Consensus Guidelines for the Prescription and Administration of Oral Bowel Cleansing Agents

The Association for Coloproctology of Great Britain and Ireland for The Royal College of Surgeons
The British Society of Gastroenterology
The British Society of Gastrointestinal and Abdominal Radiology
The Renal Association
The Royal College of Radiologists
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INTRODUCTION

Oral bowel cleansing preparations are used before colonic surgery, endoscopic and radiological assessment of large and small intestine to minimise faecal contamination. In general, these preparations are safe and well tolerated. However, in February 2009, the National Patient Safety Agency (NPSA) issued a Rapid Response Report alerting healthcare providers to the potential risk of harm associated with the use of oral bowel cleansing preparations. These risks included harm as a result of prescription of bowel preparation to patients in whom there was a definite contraindication (eg, presence of ileostomy; bowel obstruction); renal failure as a result of phosphate nephropathy; complications of hypovolaemia; and electrolyte disturbances including hypokalaemia, hyponatraemia, and hypermagnesaemia. Although there are no reliable estimates of the frequency of each of these complications, it is reasonable to put systems in place to reduce the risk of complications so long as this response is proportionate and does not greatly add to the complexity or cost of investigation.

The NPSA Report instructed Trusts that safeguards should be implemented at a local level to reduce this risk, and specifically required that all Trusts ensure that a clinical assessment of each patient for contraindications and risks occurs; that the use of a bowel cleansing preparation was authorised by a clinician; that an explanation on the safe use of the preparation was provided to the patient; and that a safe system exists for the supply of the preparation for each patient. This guidance has been prepared to help in the first of these recommendations, relating to clinical assessment. We believe that guidelines are necessary because the risk of complications depends on the choice of bowel preparation and on risk factors present in the individual patient, and there has been to date no definitive guidance on which preparation to use for which patients.

The guidelines do not include recommendations on incorporation of prescription of bowel cleansing agents into the request for investigation, nor do they cover the use of oral bowel cleansing agents in children or in pregnancy. While focused on colonic investigation, these guidelines may be also applied to use of bowel cleansing agents for radiological or endoscopic examination of the small bowel, where a reduced dose is typically administered compared to colonic examinations.

Although there are guidelines for bowel preparation prior to colonoscopy already in existence, they do not adequately address the risks identified by the NPSA.
Methodology and Terms of Reference

These recommendations are based on consensus between the authors, each of whom circulated drafts to members of their specialist society. Given the timescale imposed by the NPSA (requiring implementation of the recommendations in the Rapid Response Report by 7 September 2009), we have not performed a systematic review nor adhered in full to the guideline development methodology recommended by the National Institute for Health and Clinical Excellence (NICE). There was no representation from patient groups or from the pharmaceutical industry. The companies that market the products discussed have not been consulted for their views; some of our recommendations go beyond the Summary of Product Characteristics. The evidence for these recommendations has been assessed using the modified GRADE system.\textsuperscript{3,4} The modified GRADE system first defines the strength of the recommendations of guideline authors; expert recommendations are graded as ‘strong’ (Grade 1) or ‘weak’ (Grade 2) balanced by benefits and risks, burden and cost. Secondly, the quality or level of evidence upon which the recommendation is based is designated as high (Grade A), moderate (Grade B), low (Grade C) or very low (D), depending on study design and consistency of results. Grades of recommendation and quality of evidence may therefore range from 1A to 2D (see Appendix 1).

The NPSA supports these guidelines (Appendix 2) and we hope that NICE will develop guidelines to cover this topic in the near future.

Conflicts of interest

None of the authors have any conflict of interest to declare.
BACKGROUND

Bowel cleansing agents available for use

A number of different oral bowel cleansing agents are currently available in the UK, including:5

- **Klean Prep®** (Norgine); polyethylene glycol
- **Moviprep®** (Norgine); polyethylene glycol
- **Fleet Phospho-Soda®** (De Witt); sodium dihydrogen phosphate dehydrate and disodium phosphate dodecahydrate
- **Picolax®** (Ferring); sodium picosulphate and magnesium citrate
- **Citrafleet®** (De Witt); sodium picosulphate and magnesium citrate
- **Citramag®** (Sanochemia); magnesium carbonate and citric acid.

The ideal oral bowel cleansing agent would be convenient to administer, well tolerated, effective in cleansing, with an acceptable side-effect profile. No single agent is ideal in all clinical scenarios, and research into the ideal agent (or combination) continues. The different oral bowel cleansing agents available in the UK are summarised in Appendix 3.

Polyethylene glycols (macrogols) are non-absorbable isosmotic solutions that pass through the bowel without net absorption or secretion. Significant fluid and electrolyte shifts are therefore attenuated. The preparations must be diluted in large volumes of water (up to 4 L) to achieve the desired cathartic effect, and often carry an unpalatable taste (despite flavourings). Compliance is better with divided-dose regimens (for example, the initial 2–3 L on the night prior to the procedure and the remaining 1–2 L the following morning).6 Not all of the ingested water stays within the gut lumen; absorption of water can therefore lead to water intoxication in predisposed patients. Adequate bowel preparation can be achieved within 12 hours with Moviprep®, which is a significant advantage. Pretreatment with domperidone or metoclopramide to facilitate gastric emptying may be considered.

