosphataemia in adult patients with stage 4 and 5 chronic kidney disease.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dose

Starting dose

The recommended starting dose for patients not taking a phosphate binder is 800 to 1600 mg (Table 1), which can be administered as one to two Renagel 800 mg tablets with each meal based on serum phosphorus level.

Table 1 - Starting dose for patients not taking a phosphate binder

Serum Phosphorus	Renagel 800 mg Tablets
> 1.78 and < 2.42 mmol/L	1 tablet, three times daily with meals
≥ 2.42 and <2.91 mmol/L	2 tablets, three times daily with meals
≥ 2.91 mmol/L	2 tablets, three times daily with meals

When patients are converting from a calcium based phosphate binder, Renagel should be given in equivalent doses on a (mg to mg) weight basis compared to the patient's previous calcium based phosphate binder (Table 2). Serum phosphorus levels should be closely monitored and the dose of Renagel adjusted accordingly with the goal of lowering serum phosphorus. Serum phosphorus should be tested every 2 to 3 weeks until a stable serum phosphorus level is reached, and on a regular basis thereafter.

Table 2 - Starting dose for patients switching from calcium acetate to Renagel

Calcium Acetate 667 mg (tablets per meal)	Renagel 800 mg (tablets per meal)
1 tablet	1 tablet
2 tablets	2 tablets
3 tablets	3 tablets

Dose titration for all patients taking Renagel

The dosage should be gradually adjusted based on the serum phosphorus concentration with a goal of lowering serum phosphorus. The dose may be increased or decreased by one tablet per meal at two week intervals as necessary (Table 3). The average dose in a one year Phase 3 trial designed to lower serum phosphorus to 1.62 mmol/L or less was approximately three Renagel 800 mg tablets per meal. The average actual daily dose used in the chronic phase of a one year clinical study was 7 grams of sevelamer hydrochloride.

Table 3 - Dose titration guideline 800 mg tablets

Serum Phosphorus	Renagel Dose
> 1.78 mmol/L	Increase 1 tablet per meal at 2 week intervals
1.13 – 1.78 mmol/L	Maintain current dose
< 1.13 mmol/L	Decrease 1 tablet per meal

Paediatric population

Refer to Section 4.4 – Paediatric use

Method of administration

Patients should be advised not to chew the tablets as sevelamer hydrochloride swells on contact with moisture. Patients should swallow the tablets whole with water.

Tablets should not be crushed, chewed or broken into pieces prior to administration.

4.3 CONTRAINDICATIONS

Renagel is contraindicated in patients with hypophosphataemia or bowel obstruction.

Renagel is also contraindicated in patients known to be hypersensitive to sevelamer hydrochloride or any of the other components of the tablet listed in section 6.1.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

General

The safety and efficacy of Renagel in patients with dysphagia, swallowing disorders, severe gastrointestinal (GI) motility disorders, severe constipation, major GI tract surgery or in pre-dialysis patients have not been established. Consequently, caution should be exercised when Renagel is used in patients with these GI disorders.

Swallowing and choking difficulties

Uncommon case reports of difficulty swallowing the Renagel tablet have been reported. Many of these cases involved patients with contributing co-morbid conditions affecting the ability to swallow including swallowing disorders or oroesophageal abnormalities. Caution should be exercised when Renagel tablets are used in these patients.

Hypocalcaemia / hypercalcaemia

Patients with renal insufficiency may develop hypocalcaemia or hypercalcaemia. Renagel does not contain calcium. Serum calcium levels should be monitored as is done in routine follow - up of a dialysis patient. Elemental calcium should be given as a supplement in case of hypocalcaemia.

Metabolic acidosis

Patients with chronic kidney disease are predisposed to metabolic acidosis. Renagel does not contain alkali supplementation: serum bicarbonate and chloride levels should be monitored.

Fat-soluble vitamins

Depending on dietary intake and the nature of chronic kidney disease, dialysis patients may develop low vitamin A, D, E and K levels. Therefore, in patients not taking these vitamins, monitoring vitamin A, D and E levels and assessing vitamin K status through the measurement of thromboplastin time should be considered and these vitamins should be supplemented if necessary.

