Epsom and St. Helier University Hospitals NHS Trust

WORKING IN PARTNERSHIP WITH

NHS

Surrey (East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG & Surrey Heath) North East Hampshire & Farnham CCG, Crawley CCG and Horsham & Mid-Sussex CCG

Colesevelam

Bile Acid Malabsorption

Prescribing Clinical Network classification: Amber

N.B. The eligibility criteria included here apply to new patients commencing treatment under this guideline & not to existing patients whose treatment was initiated under the previous version. However, monitoring and discontinuation criteria apply to all patients.

NOTES to the GP

Amber drugs: Prescribing to be initiated by a hospital specialist (or if appropriate by a GP with specialist interest) but with the potential to transfer to primary care. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs**.**

The questions below will help you confirm this:

- Is the patient's condition predictable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of page 4 to the requesting consultant at the Acute Trust. Until the requesting consultant at the Acute Trust has received a signed copy of page 4 indicating that shared care has been agreed all care (including prescribing) remains with the consultant at the Acute Trust.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your PCT pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

The GP has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant

Supporting Information - **This information sheet does not replace the SPC, which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.**

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This is an unlicensed indication for colesevelam. The principle for use of bile acid binders in diarrhoea is to prevent free bile acids from stimulating secretion of sodium and water, increasing motility, inducing mucus secretion and increasing mucosal permeability in the colon.[1,2]
Colestyramine has been used for many years and remains the first line agent but unfortunately many patients find it difficult to tolerate; although the diarrhoea may improve, other symptoms such as pain and bloating may worsen. Colesevelam is therefore a useful second line agent. It is also available in tablet form which some patients may tolerate better.

Dosage and administration
In studies for bile acid diarrhoea colesevelam was shown to be effective at doses between 1.25g (2 tablets) and 3.75g (6 tablets) per day.[1,2] Colesevelam may affect bioavailability of other drugs. Therefore when a drug interaction cannot be excluded with a concomitant medication drug for which minor variations in therapeutic level would be clinically important, colesevelam should be administered at least 4 hours before or after the concomitant medication. For concomitant medication that requires administration in divided doses, the required dose of colesevelam can be taken once a day.[3]

Contraindications and Cautions

Contra-indications
• Hypersensitivity to the active substance or to any of the excipients • Bowel or biliary obstruction

Cautions
• Caution should be exercised when treating patients with triglyceride levels greater than 3.4mmol/L due to the triglyceride increasing effect with colesevelam. Safety and efficacy are not established for patients with triglyceride levels greater than 3.4mmol/L[3] • The safety and efficacy of colesevelam in patients with dysphagia, swallowing disorders, severe gastrointestinal motility disorders, inflammatory bowel disease, liver failure or major gastrointestinal tract surgery have not been established. Consequently, caution should be exercised when colesevelam is used in patients with these disorders[3] • Colesevelam can induce or worsen present constipation. The risk of constipation should especially be considered in patients with coronary heart disease and angina pectoris[3]. • Colesevelam may affect the bioavailability of other medicinal products. Therefore when a drug interaction cannot be excluded with a concomitant medicinal product for which minor variations in the therapeutic level would be clinically important, colesevelam should be administered at least four hours before or at least four hours after the concomitant medication to minimize the risk of reduced absorption of the concomitant medication. For concomitant medications which require administration via divided doses, it should be noted that the required dose of colesevelam can be taken once a day • When administering medicinal products for which alterations in blood levels could have a clinically significant effect on safety or efficacy, physicians should consider monitoring serum levels or effects.

Side Effects – See BNF/SPC for full details
The following terminologies have been used in order to classify the frequencies of adverse drug reactions: Very common (≥ 1/10) Common (≥ 1/100 to < 1/10) Uncommon (≥ 1/1,000 to < 1/100) Rare (≥ 1/10,000 to < 1/1,000) Very rare (< 1/10,000) **<u>Nervous system disorders</u>** Common: Headache.

