

Therapeutic Notes on the Management of Chronic Constipation in Primary Care

Updated September 2016



Contents

- * Introduction and background
- * Drugs used in the management of chronic constipation
- * Bulk-forming laxatives
- * Osmotic laxatives
- * Stimulant laxatives
- * Faecal softeners
- * Newer agents
- * Managing constipation in pregnancy and breastfeeding

This is an update of the 2012 COMPASS Therapeutic Note.

It has been extended to include the newer agents for the management of constipation

Successful completion of the assessment questions at the end of this issue will provide you with 3 hours towards your CPD/CME requirements. Further copies of this and any other edition in the COMPASS Therapeutic Notes series, including relevant CPD/CME assessment questions, can be found at:

www.medicinesni.com or

www.hscbusiness.hscni.net/services/2163.htm

GPs can complete the multiple choice questions on-line and print off their CPD/CME certificate at

www.medicinesni.com

Pharmacists should enter their MCQ answers at www.nicpld.org

Glossary

Chronic constipation	Constipation lasting longer than 3 months
Functional constipation	Chronic constipation without a known cause. Also known as <i>primary constipation</i> or <i>idiopathic constipation</i>
Gastrocolic response	The occurrence of peristalsis following the entrance of food into the empty stomach
IBS	Irritable Bowel Syndrome
BSFS	Bristol Stool Form Scale
Melanosis coli	Dark brownish black pigmentation of the mucous membrane of the colon due to the deposition of pigment in macrophages
Myenteric plexus	Part of the enteric nervous system with an important role in regulating gut motility
NNT	Number Needed to Treat
OTC	Over The Counter
RCT	Randomised Controlled Trial
Secondary constipation	Constipation caused by a drug or medical condition. Secondary constipation is also known as <i>organic constipation</i>
SmPC	Summary of Product Characteristics
Volvulus	A twisting or looping of the bowel resulting in obstruction; can be life-threatening

Introduction and background

Constipation means different things to different people and there is little shared understanding between patients and professionals about "normal" bowel function.¹ There is a lack of consensus in general practice regarding the optimum management strategies for chronic constipation.¹

What is meant by constipation?

Constipation can broadly be defined as the passage of stools less frequently than the patient's own normal pattern.² Stools are often dry and hard, and may be abnormally large or small.³ In the clinical consultation, if a person continues to complain about constipation after a discussion

of what is normal and what is abnormal (especially with respect to frequency), they are asking for help in managing their problem.

In *children*, the signs and symptoms of constipation may be different and may be poorly recognised. They can include infrequent bowel activity, foul smelling wind and stools, excessive flatulence, irregular stool texture, passing occasional enormous stools or frequent small pellets, withholding or straining to stop passage of stools, soiling or overflow, abdominal pain, distension or discomfort, poor appetite, lack of energy, an unhappy, angry or irritable mood and general malaise.⁴

How common is constipation?

Constipation is a common, often chronic, disorder estimated to affect 10-15% of adults in developed countries.^{12,13} The condition occurs twice as frequently in women as in men¹⁴ and is highly prevalent in the elderly,¹⁵ with up to 20% of those living in the community and 50% of those living in an institution reporting symptoms.^{9,13}

Constipation is also common in childhood. It is prevalent in around 5–30% of the child population, depending on the criteria used for diagnosis.⁴

The impact and economic burden of constipation

Constipation may often be regarded as a trivial medical problem, but for people with chronic constipation the impact on their quality of life is considerable and the burden on healthcare resources, in terms of medical care visits, GI-related procedures, investigations and medications, can be substantial.¹

Quality of life

In the most severely affected individuals, chronic constipation is accompanied by very marked impairment in quality of life and social functioning.¹⁹ Chronic constipation-associated GI symptoms significantly interfere with many aspects of sufferers' daily lives, including mood (44%), mobility (37%), normal work (42%), recreation (47%), and enjoyment of life (58%).²⁰ The impact of chronic constipation on quality of life for patients is comparable with that for conditions such as COPD, diabetes and depression.²¹

Burden on healthcare resources

Costs associated with constipation, including direct costs such as evaluation and treatment and indirect costs such as work absenteeism are high.²²

In Northern Ireland in the 12 months to June 2016 almost **700,000** prescriptions were filled for laxatives and newer agents for constipation, at a cost of nearly **£4million** - see **Table ONE**.