In clinical trials, there was no evidence of reduction in serum levels of vitamins with the exception of a one year clinical trial in which Renagel treatment was associated with reduction of 25-hydroxyvitamin D (normal range 10 to 55 µg/mL) from 39± 22 µg/mL to 34± 22 µg/mL ($p<0.01$). Most patients in Renagel clinical trials received vitamin supplements, which is typical of patients on haemodialysis. Indirect evidence of a reduction in vitamin K levels (an increase in haemorrhage corrected by vitamin K supplementation) was also seen in animals.

Gastrointestinal disorders

Cases of serious inflammatory disorders of the gastrointestinal tract (with complications including haemorrhage, perforation, ulceration, necrosis, colitis, and colonic/caecal mass) associated with the presence of sevelamer crystals have been reported (see Section 4.8). Inflammatory disorders may resolve upon Renagel discontinuation. Treatment with Renagel should be re-evaluated in patients who develop severe gastrointestinal symptoms.

Paediatric Use

The safety and effectiveness of Renagel in patients below the age of 18 years has not been established.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

Interaction studies have not been conducted in patients on dialysis.

Renagel was studied in human drug-drug interaction studies with digoxin, warfarin, enalapril, metoprolol, iron and ciprofloxacin.

In interaction studies in healthy volunteers, Renagel had no effect on the bioavailability of digoxin, warfarin, enalapril or metoprolol. However, the bioavailability of ciprofloxacin was decreased by approximately 50% when co-administered with Renagel in a single dose study. Consequently, Renagel should not be taken simultaneously with ciprofloxacin.

Reduced levels of cyclosporin, mycophenolate mofetil and tacrolimus have been reported in transplant patients when co-administered with sevelamer hydrochloride without any clinical consequences (i.e. graft rejection). The possibility of an interaction cannot be excluded and a close monitoring of blood concentrations of cyclosporin, mycophenolate mofetil and tacrolimus should be considered during the use of any of these agents in combination with sevelamer and after its withdrawal.

During post-marketing experience, very rare cases of increased TSH levels have been reported in patients co-administered Renagel and levothyroxine. Closer monitoring of TSH levels is therefore recommended in patients receiving both medications.

During post-marketing experience, very rare cases of increased phosphate levels have been reported in patients taking proton pump inhibitors co-administered with sevelamer hydrochloride.

Renagel may affect the bioavailability of other medicinal products. When administering a medicinal product where a reduction in the bioavailability of that product could have a clinically significant effect on its safety or efficacy, the medicinal product should be administered at least one hour before or three hours after Renagel, or the physician should consider monitoring blood levels.

Patients taking anti-arrhythmic medications for the control of arrhythmias and anti-seizure medications for the control of seizure disorders were excluded from clinical trials. Special precautions should be taken when prescribing Renagel to patients also taking these medications.

4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy

Category B3

The safety of sevelamer hydrochloride in human pregnancy has not been established and, because animal reproduction studies are not always predictive of human responses, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus (see section 5.3).

Breast-feeding

No adequate and controlled studies have been conducted using sevelamer in nursing mothers. Renagel tablets should be used during breastfeeding only if the potential benefit justifies the potential risks.

Fertility

There are no data about the effect of sevelamer on fertility in humans. Sevelamer hydrochloride administered orally to male and female rats prior to and throughout mating, at doses up to 4.5 g/kg/day (15 times the maximum tested human dose on a mg/kg basis of a 50 kg person) did not alter mating or fertility.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Sevelamer has no or negligible influence on the ability to drive and use machines.

4.8 UNDESIRABLE EFFECTS

Clinical trials

In a parallel design study of sevelamer hydrochloride with treatment duration of 52 weeks, adverse events reported for sevelamer hydrochloride (n=99) were similar to those reported for the active-control group (n=101), except for those in the MedDRA gastrointestinal disorders system organ class (SOC) that were more frequent (Table 4). Gastrointesintal adverse events were the most frequently occurring (≥5% of patients) treatment emergent adverse events possibly or probably related to Renagel; and a major reason for drop out in the Renagel group (Table 5).