Gastrointestinal disorders
Very common: Flatulence, constipation.
Common: Vomiting, diarrhoea, dyspepsia, abdominal pain, abnormal stools, nausea, abdominal distension.
Uncommon: Dysphagia.
Very rare: Pancreatitis

Musculoskeletal and connective tissue disorders
Uncommon: Myalgia.

Adverse reactions were generally mild or moderate in intensity[1].

Drug Interactions - See BNF/SPC for full details

Interacting Drug	Details and Action to be taken
Anticoagulant therapy	Anticoagulant therapy should be monitored closely in patients receiving warfarin or similar agents, since bile acid sequestrants have been shown to reduce absorption of vitamin K and therefore interfere with the anticoagulant effect of warfarin. Specific clinical interaction studies with colesevelam and vitamin K have not been performed[3].
Ciclosporin	Colesevelam reduces the bioavailability of ciclosporin; therefore ciclosporin blood concentrations should be closely monitored. In addition, colesevelam should be administered at least 4 hours after ciclosporin in order to further minimise the risks related to the concomitant administration. Colesevelam should consistently be taken at the same times since the timing of intake of the two drugs could influence the degree of reduced bioavailability of ciclosporin[3].
Antidiabetic agents	Co-administration of colesevelam and glibenclamide caused a decrease in the AUC_{0-inf} and C_{max} of glibenclamide by 32% and 47%, respectively. No interaction was observed when colesevelam was administered four hours after glibenclamide. Co-administration of colesevelam and repaglinide had no effect on the AUC and caused a 19% reduction in the C_{max} of repaglinide, the clinical significance of which is unknown. No interaction was observed when colesevelam was administered one hour after repaglinide. No interaction was observed when colesevelam and pioglitazone were administered simultaneously in health volunteers.
Levothyroxine	In an interaction study in healthy volunteers, colesevelam reduced the AUC and C_{max} of levothyroxine when administered either concomitantly or after 1 hour. No interaction was observed when colesevelam was administered at least four hours after levothyroxine.
Oral contraceptive pill	Colesevelam can affect the bioavailability of the oral contraceptive pill when administered simultaneously. It is important to ensure that colesevelam is administered at least 4 hours after the oral contraceptive pill to minimise the risk of any interaction.
Phenytoin	There have been very rare reports of reduced phenytoin levels in patients who have received colesevelam administered with phenytoin.
Ursodeoxycholic acid	Colesevelam predominantly binds hydrophobic bile acids. In a clinical study colesevelam did not affect the faecal excretion of endogenous (hydrophilic) ursodeoxycholic acid. However, formal interaction studies with ursodeoxycholic acid have not been performed. Colesevelam should be administered at least fours hour before or at least four hours after the concomitant medication to minimise the risk of reduced absorption of the concomitant medication. Monitoring of the clinical effects of treatment with ursodeoxycholic acid should be considered.
Verapamil	Colesevelam decreased the C_{max} and AUC of sustained-release verapamil by approximately 31% and 11%, respectively. Since there is a high degree of variability in the bioavailability of verapamil, the clinical significance of this finding is unclear.
Other interactions	Colesevelam did not induce any clinically significant reduction in the absorption of vitamins A, D, E or K during clinical studies of up to one year. However, caution should be exercised when treating patients with a susceptibility to vitamin K or fat-

	soluble vitamin deficiencies, such as patients with malabsorption. In these patients, monitoring vitamin A, D and E levels and assessing vitamin K status through the measurement of coagulation parameters is recommended and the vitamins should be supplemented if necessary.