Table ONE: Number and cost of prescriptions for laxatives in Northern Ireland for the 12 months to June 2016

Class of laxative	Number of prescriptions	Cost
Bulk-forming laxatives	50,733	£230,792
Stimulant laxatives	195,852	£1,100,658
Faecal softeners	15	£1273
Osmotic laxatives	446,822	£2,334,336
Peripheral opioid-receptor antagonists	15	875
Prucalopride	3102	£208,100
Linaclotide	2654	£115,498
Lubiprostone	50	£2,418
Total	699,243	£3,993,950

Complications

Chronic constipation may lead to additional health problems. The following complications are sometimes associated with chronic constipation.^{10,16,17}

- Haemorrhoids
- Faecal impaction
- Volvulus
- Ulcers of the colon or rectum
- Rectal prolapse
- Anal fissures
- Faecal incontinence

Features requiring further referral

It is vital to screen for "alarm features" when evaluating any patient with chronic constipation, regardless of age. Any patient

reporting the signs or symptoms listed in **Box ONE** should be referred for further investigation.¹¹ Although the predictive validity of these features for malignancy is somewhat unreliable, their presence should never be ignored.

In addition, if dietary intervention, laxatives and other approaches fail, referral to a specialist may be indicated.¹⁸



Box ONE: Signs and symptoms that might indicate a serious underlying condition:³

- Unexplained change in bowel habits lasting longer than 6 weeks
- Palpable mass in the lower right abdomen or the pelvis
- Persistent rectal bleeding without anal symptoms
- Narrowing of stool calibre
- Family history of colon cancer, or inflammatory bowel disease
- Unexplained weight loss, iron deficiency anaemia, fever, or nocturnal symptoms
- Severe, persistent constipation that is unresponsive to treatment

What is meant by "normal"?

Establishing what is 'normal' for a particular person, and whether or not the person has constipation, can be difficult. Bowel habits vary widely.⁵ The commonest reported frequency of bowel movements is once per day,^{6,7} but a Swedish survey found that this was reported by only 20% of respondents.⁷ A UK survey identified that a frequency of less than three bowel movements per week was more common in women than men.⁶

Assessing frequency, amount and consistency of stools

Because most patients understandably lack a working knowledge of normative stool consistency, it is instructive to use the **Bristol Stool Scale** when asking patients to classify their bowel movements.^{10,23,24} The scale provides 7 prototypical stool forms. Patients with constipation typically point to type 1 and type 2 bowel movements as their predominant stool form.

Definitions used for constipation (updated 2016)

The diagnosis of constipation is often arbitrary and is largely dependent on the patient's perception of "normal" bowel function. Doctors often define constipation based on stool frequency,⁸ but patients define constipation as a multi-symptom disorder that includes infrequent bowel movements, hard/lumpy stool, straining, bloating, feeling of incomplete evacuation after a bowel movement and abdominal discomfort.⁹

The **Rome IV criteria (2016)** classifies functional bowel disorders (FBD) into five categories: irritable bowel syndrome, functional constipation, functional diarrhoea, functional abdominal bloating/distention, and unspecified FBD.¹¹⁵ This classification system was developed to assist clinicians in providing working definitions of FBDs. However it is important to note that significant overlap exists between these disorders and they should be thought of as existing on a continuum, rather than discrete disorders.¹¹⁵

Functional constipation is a FBD in which symptoms of difficult, infrequent, or incomplete defecation predominate. Patients with functional constipation should not meet IBS criteria, although abdominal pain and/or bloating may be present but are not predominant symptoms.¹¹⁵