Conversely, oral sodium phosphate preparations are hyperosmotic and promote colonic evacuation by drawing large volumes of water into the colon (1–1.8 L of water per 45 ml of preparation).7 They are typically diluted in much smaller volumes of water than the polyethylene glycols (approximately 250 ml). Sodium phosphate preparations have been compared to polyethylene glycols in numerous studies and have generally been found to be safe, equally or more effective, and consistently better tolerated.8-12 One meta-analysis of eight controlled trials concluded that an ‘adequate’ preparation was equally likely with sodium phosphate or
polyethylene glycol preparations, but that an ‘excellent’ preparation was more likely with sodium phosphate preparations.9

Picosulphate is a prodrug that is metabolised within the bowel lumen to a stimulant that promotes peristalsis. It is often combined with magnesium salts (for example, in Picolax® or Citrafleet®), which act synergistically through their osmotic effects.13,14 A dose sufficient to provide adequate bowel cleansing is usually diluted in a total of 300 ml of water. Data on efficacy of cleansing are mixed when compared with other agents.15–20 It remains widely used for bowel preparation for radiological procedures.21–24

Preparations of magnesium carbonate with citric acid, such as Citramag®, are osmotic saline agents that require only 200 ml of water as a diluent. Magnesium salts are well tolerated and effective, and have been reported to be used to prepare the bowel in one in every three colonoscopies undertaken in the UK.25

Some types of bowel preparation leave a significant amount of watery residue in the gut lumen which is not a problem for endoscopic or surgical procedures. However, this may interfere with mucosal visualization at CT colonography and barium enema and these laxatives are usually avoided for radiological imaging of the colon. Picolax® produces the ‘driest’ bowel; Citramag® is intermediate; and polyethylene glycol preparations leave the highest amount of watery residue. The choice of agent therefore depends to some extent on which procedure the patient is being prepared for.

Bioavailability of some medications may be affected by bowel cleansing (eg, oral contraceptive pill). There is no evidence relating to bioavailability of immunosuppressive agents. Oral iron should be stopped at least five days before colonoscopy as it forms an adherent residue that interferes with mucosal visualisation.

Diabetic glycaemic control, particularly in patients with type 1 diabetes, can be problematic during the period of dietary restriction, requiring individualised advice from local diabetic specialists. Admission for intravenous glucose and insulin may be required in a small number of cases.

Preparations vary in the requirement for dietary restrictions; most require that a clear liquid or low residue diet should be followed for the 24 hours or longer prior to the procedure, but with Fleet Phospho-Soda® it is only necessary to avoid solid food during the dosing period.
Combinations of different bowel cleansing agents (eg, Picolax® and Klean Prep®, or combinations of senna granules with Citramag®), are used in some centres; these regimens are beyond the scope of these guidelines.

**Complications from bowel cleansing agents**

When administered correctly, all of the preparations listed have been demonstrated to be safe for use in healthy individuals without significant co-morbidity, and to effect adequate bowel cleansing. However, as hypertonic solutions, sodium phosphate preparations can cause major fluid and electrolyte shifts, and should generally be considered second line agents that should only be prescribed to patients without other co-morbidities (in particular, these preparations should be avoided in those with chronic kidney disease, congestive cardiac failure, liver failure, hypertension or patients taking renin-angiotensin blockers or diuretics) (Appendix 3).

Current practice for elective procedures is typically for patients to self-medicate oral bowel cleansing agents at home, often received through the post without formal screening of their co-morbidities, medications or hydration state. While the practice of self-medication at home should remain feasible for the majority of patients, it is clear that a screening process is necessary to ensure that patients at risk of harm from oral bowel cleansing agents are identified and prepared appropriately (Appendix 6).

1: **Hypovolaemia**

Patients receiving oral bowel cleansing agents are at risk of developing the complications of hypovolaemia and intravascular volume depletion – including syncope, myocardial ischaemia and acute kidney injury secondary to acute tubular necrosis. This risk is likely to be greatest with sodium phosphate preparations but also exists with sodium picosulphate; the risk of hypovolaemia is least with polyethylene glycol preparations.

2. **Hypokalaemia**

Hypokalaemia can occur for two reasons after bowel preparation: increased gastrointestinal loss of secreted potassium complicating the use of hyperosmotic and stimulant preparations, and, with the use sodium phosphate, increased urinary loss as a result of hyperphosphaturia. Co-administration of a carbohydrate-electrolyte solution with sodium phosphate has been reported to reduce the risk of hypokalaemia.
3. Hyponatraemia
The ingestion of large volumes of water, particularly in the context of reduced free water clearance, also predisposes patients to hyponatraemia (a risk that was highlighted specifically in the NPSA Rapid Response Report). Macrogols involve the ingestion of up to 4 L of water, but are designed to be isotonic. The risk of hyponatraemia is probably highest when large volumes of water are ingested (as a result of over-zealous adherence to advice to ‘drink plenty of fluids’) to offset water loss into the colon caused by oral sodium phosphate and sodium picosulphate preparations, but hyponatraemia has also been reported after use of macrogols.

4. Phosphate nephropathy
Acute phosphate nephropathy is an increasingly reported but under-diagnosed cause of chronic kidney disease, which may occur in up to 1 in 1,000 patients who receive sodium phosphate preparations. Oral sodium phosphate preparations provoke a transient mild hyperphosphataemia, which is most profound in elderly subjects. This is rarely associated with untoward events and may reflect the normal reduction in glomerular filtration rate (GFR) with advancing age. For this reason, the recommendations in this document are based on GFR and not on age. However, other factors which promote hyperphosphataemia predispose patients to acute phosphate nephropathy, such as inappropriate phosphate dosing, increased bowel transit time, and a reduced ability to excrete a phosphate load (such as renal impairment). Factors promoting tubular precipitation of calcium phosphate also predispose to acute phosphate nephropathy and include inadequate hydration during phosphate administration, hypertension with arteriosclerosis, and medications including non-steroidal anti-inflammatory drugs, diuretics and renin-angiotensin inhibitors. Heart failure, cirrhosis and advancing age are additional risk factors.

Recent concerns over acute phosphate nephropathy are reflected in changes made to the availability of oral sodium phosphate preparations by the United States Food and Drug Administration. These preparations are no longer available as over-the-counter medications for oral bowel cleansing, and those sodium phosphate preparations available as over-the-counter laxatives now carry a Boxed Warning.

