

Risks and wider benefits of bile acid sequestrant therapy

Bile acid sequestrants are a class of medications primarily used to lower low-density lipoprotein cholesterol (LDL-C) levels in patients with hypercholesterolemia. They function by binding bile acids in the gastrointestinal tract, preventing their reabsorption, and promoting their excretion. This process leads to increased conversion of cholesterol into bile acids in the liver, thereby reducing serum cholesterol levels. In this instance, however, they would be being used to lower serum PFAS, and any reduction in total or LDL cholesterol would be an additional benefit.

The main agents in this class include cholestyramine, colestipol, and colesevelam. These medications have varying safety and tolerability profiles.

Cholestyramine

Cholestyramine is one of the earliest bile acid sequestrants introduced for clinical use. It is available as a powder for oral suspension, often requiring multiple daily doses (Jacobson et al., 2015)

Common Side Effects

- **Gastrointestinal Disturbances:** Constipation is the most frequently reported side effect, occurring in up to 50% of patients (Hou & Goldberg, 2009). Other GI symptoms include bloating, abdominal discomfort, nausea, and flatulence.
- **Interference with Nutrient Absorption:** Cholestyramine can impair the absorption of fat-soluble vitamins (A, D, E, K) and folic acid (Glueck et al., 1972). Long-term use may lead to deficiencies if not monitored.
- **Drug Interactions:** It can bind other orally administered medications, reducing their bioavailability. Drugs such as digoxin, warfarin, and thyroxine may have decreased efficacy (Gallo et al., 1965).

Rare Side Effects

- **Hyperchloremic Acidosis:** Particularly in children and patients with renal impairment (Kamar & McQuillan, 2015).
- **Bleeding Tendencies:** Due to vitamin K deficiency from prolonged use (Vroonhof et al., 2003).

Colestipol

Colestipol is available in granule and tablet forms. Similar to cholestyramine, it binds bile acids in the intestine.

Common Side Effects

- **Gastrointestinal Symptoms:** Constipation is also common, though some studies suggest a slightly lower incidence compared to cholestyramine (Lent-Schochet D, 2023) Other GI side effects include indigestion, nausea, and haemorrhoids due to straining.
- **Nutrient Absorption Interference:** Like cholestyramine, it can reduce the absorption of vitamins and some medications (Hameed MH, 2024).

Colesevelam

Colesevelam is a newer bile acid sequestrant with a high affinity for bile acids and is available in tablet and oral suspension forms. It has an advantage over the other agents in that it has been shown to improve glycaemic control in type 2 diabetes mellitus (Fonseca et al., 2008).

Common Side Effects

- **Gastrointestinal Effects:** Studies have shown that colesevelam has a lower incidence of GI side effects compared to cholestyramine and colestipol (Puleston et al., 2005). Constipation remains the most common, but occurs less frequently.
- **Drug Interactions:** Colesevelam can affect absorption of other medicines

Comparative Analysis of Side Effects and tolerability

Gastrointestinal Side Effects: Cholestyramine and colestipol have higher rates of GI side effects, particularly constipation, compared to colesevelam (Puleston et al., 2005). The severity of constipation and abdominal discomfort is often greater with cholestyramine due to its formulation and higher required doses (Insull, 2006).

Drug and Nutrient Interactions: Cholestyramine and Colestipol can both bind other drugs and reduce absorption of vitamins, necessitating careful timing of medication administration and possible supplementation. Colesevelam exhibits somewhat fewer interactions, potentially allowing for more flexibility in dosing schedules (Drugs.com, 2024).

Patient Compliance: Cholestyramine's powder form can be unpalatable, affecting adherence. Colestipol tablets and colesevelam tablets/suspension offer improved compliance (Brunetti & DeSantis, 2015). Colesevelam requires fewer daily doses, enhancing tolerability (Drugs.com, 2024).

Capital and revenue requirements for establishing and running a service to prescribe bile acid sequestrants to reduce PFAS body burden

Necessary Equipment

None

Required Personnel

Any doctor can prescribe bile acid sequestrants and so the service could be delivered using existing resources in primary care, Some training may be required.

Maintenance and Regulatory Compliance

No additional requirement over the status quo

Cost of prescribing bile acid sequestrant therapies to reduce PFAS body burden

Capital cost

There are no capital costs

Additional Costs to Consider

- **Training:** There may be some training costs around the safe and appropriate prescribing of bile acid sequestrants. While it is likely that this could be delivered within existing resources, it would be reasonable to assume an additional cost of £5,000 per annum.
- **Drug costs:** The estimated costs of the different bile acid sequestrants, in generic formulations are outlined below. These are per person per year estimates and do not include any discounts that might be available.

Medication	Daily Dose	Annual Cost (£)
Cholestyramine (Generic)	12 g (3 sachets)	£350.40
Colestipol (Generic)	10 g (2 sachets)	£438.00
Colesevelam (Generic)	3.75 g (6 tablets)	£730.20

In summary

Bringing all of this together, there is zero capital outlay. Assuming that 50 people are treated and they require six months of treatment each, total drug costs vary from £8,760 for cholestyramine to £18,255.50 for colesevelam. On this basis, the maximum total programme cost would be £23,255.50 per annum.

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