Table 4 - Treatment emergent adverse events ≥ 10% from a parallel design trial of Renagel tablets versus calcium acetate for 52 weeks of treatment regardless of causality

Adverse Event	Renagel (N=99)	Calcium (N=101)
	Patients (%)	Patients (%)
Gastrointestinal Disorders		
Vomiting	22.2	21.8
Nausea	20.2	19.8
Diarrhoea	19.2	22.8
Dyspepsia	16.2	6.9
Constipation	8.1	11.9
Infections and Infestations		
Nasopharyngitis	14.1	7.9
Bronchitis	11.1	12.9
Upper Respiratory Tract Infection	5.1	10.9
Musculoskeletal Connective Tissue and Bone Disorders		
Pain in Limb	13.1	14.9
Arthralgia	12.1	17.8
Back Pain	4.0	17.8
Skin Disorders		
Pruritus	13.1	9.9
Respiratory, Thoracic and Mediastinal Disorders		
Dyspnoea	10.1	16.8
Cough	7.1	12.9
Vascular Disorders		
Hypertension	10.1	5.9
Nervous System Disorders		
Headache	9.1	15.8
General Disorders and Site Administration Disorders		

Adverse Event	Renagel (N=99)	Calcium (N=101)
	Patients (%)	Patients (%)
Mechanical Complication of Implant	6.1	10.9
Pyrexia	5.1	10.9

Table 5 - Summary of frequently occurring (≥ 5% of patients) treatment emergent adverse events possibly or probably related to Renagel

System Organ Class (SOC)	Event Description	Patient %
Gastrointestinal Disorders	Vomiting	10.1
	Nausea	10.1
	Dyspepsia	9.1
	Diarrhoea	8.1
	Abdominal pain	5.1
	Flatulence	5.1

In a placebo-controlled study with a treatment duration of two weeks, treatment emergent adverse events possibly or probably related to Renagel (N=24) included dyspepsia (8.3%) and vomiting (4.2%). In a cross-over study with treatment durations of eight weeks each, the treatment emergent events possibly or probably related to Renagel (N=82) included dyspepsia (8.5%), diarrhoea (4.9%), nausea (4.9%), vomiting (4.9%), anorexia (3.7%), and gastrointestinal disorder (3.7%). In a long term, open label extension trial the treatment emergent events possibly or probably related to Renagel (N=192) included nausea (7.3%), abdominal pain (5.2%) and dyspepsia (4.7%).

In a parallel design study with a treatment duration of 12 weeks, the adverse events reported for sevelamer hydrochloride in peritoneal dialysis patients (N=97) were similar to adverse events observed in haemodialysis patients. Adverse events possibly related to sevelamer hydrochloride included dyspepsia (12.4%), diarrhoea (5.2%), nausea (5.2%), constipation (4.1%), pruritus (4.1%), abdominal distension (3.1%), vomiting (3.1%), fatigue (3.1%), anorexia (3.1%) and arthralgia. The most frequently occurring serious adverse event was peritonitis (8.2%) reported as unrelated to sevelamer hydrochloride.

Post-marketing experience

Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

During post marketing experience, the following adverse events have been reported in patients receiving Renagel: Hypersensitivity, pruritus, rash, abdominal pain and uncommon cases of ileus, intestinal obstruction and intestinal perforation. Constipation might be a preceding symptom indicating the development of intestinal obstruction. Hence, patients with severe constipation should be monitored carefully while being treated with Renagel.

Cases of serious inflammatory disorders of the gastrointestinal tract (with complications including haemorrhage, perforation, ulceration, necrosis, colitis, and intestinal mass) associated with the presence of sevelamer crystals have been reported (see Section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 OVERDOSE

Renagel has been given to normal healthy volunteers in doses of up to 14.4 grams per day for 8 days with no adverse effects. There are no reported overdoses of Renagel in patients. Since Renagel is not absorbed, the risk of systemic toxicity is low.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

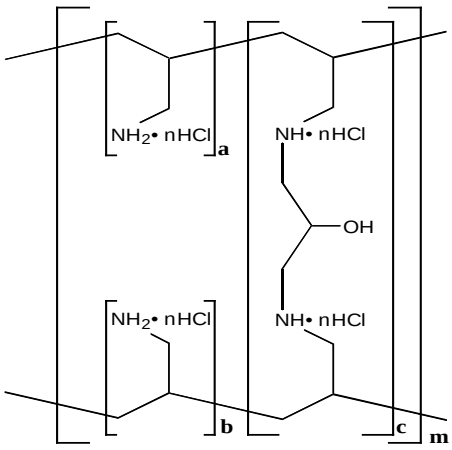
5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Treatment of hyperphosphatemia. ATC code: V03AE02.