5. Hypocalcaemia
Hypocalcaemia is a direct result of hyperphosphataemia and occurs in all patients who receive oral sodium phosphate. Hypoparathyroidism is a risk factor for severe hypocalcaemia in this situation.
6. Hypernatraemia

Hypernatraemia is uncommon, but can occur as a result of the sodium load in oral sodium phosphate preparations in combination with inadequate water intake.\textsuperscript{31}

**Is a bowel cleansing agent required?**

Oral bowel cleansing agents have traditionally been prescribed (predominantly on the basis of observational data and expert opinion) prior to elective colorectal surgery in an effort to reduce the likelihood of surgical complications arising from anastomotic leakage. However, opinion is increasingly divided on the merits of bowel preparation in this context. There is an increasing body of evidence to suggest that bowel preparation is not required for most procedures. Two recent trials are particularly noteworthy. Firstly, in a trial randomising over 1,300 patients, Jung \textit{et al} found no appreciable difference in clinical anastomotic leaks and intra-abdominal abscesses between those patients receiving bowel preparation or no bowel preparation (2.6\% vs 4.3\%, effect difference 1.7\%, 95\% CI 0.7–2.7).\textsuperscript{42} Similar conclusions were reached by Contant \textit{et al}, who randomised 1,431 patients undergoing elective colorectal surgery to receive an oral bowel cleansing agent (polyethylene glycol or oral sodium phosphate) or no bowel preparation.\textsuperscript{43} While the rate of intra-abdominal abscesses was slightly higher in the group not receiving bowel preparation (4.7\% vs 2.2\%, \textit{p}=0.02), the general incidence was low. All other endpoints (mortality, length of hospital stay, re-intervention rate) were similar among the two groups.

At present, patients who undergo abdominoperineal excision of the rectum, right hemicolectomy, total proctocolectomy and ileo-anal pouches, are generally not prescribed oral bowel cleansing agents. However, oral bowel cleansing agents are used more widely in patients undergoing anterior resection and left-sided resections. Postoperative rapid recovery programmes are being increasingly employed and usually avoid bowel preparation. In the light of these uncertainties, we recommend that the prescription of oral bowel cleansing agents is discussed with the patient.

In patients requiring bowel investigation, with co-morbidity that may increase the risk of complications from bowel preparation, it is worth considering the role of investigations that require minimal or no formal bowel purgation. CT colonography with faecal tagging is an area of growing clinical interest and research, using iodinated or barium-based contrast to mark faeces in the colon. It is an effective method of diagnosing and excluding colon cancer and other colonic diseases and potentially avoids the complications of bowel preparation. CT colonography is likely to have an increasingly prominent role in the future, particularly if bowel purgation can be avoided.
Gastrografin® is commonly used for small bowel studies (for instance, the investigation of postoperative ileus) and sometimes for CT colonography. It is hyperosmolar and, when used undiluted and/or with high doses, may cause an osmotic diarrhoea. Recommendations on its use are beyond the scope of these guidelines, but clinicians should be aware of the potential risk of causing hypovolaemia.

Finally, these guidelines are intended to reduce the risk of complications from the use of oral bowel cleansing agents, but they do not address every situation and are not a substitute for sound clinical judgement.
SUMMARY OF GUIDELINE STATEMENTS

1. Absolute contraindications to the use of oral bowel cleansing agents.

2. The choice of oral bowel cleansing agent.

3. The administration of oral bowel cleansing agents. (3.1–3.6).

4. Relative contraindications: circumstances in which the choice of a particular oral bowel cleansing agent or administration protocol may confer significant benefits.

   4.1 Chronic kidney disease (4.1.1–4.1.8)
   4.2 Haemodialysis patients (4.2.1–4.2.2)
   4.3 Peritoneal dialysis patients (4.3.1–4.3.2)
   4.4 Renal transplant patients (4.4.1–4.4.2)
   4.5 Congestive cardiac failure (4.5.1–4.5.2)
   4.6 Liver cirrhosis and/or ascites (4.6.1)
   4.7 Patients taking particular medications
      4.7.1 Renin-angiotensin blockers
      4.7.2 Diuretics
      4.7.3 Non-steroidal anti-inflammatory drugs
      4.7.4 Medications known to induce the Syndrome of Inappropriate ADH secretion

5. Areas in which further research is needed.
GUIDELINE STATEMENTS

1. The following conditions are absolute contraindications for the use of all oral bowel cleansing preparations:

   • Gastrointestinal obstruction or perforation, ileus, or gastric retention
   • Acute intestinal or gastric ulceration
   • Severe acute inflammatory bowel disease or toxic megacolon
   • Reduced levels of consciousness
   • Hypersensitivity to any of the ingredients
   • Inability to swallow without aspiration (in this situation a nasogastric tube may be used for administration)
   • Ileostomy

   Grade 1D

2. The choice of oral bowel cleansing agent

Magnesium salt preparations should be avoided in patients with stage 4 and 5 chronic kidney disease (see Appendix 4 for the definition of chronic kidney disease). Grade 2D

Sodium picosulphate preparations should be avoided in patients at risk of, or suffering from, hypovolaemia, including those patients taking high-dose diuretics, those with congestive cardiac failure and advanced cirrhosis, and those with chronic kidney disease.