Box TWO: Diagnostic Criteria for Functional Constipation Rome IV criteria^{115*}

1. Must include two or more of the following:
 - a. Straining during >25% of defecations
 - b. Lumpy or hard stools (BSFS 1-2) for > 25% of defecations
 - c. Sensation of incomplete evacuation for > 25% of defaecations
 - d. Sensation of anorectal obstruction / blockage for > 25% of defecations
 - e. Manual manoeuvres to facilitate > 25% of defecations (e.g. digital evacuation, support of the pelvic floor)
 - f. Fewer than 3 spontaneous bowel movements per week
2. Loose stools are rarely present without the use of laxatives.
3. Insufficient criteria for irritable bowel syndrome.

*Criteria have to have been met for the previous three months, with the onset of symptoms six months prior to diagnosis

What is the difference between chronic constipation and irritable bowel syndrome with constipation (IBS-C)?

It is useful to note the difference between chronic constipation and irritable bowel syndrome with constipation (IBS-C). Whereas the hallmark symptom of IBS-C is abdominal pain in association with constipation, patients with chronic constipation do not report pain as a predominant feature.^{10,11,115} Practically, however, many patients do not comply with this tidy dichotomy. It is common to encounter patients who have mild or moderate abdominal discomfort in chronic constipation but who do not report discomfort as a *predominant* symptom. Similarly, patients with IBS-C may have abdominal pain on some occasions but not consistently. These variations in patient assessment of abdominal discomfort make it difficult to clearly distinguish IBS-C from chronic constipation. If in doubt, ask the patient whether pain or discomfort is a *predominant* feature or whether the "main problem" is limited to the constipation itself. Patients who acknowledge that abdominal pain is a major factor are more likely to have IBS-C than chronic constipation. Those principally concerned with improving stool frequency or form independent of abdominal pain probably have chronic constipation.¹¹ This supports the concept that functional constipation and IBS-C are disorders that exist on a continuous spectrum.¹¹⁵

What causes constipation? (updated 2016)

Constipation may be primary or secondary to other medical conditions, including metabolic, neurological or endocrine diseases. Furthermore, medication used in the treatment of other conditions may cause secondary constipation. **Box THREE** summarises the causes of secondary constipation. Secondary causes should be addressed first as the likely aetiology.¹¹⁵

Box THREE: Causes of secondary constipation

Dietary

- Low fibre, dieting, anorexia, fluid depletion, change to diet with chronic diseases such as dementia, depression

Metabolic

- Diabetes mellitus, hypercalcaemia, hypokalaemia, hypothyroidism, porphyria

Neurological

- Parkinson's disease, spinal cord pathology, multiple sclerosis

Iatrogenic

- Aluminium antacids
- Antimuscarinic (e.g. procyclidine, oxybutynin)
- Antidepressants (most commonly tricyclic antidepressants)
- Antiepileptics (e.g. carbamazepine, gabapentin, oxcarbazepine, pregabalin, phenytoin)
- Sedating antihistamines
- Antipsychotics
- Antispasmodics (e.g. dicycloverine, hyoscine)
- Calcium supplements
- Diuretics
- Iron supplements
- Opioids
- Verapamil

Painful anorectal conditions

- Anal fissure, haemorrhoids, abscess, fistula, levator ani syndrome, proctalgia fugax.