The structure is represented in Figure 1.

Figure 1 - Structure of Sevelamer Hydrochloride



a, b = number of primary amine groups	a + b = 9
c = number of crosslinking groups	c = 1
n = fraction of protonated amines	n = 0.4

m = large number to indicate extended polymer network

The primary amine groups shown in the structure are derived directly from poly (allylamine hydrochloride). The cross-linking groups consist of two secondary amine groups derived from poly (allylamine hydrochloride) and one molecule of epichlorohydrin.

CAS Registry Number: 152751-57-0.

Sevelamer, or poly(allylamine-co-N,N'-diallyl-1,3-diamino-2-hydroxypropane), a cross-linked polymer, is a white to off-white, water insoluble powder. Sevelamer is a partial hydrochloride salt, approximately 40% amine hydrochloride and 60% free base. Sevelamer hydrochloride is hydrophilic, but also insoluble in water.

Mechanism of Action

Patients with end-stage renal disease (ESRD) retain phosphorus and can develop hyperphosphataemia. Renagel contains sevelamer, a non-absorbed phosphate binding poly(allylamine hydrochloride) polymer, free of metal and calcium. It contains multiple amines separated by one carbon from the polymer backbone. These amines become partially protonated in the intestine and interact with phosphorus molecules through ionic and hydrogen bonding. By binding phosphorus in the dietary tract, sevelamer lowers the phosphorus concentration in the serum. Renagel decreases the incidence of hypercalcaemic episodes as compared to patients using calcium based phosphate binders alone, probably because the product itself does not contain calcium.

Renagel treatment also results in a lowering of low-density lipoprotein (LDL) and total serum cholesterol levels by increasing faecal excretion of bile acids.

High serum phosphorus can precipitate serum calcium resulting in ectopic calcification. When the product of serum calcium and phosphorus concentrations (Ca x P) exceeds 4.46 $(mmol/L)^2$, there is an increased risk that ectopic calcification will occur. Hyperphosphataemia plays a role in the development of secondary hyperparathyroidism in renal insufficiency. An increase in parathyroid hormone (PTH) levels is characteristic of patients with chronic renal failure. Increased levels of PTH can lead to the bone disease osteitis fibrosa. A decrease in serum phosphorus may decrease serum PTH levels.

Clinical efficacy and safety

In vitro studies have shown that the capsule and tablet formulations bind phosphate to a similar extent. Since Renagel does not contain aluminium, it does not cause aluminium intoxication.

The ability of Renagel to lower serum phosphorus in end stage renal disease (ESRD) patients on haemodialysis was demonstrated in three Phase 2 studies with treatment duration ranging from 2 to 12 weeks and two Phase 3 studies with treatment duration of 8 weeks each. Four of the five studies were open-label dose-titration studies. One of the Phase 2 studies was a placebo-controlled study. The Phase 3 cross-over study, described below, had a control arm. About half the patients

from these studies (N=192) were treated with Renagel capsules in a long-term open-label extension study of 44 weeks.

In a cross-over study of sevelamer and calcium acetate, 84 ESRD patients on haemodialysis who were hyperphosphataemic (serum phosphorus > 1.94 mmol/L) following a 2-week phosphate binder washout period were randomised to receive either Renagel for 8 weeks followed by calcium acetate for 8 weeks or calcium acetate for 8 weeks followed by Renagel for 8 weeks. Treatment periods were separated by a 2-week phosphate binder washout period. Patients started on Renagel capsules or calcium acetate tablets 3 times per day with meals. Over each 8-week treatment period, at three separate time points the dose of either agent could be titrated up one capsule or tablet per meal (3 per day) to control serum phosphorus. Renagel and calcium acetate both significantly decreased mean serum phosphorus by about 0.65 mmol/L (Table 6).