The use of oral sodium phosphate preparations is strongly discouraged in patients with chronic kidney disease, pre-existing electrolyte disturbances, congestive cardiac failure, cirrhosis or with a history of hypertension. Grade 1C

The use of oral sodium phosphate preparations in otherwise healthy patients is currently acceptable in cases where sodium picosulphate, magnesium salts and polyethylene glycols are contraindicated or have proven ineffective or intolerable. Grade 2C

3. The administration of oral bowel cleansing agents

   3.1 The appropriate doses of oral bowel cleansing preparations should not be exceeded. Grade 1C
Where sodium phosphate preparations are prescribed, modification of the standard dose (two 45 ml doses 9–12 hrs apart) to a 45 ml dose followed by a 30 ml dose should be considered. Grade 1C. The latter regime provides equally effective bowel cleansing but a significantly lower serum phosphate level.\textsuperscript{44} Furthermore, increasing the interval between doses to 24 hours reduces the incidence of clinically relevant hyperphosphataemia (>2.1 mmol/L) without compromising efficacy.\textsuperscript{45} Therefore, when administering sodium phosphate preparations, a regime of a 45 ml dose followed by a 30 ml dose 24 hours later should be used. Grade 2C

3.2 The period of bowel cleansing should never exceed 24 hours. Grade 1C

To improve both tolerability and efficacy, consideration should be given to splitting the dose of oral bowel cleansing agent over 12 hours when polyethylene glycol preparations are utilised. Grade 2B

3.3 Hypovolaemia must be corrected prior to administration of oral bowel cleansing preparations. Grade 1C

Patients with co-morbidities indicating a predisposition to hypovolaemia should be assessed prior to commencing administration of oral bowel cleansing agents. Patients at particular risk of hypovolaemia include (but are not limited to) those with chronic or severe diarrhoea, chronic vomiting, dysphagia, those with persistent hyperglycaemia and those taking high-dose diuretics (see Section 4.7.2). Admission to hospital for pre-hydration may be necessary. Grade 2D

Where intravenous fluid replacement is undertaken, isotonic fluid (for example, Hartmann’s solution) may be preferable.\textsuperscript{46} Grade 2D

3.4 Hypovolaemia must be prevented during administration of oral bowel cleansing preparations. Grade 1C

Patients should receive clear instructions regarding oral fluid intake and these instructions should also be provided in writing. Grade 1D

Some patients receiving polyethylene glycol may achieve adequate bowel preparation without consuming the full 4 litres of fluid that are generally suggested.\textsuperscript{47} It is reasonable to advise patients to discontinue drinking fluids if their bowel motions become watery and clear. Grade 2C
Isotonic electrolyte oral rehydration solutions may be of benefit, and should be considered in place of high water intake for patients at risk of hyponatraemia being prescribed sodium picosulphate or sodium phosphate. Grade 2C

Admission for intravenous fluid replacement should be considered in all patients who may be unable to maintain adequate oral intake at home (for example, the elderly and those with reduced mobility). Grade 1C

3.5 Renal function should be measured (using an estimated GFR from serum creatinine concentration) in all patients in whom the use of oral bowel cleansing agents is considered. Grade 1C

3.6 Advice regarding regular medications

Patients should be advised that their regular oral medications should not be taken one hour before or after administration of bowel cleansing preparations due to the possibility of impaired absorption. Grade 1C

Patients taking the oral contraceptive pill should be advised to take alternative precautions during the week following the administration of the oral bowel cleansing agent. Grade 1C

Patients in whom the possibility of a reduction in the absorption of their regular medications may prove catastrophic (for example, patients taking immunosuppression for transplants) may require admission for the administration of intravenous preparations. Grade 2D

Patients with diabetes mellitus receiving treatment with insulin will also require specific advice, which should be agreed locally so as to be consistent with local practice and guidance for management of diabetes mellitus while ‘nil by mouth’ or on reduced oral intake.

4. The following conditions are relative contraindications for the use of oral bowel cleansing preparations; consideration should be given to the choice and manner of administration of oral bowel cleansing agent in accordance with the recommendations outlined below.
Polyethylene glycol is generally safer than sodium phosphate preparations for patients with electrolyte or fluid imbalances, as may be seen in conditions such as chronic kidney disease, congestive heart failure and liver failure.

Moviprep® requires a smaller total volume of fluid (3 L) to be consumed than Klean Prep® (4 L) and may be preferable in patients in whom the ability to ingest high volumes of fluid causes concern.

4.1 Chronic kidney disease (CKD)

Knowledge of an individual’s excretory renal function is an essential consideration when identifying the most appropriate oral bowel cleansing preparation. Pre-existing CKD (sometimes unrecognised) is the single most important factor in the development of acute phosphate nephropathy in patients receiving oral sodium phosphate preparations.

4.1.1 Patients with Stage 3, 4 or 5 CKD (an eGFR less than 60 ml/min/1.73m²) should not receive oral sodium phosphate preparations. Grade 1C

4.1.2 Patients with pre-existing electrolyte imbalances should not receive oral sodium phosphate preparations. Grade 1C

4.1.3 For patients with early CKD (Stages 1—3), polyethylene glycols, Picolax® and Citramag® are the preferred oral bowel cleansing agents. Grade 1C

4.1.4 In patients with Stage 4 or 5 CKD, who are not receiving dialysis, the use of either polyethylene glycol preparations or Picolax® may be considered. Grade 2C

4.1.5 Polyethylene glycol preparations may be preferable in those patients with Stage 4 or 5 CKD, who are not receiving dialysis, and who are expected to be able to tolerate the ingestion of the larger volumes of fluid required with these agents. Moviprep® requires a smaller total volume of fluid (3 L) to be consumed than Klean Prep® (4 L) and may be preferable these patients. Grade 1D

4.1.6 In patients with Stage 4 CKD, or patients with Stage 5 CKD who are not receiving dialysis, the use of Picolax® or Citramag® is associated with a small risk of magnesium accumulation and should therefore be reserved for those patients likely to be unable to tolerate the ingestion of the volume of fluid required to administer polyethylene glycol preparations. Grade 2D

4.1.7 In patients with Stage 5 CKD, who are not receiving haemodialysis, the use of Picolax® is associated with a small risk of magnesium accumulation and should therefore be reserved for those patients likely to be unable to
tolerate the ingestion of the volume of fluid required to administer polyethylene glycol preparations. Grade 2D

4.1.8 Due to the possibility of magnesium accumulation, the use of Citramag® and Citra-Fleet® should be avoided in patients with stage 5 CKD who are not receiving haemodialysis. Grade 1D

It should be noted that Klean Prep® is currently the only oral bowel cleansing agent available in the UK not stated to be absolutely or relatively contraindicated in CKD in the summary of product characteristics.