Chronic constipation may be affected by personality, stress, and early toilet training.¹¹⁵ Constipation behaviour can be learned in early life; deliberate suppression of defecation leads to reduced stool frequency and weight and increased transit time.¹¹⁵ Chronic constipation can be divided into three broad categories: normal-transit constipation, slow-transit constipation, and defecatory or rectal evacuation disorders.¹¹⁵

What is dyssynergic defecation or outlet delay? (2016)

Outlet delay is a form of idiopathic constipation in which markers move normally through the colon but stagnate in the

rectum. This is seen in persons who demonstrate abnormal responses of the pelvic floor muscles during defecation (also known as pelvic floor dyssynergia or dyssynergic defecation).¹¹⁴

In patients with **dyssynergic defecation**, there is a failure to relax, or inappropriate contraction of, the puborectalis and external anal sphincter muscles. This narrows the anorectal angle and increases the pressures of the anal canal so that evacuation is less effective. This pattern may represent a conscious or unconscious act. The cause is not completely understood, but is probably multifactorial. It is thought to be an acquired, learned dysfunction rather than an organic or neurogenic disease.¹¹⁴

Whilst colonic transit time can be estimated by using BSFS, diagnosis of slow transit constipation or dyssynergic defecation requires diagnostic tests.¹¹⁵ This is neither required nor justified in all patients. However, patients who do not respond to reasonable trials of empiric therapy should be referred to a specialist in gastroenterology for diagnostic evaluation.¹¹⁵

What lifestyle measures should be recommended to prevent and treat constipation?

Many guidelines recommend general lifestyle modifications before considering drug treatment. Traditionally, individuals with chronic constipation are told to increase dietary fibre intake in order to alleviate symptoms, but there is little evidence from randomised controlled trials (RCTs) that this approach is of any benefit.^{25,26} However, observational studies suggest a beneficial effect of dietary fibre in constipated patients.^{27,28}

In general, the diet should be balanced and contain whole grains, fruits, and vegetables. This is recommended as part of the treatment for constipation. It is also recommended for general health and promoted by the 'five-a-day' policy. Fibre intake should be increased gradually (to minimise flatulence and bloating) and maintained for life. Adults should aim to consume 18–30g fibre per day. (As a guide, a medium-sized bowl of porridge contains around 2g of fibre; 2 slices of brown bread contain 2.5g of fibre).

Although the effects of a high fibre diet may be seen in a few days, it may take as long as 4 weeks. Adequate fluid intake is important (particularly with a high fibre diet or fibre supplements), but can be difficult for some people (e.g. frail or elderly). Fruits high in fibre and sorbitol, and fruit juices high in sorbitol can help prevent and treat constipation. Fruits (and their juices) that have a high sorbitol content include apples, apricots, gooseberries, grapes (and raisins), peaches, pears, plums (and prunes), raspberries, and strawberries. The concentration of sorbitol is about 5–10 times higher in dried fruit.

Another behavioural modification to consider includes ensuring that patients set aside regular scheduled time for a bowel movement (typically in the morning to coincide with the body's natural gastrocolic response).

In **children**, NICE⁴ indicate that dietary interventions alone should NOT be used as first-line treatment for idiopathic constipation. Constipation in children should be treated with laxatives and a combination of:

- Negotiated and non-punitive behavioural interventions suited to the child or young person's stage of development. These could include scheduled toileting and support to establish a regular bowel habit, maintenance and discussion of a bowel diary, information on constipation, and use of encouragement and rewards systems.
 - Dietary modifications to ensure a balanced diet and sufficient fluids are consumed.
- Advise parents, children and young people that a balanced diet should include:
- Adequate fluid intake.
 - Adequate fibre. Recommend including foods with high fibre content. Do not recommend unprocessed bran, which can cause bloating and flatulence and reduce the absorption of micronutrients.

Drugs used in the Management of Chronic Constipation

A variety of treatment options are available for patients with chronic constipation, ranging from older over-the-counter (OTC) laxatives to more recently developed prescription drugs. A majority (96%) of patients who seek consultation for constipation will have already attempted self-medication with OTC products.³³ In spite of these different treatment approaches, there remains a substantial unmet need in the treatment of chronic constipation.³⁴

Laxatives are divided into the following main groups:

- Bulk-forming laxatives
- Stimulant laxatives
- Faecal softeners
- Osmotic laxatives
- Bowel cleansing preparations (not covered in this review)

This simple classification disguises the fact that some laxatives have a complex action.