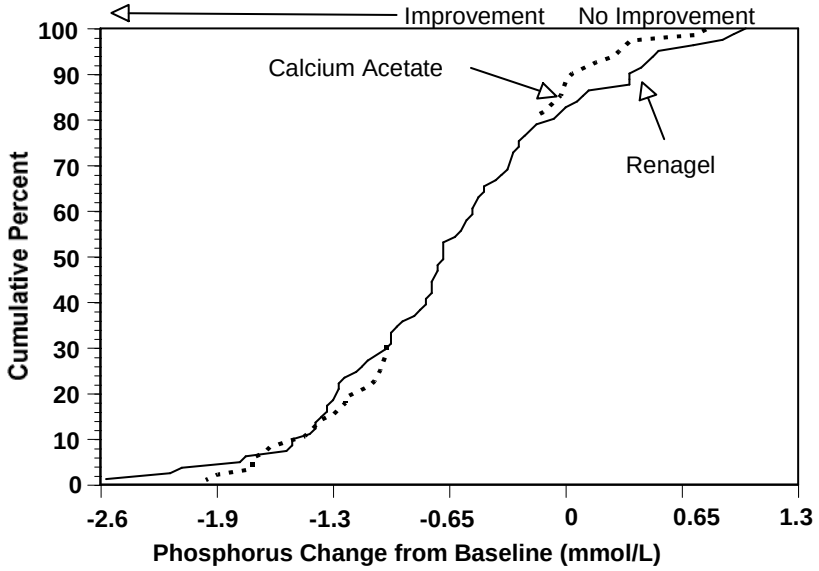
Table 6 - Mean serum phosphorus at baseline and endpoint

	Renagel (n=81)	Ca Acetate (N=83)
Baseline at End of Washout	2.7 mmol/L	2.6 mmol/L
Change from Baseline at Endpoint (95% Confidence Interval)	- 0.65 mmol/L* (-0.81, -0.48)	- 0.68 mmol/L* (-0.84, -0.55)

*p < 0.0001, within treatment group comparison

Figure 2 illustrates that the proportion of patients achieving a given level of serum phosphorus lowering is comparable between the two treatment groups. For example, about half the patients in each group had a decrease of at least 0.65 mmol/L at endpoint. Successful control of serum phosphorus in chronic kidney disease patients is multifactorial including reduction of dietary phosphate intake, removal of phosphate with dialysis and inhibition of intestinal phosphate absorption with phosphate binders. As seen in Figure 2, some of the patients in GTC 36-301 did not respond to sevelamer treatment. Not all patients achieve phosphorus control with sevelamer alone, especially at the doses administered in this study (average actual daily dose 4.3 g/day). Later studies which employed higher doses of sevelamer (i.e. GTC 49-301-average actual daily dose 6.5 g/day) had a better rate of phosphorus response.

Figure 2 - Cumulative percent of patients (y-axis) attaining a phosphorus change from baseline at least as great as the value of the x-axis. A shift to the left of a curve indicates a better response.



Average daily consumption at the end of treatment was 4.9 g sevelamer (range of 0.0 to 12.6 g) and 5.0 g of calcium acetate (range of 0.0 to 17.8 g). During calcium acetate treatment, 22% of patients developed serum calcium ≥ 2.75 mmol/L on at least one occasion versus 5% for sevelamer ($p < 0.05$). Thus the risk of developing hypercalcaemia is less with Renagel compared to calcium acetate.

Mean LDL cholesterol and mean total cholesterol declined significantly on Renagel capsules treatment (-24% and -15% respectively). Neither LDL nor total cholesterol changed on calcium acetate treatment. Triglycerides, high-density lipoprotein (HDL) cholesterol, and albumin did not change on either treatment.

Similar reductions in serum phosphorus and LDL cholesterol were observed in an 8-week open - label, uncontrolled study of 172 end-stage renal disease patients on haemodialysis.