Subgroups of patients with CKD requiring further consideration include the following.

4.2 Patients undergoing chronic haemodialysis

4.2.1 Although acute kidney injury is rarely a concern in these patients, the possibility of intravascular depletion secondary to oral bowel cleansing agents has other implications in patients receiving chronic haemodialysis. Firstly, in those patients dialysing through arteriovenous fistulae or PTFE grafts, a period of intravascular depletion, if it causes hypotension, may risk causing thrombosis of the dialysis access. Secondly, the combination of dialysis (which is itself often associated with significant fluid and electrolyte shifts) and administration of oral bowel cleansing agents, may provoke more profound hypovolaemia than would otherwise occur. Furthermore, the significant oral fluid intake required with polyethylene glycol preparations may provoke fluid overload in anuric patients. For these reasons, each case should be considered on an individual basis, and the timing of dialysis sessions should be tailored to the situation. Admission to hospital to co-ordinate and oversee dialysis prescription and administration of oral bowel cleansing agents may be necessary for some patients receiving chronic haemodialysis. Grade 2D

4.2.2 Although contraindicated in Stage 4 and 5 CKD in pre-dialysis patients, sodium picosulphate and magnesium salts can be used safely as oral bowel cleansing agents in patients receiving haemodialysis. Grade 2D

4.3 Patients undergoing peritoneal dialysis

4.3.1 Peritoneal dialysis is generally associated with less significant fluid shifts than haemodialysis. Admission to hospital for administration of oral bowel cleansing agents is therefore less likely to be necessary for the majority of peritoneal
dialysis patients. However, a small proportion of patients undertaking peritoneal dialysis have a small but important degree of residual native renal function. This must be assessed on an individual basis. Measures to avoid significant fluid shifts and possible intravascular volume depletion are therefore important in this group. **Admission to hospital to oversee administration of oral bowel cleansing agents should be considered in those considered to have important residual renal function. Grade 2D**

4.3.2 Patients undertaking peritoneal dialysis should continue to dialyse in the normal way during the administration of the oral bowel cleansing agent. The dialysis fluid should be drained out prior to the procedure for which the bowel preparation has been prescribed.

4.4 Renal transplant recipients

4.4.1 These patients should not receive sodium phosphate preparations unless all the alternative agents are contraindicated. Grade 1D

4.4.2 Admission to hospital may be advisable on an individual patient basis when concerns exist over the absorption of immunosuppressants during concomitant administration of oral bowel cleansing agents. Grade 2D

4.5 Congestive cardiac failure

Congestive cardiac failure is associated with a reduction in renal blood flow and an associated fall in GFR; the ability of these patients to excrete a phosphate load is therefore reduced, leading to an increased risk of acute phosphate nephropathy. Furthermore, these patients are at particular risk of hyponatraemia caused by the combination of hypovolaemia and high water intake.

4.5.1 Macrogol preparations are the preferred oral bowel cleansing agents in patients with congestive cardiac failure. Grade 2D

4.5.2 Patients with significant congestive cardiac failure (NYHA Class III or IV, or an Ejection Fraction below 50%) should not receive oral sodium phosphate preparations. Grade 1C

Many medications commonly prescribed to treat heart failure require evaluation prior to administration of an oral bowel cleansing agent. For example, where possible, diuretics, angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers should be discontinued in accordance with the guidance below.
4.6 Liver cirrhosis and/or ascites

4.6.1 Cirrhosis has been identified as a possible risk factor for acute phosphate nephropathy. Polyethylene glycol is the preferred oral bowel cleansing agent for use in patients with liver cirrhosis or ascites. Grade 2D

4.7 Caution is advised in the administration of oral bowel cleansing preparations to patients taking certain medications.

4.7.1 Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers
An increase in efferent glomerular arteriolar tone is an important physiological response to hypotension and/or volume depletion, enabling the GFR to be maintained. In the presence of angiotensin-converting enzyme inhibition, this compensatory response is ameliorated. Patients established on angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are prone to deterioration in renal function during periods of hypovolaemia (eg, precipitated by oral bowel cleansing agents).

Furthermore, renin-angiotensin blockers also accentuate bicarbonaturia through inhibition of angiotensin II, enhancing alkalinisation of the urine. This promotes calcium and phosphate precipitation, increasing the risk of acute phosphate nephropathy in the presence of oral sodium phosphate preparations.50

Where possible, therefore, renin-angiotensin blockers should be discontinued on the day of administration of oral bowel cleansing agents and not reinstated until 72 hours after the procedure. Grade 2D

4.7.2 Diuretics
Diuretics may alter electrolyte balance and predispose to intravascular volume depletion. Therefore, as for all patients, it is advised that a patient’s hydration status is assessed prior to administration of oral bowel cleansing preparations in patients taking diuretics.
Unless there is judged to be a significant risk of pulmonary oedema, **diuretics should be temporarily discontinued on the day of the administration of oral bowel cleansing preparation. Grade 1D**

4.7.3 Non-steroidal anti-inflammatory drugs (NSAIDs)

These medications reduce renal perfusion and therefore limit the kidneys’ capacity to compensate for reduced renal perfusion through volume depletion. Where possible, therefore, **NSAIDs should be discontinued on the day of administration of oral bowel cleansing preparations and withheld until 72 hours after the procedure. Grade 1D**

4.7.4 Medications known to induce the Syndrome of Inappropriate Anti-diuretic Hormone (SIADH) secretion

These medications increase the risk of water retention and/or electrolyte imbalance, and include tricyclic anti-depressants, selective serotonin reuptake inhibitors, many anti-psychotic drugs and carbamazepine. While these medications need not be discontinued, **serum urea and electrolytes should be checked prior to administration of oral bowel cleansing preparations in patients taking these medications. Grade 2D**
AREAS REQUIRING FURTHER RESEARCH

1. Should the serum creatinine concentration be re-checked after a patient has received oral sodium phosphate, and when should this be undertaken?