There are also newer agents for managing constipation that do not fit into any of these traditional groups:

- Peripheral opioid-receptor antagonists
- 5HT₄-receptor agonists
- Chloride-channel activator
- Guanylate cyclase-C receptor agonist

Guidance about which laxative(s) to use in adults

With the exception of evidence comparing the efficacy of macrogols with lactulose (see later), there is limited clinical evidence on which to judge the comparative efficacy of individual laxatives. Therefore management of chronic constipation in adults is largely based on expert opinion.³

Begin by relieving faecal loading/impaction, if present. Set realistic expectations for the results of treatment of chronic constipation. Advise people about lifestyle measures and adjust any constipating medication, if possible. Exclude underlying causes (e.g. hypothyroidism, metabolic disease, anal fissure, haemorrhoids).

Disimpaction in adults

The aim is to achieve complete disimpaction, with the minimum of discomfort. This can take several days in which doses and combinations of laxatives are adjusted.¹¹⁷

Offer the following regimen for disimpaction if indicated:

- For hard stools, consider using a high dose of an oral macrogol (licensed for use in faecal loading/impaction).
- For soft stools, or for hard stools after a few days treatment with a macrogol, consider starting or adding an oral stimulant laxative.
- If the response to oral laxatives is insufficient or not fast enough, consider:
 - Using a suppository: bisacodyl for soft stools; glycerol alone, or glycerol plus bisacodyl for hard stools.
 - Using a mini enema: docusate (softener and weak stimulant) or sodium citrate (osmotic).
- If the response is still insufficient:
 - Consider using a sodium phosphate or arachis oil retention enema (place high if the rectum is empty but the colon is full).
 - For hard faeces it can be helpful to give the arachis oil enema overnight before giving a sodium phosphate (large volume) or sodium citrate (small volume) enema the next day.
 - Enemas may need to be repeated several times to clear hard impacted faeces.
 - A district nurse or a carer to administer enemas.¹¹⁷

Laxatives are recommended:

- if lifestyle measures are insufficient, or whilst waiting for them to take effect
- for people taking a constipating drug that cannot be stopped
- for people with other secondary causes of constipation
- as 'rescue' medicines for episodes of faecal loading.

The aim of treatment with laxative agents is to adjust the dose, choice, and combination of laxative to produce comfortable defecation with soft, formed stools once or twice a day.

Expert consensus opinion³⁵ tends to favour starting treatment with a **bulk-forming laxative**. It is important to maintain good hydration when taking bulk-forming laxatives. This may be difficult for some people (e.g. the frail or elderly). If stools remain hard, add or switch to an **osmotic laxative**. If stools are soft but the person still finds them difficult to pass or complains of inadequate emptying, add a **stimulant laxative**. Adjust the dose, choice, and combination of laxative according to symptoms, speed with which relief is required, response to treatment, and individual preference. The dose of laxative should be gradually titrated upwards (or downwards) to produce one or two soft, formed stools per day.

Guidance on managing constipation in children

All children and young people with idiopathic constipation should be assessed for faecal impaction.⁴ Use a combination of history-taking and physical examination to diagnose faecal impaction – look for overflow soiling and/or faecal mass palpable abdominally and/or rectally if indicated. If impaction is present, see the section on disimpaction if needed.

Disimpaction in children

Offer the following oral medication regimen for disimpaction if indicated:⁴

- polyethylene glycol, using an escalating dose regimen as the first-line treatment
- add a stimulant laxative if polyethylene glycol does not work
- substitute a stimulant laxative if polyethylene glycol is not tolerated by the child or young person. Add another laxative such as lactulose or docusate if stools are hard.

Please note:

- **do not** use rectal medications for disimpaction unless all oral medications have failed and only if the child or young person and their family consent
- administer **sodium citrate** enemas only if all oral medications for disimpaction have failed
- **do not** administer phosphate enemas for disimpaction unless under specialist supervision in hospital/health centre/clinic, and only if all oral medications and sodium citrate enemas have failed.