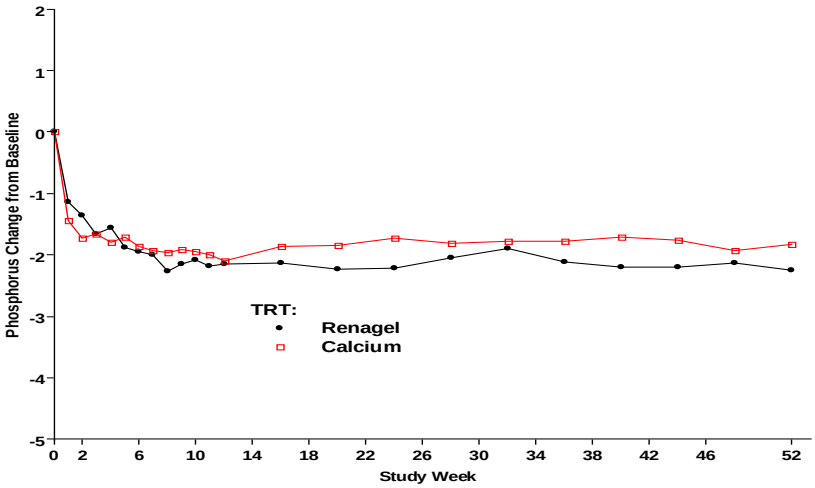
In a parallel study of Renagel and calcium acetate or calcium carbonate, two hundred ESRD patients on haemodialysis who were hyperphosphataemic (serum phosphorus > 1.78 mmol/L) following a two-week phosphate binder washout period were randomised to receive Renagel 800 mg tablets (N=99) or calcium, either calcium acetate (N=54) or calcium carbonate (N=47). Seventy-seven percent of Renagel patients (N=76) and 80% of the calcium patients (N=81) completed the full 52 weeks of treatment with the major reason for dropout in the Renagel group was gastrointestinal adverse events. Calcium acetate and calcium carbonate produced comparable decreases in serum phosphorus. At week 52, using last observation carried - forward, Renagel and calcium both significantly decreased mean serum phosphorus (Table 7).

Table 7 - Mean serum phosphorus at baseline and end of treatment (52 weeks)

Serum Phosphorus	Renagel (N=76)	Calcium (N=81)
Baseline	2.38 mmol/L	2.33 mmol/L
Change from baseline at 52 weeks	-0.72 mmol/L	-0.64 mmol/L
Mean serum phosphorus levels at 52 weeks	1.67 mmol/L	1.68 mmol/L

Figure 3, a plot of the phosphorus change from baseline for the completers, illustrates the durability of response for patients who are able to remain on treatment.

Figure 3 - mean phosphorus change from baseline for patients who completed 52 weeks of treatment



Average daily consumption at the end of the treatment was 6.5 g of sevelamer (range of 0.8 to 13 g) or approximately eight 800 mg tablets (range of 1 to 16 tablets), 4.6 g of calcium acetate (range of 0.7 to 9.5 g) and 3.9 g of calcium carbonate treatment, 34% of patients developed serum calcium corrected for albumin ≥ 2.75 mmol/L on at least one occasion versus 7% for Renagel ($p<0.05$). Thus the risk of developing hypercalcaemia is less with Renagel compared to calcium salts.

Mean LDL cholesterol and mean total cholesterol declined significantly ($p<0.05$) on Renagel treatment (-32% and -20%, respectively) compared to calcium (+0.2% and -2%, respectively) triglycerides, HDL cholesterol, and albumin did not change.

In a parallel study of sevelamer hydrochloride or calcium acetate in peritoneal dialysis patients, one hundred and forty three patients on peritoneal dialysis who were hyperphosphatemic (serum phosphorus > 5.5 mg/dL) following a two-week phosphate binder washout period were randomized to receive Renagel 800 mg tablets (N=97) or calcium acetate (N=46). Treatment for 12 weeks with Renagel was non-inferior to calcium acetate in reducing serum phosphorus. There were statistically significant changes in serum phosphorus ($p< 0.001$) from baseline for both the

Renagel (1.61 mg/dL from 7.48 mg/dL) and calcium acetate (-1.81 mg/dL from 7.29 mg/dL) groups.

Average daily consumption at the end of treatment was 5.9 g for Renagel (range of 0.8 to 14.3 g) and 4.3 g for calcium acetate (range of 1.7 to 9.0 g). During calcium acetate treatment, 18% of patients had a serum calcium corrected for albumin ≥ 11.0 mg/dL at the end of the study versus 2% for Renagel (p=0.001).