Best practice remains unclear. Identification at a later date of non-progressive chronic kidney disease in a typical patient who has developed acute phosphate nephropathy (an elderly person with hypertension and minimal proteinuria) is unlikely to provide a strong indication for renal biopsy; the link between oral bowel cleansing preparation and renal impairment is less likely to be noticed as time elapses. A decision not to check the serum creatinine concentration following oral sodium phosphate preparations may lead to cases of acute phosphate nephropathy being missed. This may result in the patient receiving further sodium phosphate preparations. The optimal timing of such a blood test has not been established. Furthermore, it is unclear whether it should be undertaken in all patients receiving oral sodium phosphate preparations or simply those at higher risk for acute phosphate nephropathy. A cost–benefit analysis is also required.

2. How safe is the use of oral sodium phosphate preparations in patients without those co-morbidities currently identified as risk factors of acute phosphate nephropathy?

Given the current evidence base, and their superior tolerability, the use of oral sodium phosphate preparations as oral bowel cleansing agents in patients without chronic kidney disease, congestive heart failure or liver failure probably remains acceptable. However, further studies are required to ascertain the true safety of sodium phosphate preparations as bowel cleansing preparations for screening investigations (which, by their nature, are often repeated over time) and in patients with very early (Stage 1 or 2) chronic kidney disease.

3. In the presence of predisposing conditions such as heart failure, what is the risk of acute electrolyte disorders with each preparation?

Hyponatraemia appears most likely to occur when predisposed patients drink large volumes of water, causing water intoxication, as a result of over-enthusiastic adherence to advice to drink ‘plenty of water’. Use of macrogols involves ingestion of up to 4 litres of fluid, but this is as an isotonic solution and as such, is designed not to cause electrolyte abnormalities. However, how effective these preparations are at preventing electrolyte disorders requires further study.
REFERENCES

2. Wexner SD, Beck DE, Baron TH et al; American Society of Colon and Rectal Surgeons; American Society for Gastrointestinal Endoscopy; Society of American Gastrointestinal and Endoscopic Surgeons. A consensus document on bowel preparation before colonoscopy: prepared by a task force from the American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). *Gastrointest Endosc* 2006;63(7):894-909.


## APPENDIX 1: THE MODIFIED GRADE SYSTEM

<table>
<thead>
<tr>
<th>Grade of Recommendation</th>
<th>Clarity of risk/benefit</th>
<th>Quality of supporting evidence</th>
<th>Implications for clinical practice</th>
</tr>
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<tbody>
<tr>
<td><strong>1A</strong> Strong recommendation. High quality evidence.</td>
<td>Benefits clearly outweigh risk and burdens, or vice versa</td>
<td>Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.</td>
<td>Strong recommendations, can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless there is a clear rationale for an alternative approach.</td>
</tr>
<tr>
<td><strong>1B</strong> Strong recommendation. Moderate quality evidence.</td>
<td>Benefits clearly outweigh risk and burdens, or vice versa</td>
<td>Evidence from randomized, controlled trials with important limitations (inconsistent results, methods flaws, indirect or imprecise), or very strong evidence of some other form. Further research may impact on our confidence in the estimate of benefit and risk.</td>
<td>Strong recommendation and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.</td>
</tr>
<tr>
<td><strong>1C</strong> Strong recommendation. Low quality evidence.</td>
<td>Benefits appear to outweigh risk and burdens, or vice versa</td>
<td>Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.</td>
<td>Strong recommendation, and applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality.</td>
</tr>
<tr>
<td><strong>1D</strong> Strong recommendation Very low quality evidence</td>
<td>Benefits appear to outweigh risk and burdens, or vice versa</td>
<td>Evidence limited to case studies</td>
<td>Strong recommendation based mainly on case studies and expert judgement</td>
</tr>
<tr>
<td><strong>2A</strong> Weak recommendation. High quality evidence.</td>
<td>Benefits closely balanced with risks and burdens</td>
<td>Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.</td>
<td>Weak recommendation, best action may differ depending on circumstances or patients’ or societal values</td>
</tr>
<tr>
<td><strong>2B</strong> Weak recommendation. Moderate quality evidence.</td>
<td>Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks and burdens</td>
<td>Evidence from randomized, controlled trials with important limitations (inconsistent results, methods flaws, indirect or imprecise), or strong evidence of some other research design. Further research may change the estimate of benefit and risk.</td>
<td>Weak recommendation, alternative approaches likely to be better for some patients under some circumstances</td>
</tr>
<tr>
<td><strong>2C</strong> Weak recommendation. Low quality evidence.</td>
<td>Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens</td>
<td>Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.</td>
<td>Weak recommendation; other alternatives may be reasonable</td>
</tr>
<tr>
<td><strong>2D</strong> Weak recommendation Very low quality evidence</td>
<td>Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens</td>
<td>Evidence limited to case studies and expert judgement</td>
<td>Very weak recommendation; other alternatives may be equally reasonable.</td>
</tr>
</tbody>
</table>
APPENDIX 2: STATEMENT OF SUPPORT FOR THE GUIDELINES BY THE NPSA

"The NPSA welcomes the helpful guidelines developed by independent clinical experts which provide additional information to help in reducing risks to patients. The NPSA issued a Rapid Response Report in response to the death of a patient with known contra-indications and reports of 218 other incidents relating to oral bowel cleaning preparations. A key recommendation was assessing the risks to patients (such as renal failure or pre-existing bowel conditions) before prescribing these medicines. Given the complexity of these decisions, weighing the evidence on individual preparations and particular risk factors for each patient, these practical clinical guidelines from experts following review of existing evidence and current practice are highly valuable. The NPSA alerted the service to the risks and the need for vigilance - these guidelines provide further detailed information for individual clinicians to make the safest decisions for their patients. We also support the case for further robust review of evidence by NICE on the effectiveness of particular preparations for specific groups of patients and conditions and to address gaps in current guidelines identified by this work."
## APPENDIX 3: COMMENTS REGARDING POTENTIAL ADVANTAGES AND COMPLICATIONS OF INDIVIDUAL ORAL BOWEL CLEANSING AGENTS