References

1. Walters J, Pattni S. Managing bile acid diarrhoea. Therapeutic Advances in Gastroenterology 2010; 3:349.
2. Pattni S and Walters J. Recent advances in the understanding of bile acid malabsorption. British Medical Bulletin 2009; 92:79-93.
3. Summary of Product Characteristics Cholestagel® Sanofi http://www.medicines.org.uk/emc/

Criteria for Use:

RESPONSIBILITIES and ROLES

Specialist responsibilities	
1	Diagnosis of condition and assessment of suitability of patient for Colesevelam treatment, also ensure all other treatment options have been fully explored.
2	Discuss the aims, benefits and side effects of treatment with the patient as well as their role
3	Make patients aware that colesevelam is being prescribed for an unlicensed indication, obtain informed consent and provide information about colesevelam and standard alternatives. Document consent in patient records.
4	Explain to the patient their treatment plan including the dosing schedule.
5	Initial monitoring of triglyceride levels with follow up monitoring arranged if raised
6	Initiate treatment with colesevelam and prescribe an initial 3 months' supply. Ensure efficacy in terms of symptom control and identify the lowest dose at which patients remain comfortable.
7	Monitor the INR and vitamin D levels if clinically indicated due to risk of colesevelam causing a reduction in absorption.
8	Advise patients to take a daily multivitamin preparation if appropriate.
9	Monitor and evaluate response to colesevelam treatment, including adverse drug reactions, with the patient and continue/discontinue treatment in line with agreed treatment plan
10	Discuss the possibility of shared care with the patient and ensure they understand the plan for their subsequent treatment when a proven benefit has been established.
11	Supply GP with summary of patient review (including anticipated length of treatment which is likely to be long term if treatment is effective) and a copy of the shared care guidelines recommending that a shared care arrangement is initiated.
12	Advising GP and the patient on related issues such as drug interactions and timing of administration of concomitant medications.
13	Responding to issues raised by GP after care of patient has been transferred.
14	Advise GP if treatment is to discontinue at any point.
15	Inform GP if patient does not attend planned follow-up appointment

General Practitioner responsibilities	
1	Subsequent prescribing of colesevelam at the dose recommended.
2	Monitoring the patient's overall health and well being and observing patient for evidence of ADRs/abnormalities and liaising with secondary care clinician if necessary.
3	Ensuring advice is sought from the secondary care clinician if there is any significant change in the patient's physical health status that may affect prescribing or appropriateness of the drug.
4	Monitoring triglyceride levels if level is greater than 3.4mmol/L. Consider annual check. Discuss the risks and benefits with the patient of raised triglyceride levels.
5	Refer patient back to secondary care if symptoms of diarrhoea recur.

Patient's / Carer's roles	
1	Ask the specialist or GP for information, if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with colesevelam.
3	Tell the specialist or GP of any other medication being taken, including over-the-counter products.
4	Report any side effects or concerns you have to the specialist or GP.

BACK-UP ADVICE AND SUPPORT

Contact details	Specialist	Telephone No.	Email address:
Specialist:			
Hospital Pharmacy:			
Out of hours contact			

SHARED CARE PRESCRIBING GUIDELINE

Colesevelam for Bile Salt Absorption

Agreement for transfer of prescribing to GP

Patient details / addressograph:

Name……..

Address……..
……..
……..

DOB…….

Hospital No…….

Drug name and dose:

The following tests, investigations have been carried out:

List any relevant tests:

Date initiated:…….

At the last patient review the drug appeared to be effectively controlling symptoms/ providing benefit:
Yes / No

The patients has now been stabilised on a dose of: ……..

I will arrange to review this patient regularly. Date of next clinic appointment:……

Consultant: Address: Contact Number	**Agreement to shared care, to be signed by GP and Consultant.** **Consultant Signature:** **……..** **Date:**
GP: Address: Contact Number	**GP Signature:** **……** **Date:**
Main Carer: Contact Number:	**If shared care is agreed and GP has signed above please return a copy of this page to the requesting consultant or alternatively fax to:** **Acute Trust please insert appropriate Fax Number**:
Key worker if appropriate: Contact Number: **PD CNS:**	