There appeared to be a trend for a decrease from baseline for total, LDL, and non-HDL cholesterol levels. The long term impact of Renagel on cardiovascular related morbidity and mortality, as a result of total, LDL and non-HDL reduction, is unclear.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

A mass balance study using ^{14}C-sevelamer hydrochloride in 16 healthy male and female volunteers showed that sevelamer is not systemically absorbed. No absorption studies have been performed in patients with renal disease.

5.3 PRECLINICAL SAFETY DATA

Acute toxicity

In non-clinical studies in rats and dogs, sevelamer hydrochloride reduced vitamin D, E and folic acid levels at doses of 0.6 -10 g/kg/day which are 6-100 times the recommended average clinical dose based on a mg/kg basis.

Carcinogenicity

Sevelamer hydrochloride was administered in the diet to rats and mice for two years. In mice and female rats, there was no increase in the incidence of tumours. In male rats, there was an increased incidence of transitional cell papillomas and transitional cell carcinomas in the urinary bladder at a dose of 3 g/kg/day, which is 10 times the maximum daily human dose (mg/kg basis) for a 50 kg person examined in clinical trials. These findings were considered likely to be secondary to increased serum and urinary calcium levels and inflammatory responses in the urinary bladder and their relevance to humans is unknown.

Mutagenicity

In an *in vitro* mammalian cytogenetics test with metabolic activation, sevelamer hydrochloride caused a statistically significant increase in the number of structural chromosome aberrations. Sevelamer hydrochloride was not mutagenic in the Ames bacterial mutation assay. Based on the available evidence, sevelamer hydrochloride is considered unlikely to be genotoxic *in vivo* following oral administration.

Teratogenicity

There was no evidence of teratogenicity in rabbits or rats following oral administration of sevelamer hydrochloride during the period of organogenesis at respective doses 1.5 and 4.5 g/kg/day (5 and 15 times respectively on a mg/kg basis for a 50 kg human). In rats receiving doses of 1.5 and 4.5 g/kg/day during organogenesis, there was reduced or irregular ossification of foetal bonds at exposures of 5 and 15 times the maximum tested human dose. In rabbits receiving 1 g/kg/day during organogenesis, there was an increase in early resorptions leading to a reduction in the number of live foetuses per liter at an exposure 3.3 times the maximum recommended human dose.

Oral administration of sevelamer hydrochloride to female rats throughout gestation and lactation at doses of 0.1-1 g/kg/day (exposure 0.3 - 3.3 times the maximum recommended human dose) did not affect the birth or growth of their offspring or their postnatal development.

In pregnant rats given dietary doses of 0.5, 1.5 or 4.5 g/kg/day of sevelamer hydrochloride during organogenesis, reduced or irregular ossification of foetal bones, probably due to a reduced absorption of fat-soluble vitamin D, occurred in mid-and high-dose groups (human equivalent doses less than the maximum clinical trial dose of 13 g). In pregnant rabbits given oral doses of 100, 500 or 1000 mg/kg/day of sevelamer hydrochloride by gavage during organogenesis, an increase of early resorptions occurred in the high-dose group (human equivalent dose twice the maximum clinical trial dose.)

Oral administration of sevelamer hydrochloride to female rats throughout gestation and lactation did not have any adverse effects on offspring (see section 4.6).

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The inactive ingredients in Renagel tablets are:

hypromellose

diacetylated monoglycerides

colloidal anhydrous silica

stearic acid.

The imprint contains:

iron oxide black ink

propylene glycol

isopropyl alcohol.

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

3 years

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Do not refrigerate. Protect from moisture. Keep the container tightly closed.

6.5 NATURE AND CONTENTS OF CONTAINER

Renagel tablets are packaged in white high density polyethylene bottles, with a child resistant polypropylene cap and an induction seal.

Renagel 800 mg tablets are available in pack sizes of 180 and 30*[§] tablets.

* Presentations currently not-marketed.

[§] Physician starter pack.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements for disposal.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics
PO Box 62027
Sylvia Park Auckland 1644
Freecall: 0800 283 684
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

19 October 2006

10 DATE OF REVISION OF THE TEXT

20 June 2022

Summary of changes

Section changed	Summary of new information
8	Change of sponsor