<table>
<thead>
<tr>
<th>Oral Bowel Cleansing Agent (OBCA)</th>
<th>Potential advantages of this OBCA</th>
<th>Tolerability and ease of use</th>
<th>Is a low residue diet advised prior to dosing?</th>
<th>Are there complications specific to this OBCA?</th>
<th>Are there any contraindications specific to this OBCA?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Picolax® or Citrafleet®</strong></td>
<td>Produces the lowest watery residue; potentially advantageous for radiological investigation.</td>
<td>Powder is reconstituted with a low volume of water. It then arms on mixing.</td>
<td>Yes</td>
<td>1. Higher risk of hyponatraemia (if excessive water ingestion) than with other OBCA's. 2. Risk of hypermagnesaemia in patients with advanced chronic kidney disease.</td>
<td>It is particularly important that patients with conditions predisposing to hypovolaemia are evaluated prior to receiving this OBCA.</td>
</tr>
<tr>
<td>(Sodium picosulphate &amp; magnesium citrate)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Citramag®</strong></td>
<td>Produces a low watery residue (although not as low as Picolax®).</td>
<td>Powder is reconstituted with a low volume of hot water.</td>
<td>Yes</td>
<td>1. Higher risk of hyponatraemia (if excessive water ingestion) than with other OBCA's. 2. Risk of hypermagnesaemia in patients with advanced chronic kidney disease.</td>
<td>It is particularly important that patients with conditions predisposing to hypovolaemia are evaluated prior to receiving this OBCA.</td>
</tr>
<tr>
<td>(magnesium carbonate and citric acid)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Klean Prep®</strong></td>
<td>Less likely to cause hypovolaemia.</td>
<td>Powder is reconstituted with a high volume of water (up to 4 litres).</td>
<td>Yes</td>
<td><strong>Lowest risk of provoking hypovolaemia and/or hyponatraemia.</strong></td>
<td></td>
</tr>
<tr>
<td>(polyethylene glycol)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moviprep®</strong></td>
<td>1. Less likely to cause hypovolaemia 2. Bowel preparation can be completed within 12 hrs.</td>
<td>Powder is reconstituted with a moderate volume of water (approx 2 litres).</td>
<td>Yes</td>
<td><strong>Lowest risk of provoking hypovolaemia and/or hyponatraemia.</strong></td>
<td>G6PD deficiency.</td>
</tr>
<tr>
<td>(polyethylene glycol)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fleet Phosphosoda®</strong></td>
<td>Well tolerated.</td>
<td>A low volume of liquid (45 ml) is mixed with a low volume of water (120 ml).</td>
<td>No. It is sufficient to simply avoid solid food during the dosing period.</td>
<td>1. Acute phosphate nephropathy. 2. Hypocalcaemia resulting from hyperphosphataemia. 3. Highest risk of hypovolaemia.</td>
<td>Should not be prescribed to patients with: 1. hypovolaemia 2. eGFR &lt;60 ml/min/1.73m² 3. hepatic cirrhosis 4. cardiac failure 5. hypertension 6. renin-angiotensin blockade … unless all other OBCA's are contraindicated.</td>
</tr>
<tr>
<td>(sodium phosphate)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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1. It should be remembered that the administration of ALL types of OBCA may be complicated by hypovolaemia and/or electrolyte disturbances (including hypokalaemia, hyponatraemia and hypernatraemia).

2. The following are absolute contraindications to ALL types of OBCA: gastrointestinal obstruction, perforation or ileus; acute intestinal ulceration; severe inflammatory bowel disease; reduced consciousness; hypersensitivity to any of the ingredients; ileostomy.
The diagnosis of chronic kidney disease (CKD) is based on two parameters. The first is the glomerular filtration rate (GFR). An estimated GFR (eGFR), calculated from the serum creatinine concentration, is commonly employed. To ensure that the impairment in renal function is chronic in nature rather than acute, the GFR should be calculated on two occasions over 90 days apart. The second parameter is the presence of markers of kidney damage, which include abnormalities evident on urinalysis (e.g., proteinuria) or radiological investigation.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR mL/min/1.73m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage evident</td>
<td>&gt;90</td>
</tr>
<tr>
<td></td>
<td>Normal or elevated GFR</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage evident</td>
<td>60–89</td>
</tr>
<tr>
<td></td>
<td>Mildly reduced GFR</td>
<td></td>
</tr>
<tr>
<td>3A</td>
<td>Moderately reduced GFR</td>
<td>45–59</td>
</tr>
<tr>
<td></td>
<td>+/- documented kidney damage</td>
<td></td>
</tr>
<tr>
<td>3B</td>
<td>Moderately reduced GFR</td>
<td>44–30</td>
</tr>
<tr>
<td></td>
<td>+/- documented kidney damage</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Severely reduced GFR</td>
<td>15–29</td>
</tr>
<tr>
<td></td>
<td>+/- documented kidney damage</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or on dialysis</td>
</tr>
<tr>
<td></td>
<td>+/- documented kidney damage</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX 5: ORAL BOWEL CLEANSING AGENT PATIENT ADVICE SHEET

The following Patient Advice Sheet is not intended to replace instruction sheets already in existence at a local level. Individual units may wish to use it alongside their existing instruction sheets, or to consider including the information it contains within their existing instruction sheets.

This Patient Advice Sheet provides information that is frequently omitted from the instructions provided by the manufacturers of the oral bowel cleansing agents. It is intended to augment these instructions, not to replace them.

Local contact details should be included on the template to allow patients to raise concerns or uncertainties.
AN ADVICE SHEET FOR PATIENTS WHO HAVE BEEN PRESCRIBED AN ORAL BOWEL CLEANSING AGENT.

You have been prescribed an oral bowel cleansing agent (sometimes also called a ‘bowel prep’). Its role is to clear out your bowels. This is important to ensure the safety and effectiveness of the planned procedure. There is a risk of developing dehydration, low blood pressure or kidney problems with this medication. The doctor prescribing the oral bowel cleansing agent will have assessed your risk and identified the most appropriate medication for you. You should also have had a blood test to check your kidney function. A number of oral bowel cleansing agents are available. You should refer to the manufacturer’s instructions when taking your preparation. However, the following rules apply in all cases.

The prescribed dose of oral bowel cleansing agent should not be exceeded. The oral bowel cleansing agent should not be taken over a period longer than 24 hours.

Oral bowel cleansing agents predispose to dehydration. You should maintain a good fluid intake whilst taking these medications. If you develop the symptoms of dehydration, and cannot increase your fluid intake, then you should seek medical attention. These symptoms include dizziness or light-headedness (particularly on standing up), thirst, or a reduced urine production.

You should follow any specific advice you have been given with regard to your regular medications. Medications that you may have been asked to temporarily discontinue include:

- **Antihypertensives** (to lower your blood pressure) such as ACE inhibitors like Ramipril®
- **Diuretics** (‘water tablets’, such as furosemide)
- **Non-steroidal anti-inflammatory drugs** (a type of pain killer, such as ibuprofen)
- **Iron preparations** (for anaemia, such as ferrous sulphate)
- **Aspirin, dipyridamole, clopidogrel or warfarin** (these agents thin your blood out; you may have been asked to discontinue them depending on the nature of the procedure that is planned).

If you have not received specific advice regarding your regular medications then you should continue to take them as normal. However, you may need to amend the timing as it is preferable to avoid taking them less than one hour either side of any dose of oral bowel cleansing agent.

Patients taking immunosuppression for transplanted organs should seek the advice of their doctor before taking an oral bowel cleansing agent.

Patients taking the oral contraceptive pill should take alternative precautions during the week following taking the oral bowel cleansing agent.

*If you experience problems, advice from a healthcare professional is available on (tel no).*
APPENDIX 6: ORAL BOWEL CLEANSING AGENT PRESCRIPTION

ORAL BOWEL CLEANSING AGENT PRESCRIPTION CHECKLIST
This checklist is to be completed by the clinician authorising the oral bowel cleansing agent and should then be filed in the patient’s medical records.

**NAME** ……………………………
**HOSPITAL NO.** ……………………………
**Date of Birth** ……………………………

**STEP 1: ABSOLUTE CONTRAINDICATIONS**
- GI Obstruction, ileus or perforation Y / N
- Severe IBD Y / N
- Toxic megacolon Y / N
- Reduced conscious level Y / N
- Hypersensitivity to any ingredients Y / N
- Dysphagia (unless via NGT) Y / N
- Ileostomy Y / N

If yes to any question, do not continue.

**STEP 2: Review the BLOOD RESULTS**
- Na …… eGFR 30-60 = CKD 3
- K ……… eGFR 15-29 = CKD 4
- eGFR ……. eGFR 0-14 = CKD 5

**STEP 3: Review MEDICATIONS**
- ACEi/ARB Y/N Safe to stop for 72 hrs? Y/N
- Diuretics Y/N Safe to stop for 24 hrs? Y/N
- NSAIDs Y/N Safe to stop for 72 hrs? Y/N

**STEP 4: Consider CO-MORBIDITIES & RISK FACTORS**

<table>
<thead>
<tr>
<th>Co-morbidities</th>
<th>Optimal</th>
<th>Acceptable</th>
<th>Avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kidney Disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD 3</td>
<td>PEG / Picolax / Citramag</td>
<td></td>
<td>OSP</td>
</tr>
<tr>
<td>CKD 4</td>
<td>PEG (if fluid status allows)</td>
<td>Picolax / Citramag</td>
<td>OSP</td>
</tr>
<tr>
<td>CKD 5</td>
<td>PEG (if fluid status allows)</td>
<td>Picolax</td>
<td>OSP, Citramag</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>Discuss with nephrologist</td>
<td>Discuss with nephrologist</td>
<td></td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>Discuss with nephrologist</td>
<td>Discuss with nephrologist</td>
<td></td>
</tr>
<tr>
<td>Renal Transplant</td>
<td>Discuss with nephrologist</td>
<td>Discuss with nephrologist</td>
<td></td>
</tr>
<tr>
<td><strong>Electrolyte Imbalance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEG</td>
<td></td>
<td></td>
<td>OSP</td>
</tr>
<tr>
<td><strong>Cardiac Failure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEG</td>
<td>Picolax / Citramag</td>
<td>OSP</td>
<td></td>
</tr>
<tr>
<td><strong>Liver Cirrhosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEG</td>
<td>Picolax</td>
<td>OSP</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEG / Picolax / Citramag</td>
<td></td>
<td>OSP</td>
<td></td>
</tr>
</tbody>
</table>

**STEP 5: TYPE OF BOWEL PREP ISSUED?**
- Picolax / Citramag / Klean Prep / Moviprep / Fleet Phospho-soda

**STEP 6: INSTRUCTIONS PROVIDED TO THE PATIENT**
- Verbally Y/N
- Leaflet Y/N

**STEP 7: OTHER COMMENTS**

**STEP 8: SIGNATURE…………………………….

KEY
ACEi Angiotensin converting enzyme inhibitors, ARB Angiotensin II Receptor Blockers, CKD chronic kidney disease, OSP oral sodium phosphate preparations (Fleet Phospho-soda), PEG polyethylene glycol (Klean Prep, Moviprep).