If impaction is not present or has been treated, treat the child promptly with a laxative (even if the history of constipation is very short). Delays of greater than 3 days between stools may increase the likelihood of pain on passing hard stools leading to anal fissure, anal spasm and eventually to a learned response to avoid defecation.³⁶

NICE recommend polyethylene glycol 3350 (**Movicol® Paediatric Plain** or **Laxido® Paediatric Plain**) as the preferred first-line agent for the management of constipation in children.⁴ Ensure that an effective dose is used, by adjusting the dose according to response to treatment. (If the child has needed disimpaction, the usual dose is half the disimpaction dose). If this approach does not work, *add in* a stimulant laxative; if this approach is not tolerated, *substitute for* a stimulant laxative. If stools are hard, consider adding in lactulose or another laxative with softening effects, such as docusate.

Do not use suppositories or enemas in primary care unless all oral medications have failed and preferably following specialist advice. Doses above the licensed maximum dose may be needed, so informed consent should be verbally obtained and documented.⁴

Continue medication at maintenance dose for several weeks after regular bowel habit is established – this may take several months.⁴ Children who are toilet training should remain on laxatives until toilet training is well established. Some children may require laxative therapy for several years. A minority may require ongoing laxative therapy.⁴

Review children and young people undergoing disimpaction within 1 week. Start **maintenance therapy** as soon as the child or young person's bowel is disimpacted. Reassess children frequently during maintenance treatment to ensure they do not become re-impacted and assess issues in maintaining treatment such as taking medicine and toileting. Tailor the frequency of assessment to the individual needs of the child and their families (this could range from daily contact to contact every few weeks). Where possible, reassessment should be provided by the same person/team.

Please note: At the time of this review (July 2016), neither Movicol® Paediatric Plain nor Laxido® Paediatric Plain had UK marketing authorisations for use in faecal impaction in children under 5 years, or for chronic constipation in children less than 2 years. Informed consent should be obtained and documented.

Stopping laxatives

Laxatives should not be stopped abruptly. Laxatives should be **gradually withdrawn** when regular bowel movements occur without difficulty (e.g. 2 - 4 weeks after defecation has become comfortable and a regular bowel pattern with soft, formed stools has been established). The rate at which doses are reduced should be guided by the frequency and consistency of the stools. Doses should be reduced in a gradual manner in order to minimise the risk of requiring 'rescue therapy' for recurrent faecal loading. If a combination of laxatives has been used, reduce and stop one laxative at a time. Stimulant laxative doses should be reduced first, if possible. However, it may be necessary to also adjust the dose of the osmotic laxative to compensate. The patient should be advised that it can take several months to be successfully weaned off all laxatives. It is common to get relapses and these should be treated early with increased doses of laxatives.

Prescribing Notes: Laxatives²

- ▶ Before prescribing laxatives it is important to be sure that the patient *is* constipated and that the constipation is *not* secondary to an underlying undiagnosed complaint
- ▶ It is important for those who complain of constipation to understand that bowel habits can vary considerably in frequency without doing harm. Some people tend to consider themselves constipated if they do not have a bowel movement each day. A useful definition of constipation is the passage of hard stools less frequently than the patient's own normal pattern and this can be explained to the patient
- ▶ Misconceptions about bowel habits have led to excessive laxative use. Abuse may lead to hypokalaemia
- ▶ The BNF recommends that laxatives should generally be **avoided** except where straining will exacerbate a condition (such as angina) or increase the risk of rectal bleeding as in haemorrhoids
- ▶ Laxatives are of value in *drug-induced constipation*, for the expulsion of *parasites* after anthelmintic treatment, and to clear the alimentary tract before *surgery and radiological procedures*
- ▶ Prolonged treatment of constipation is sometimes necessary.

Bulk-forming laxatives

(ispaghula, methylcellulose and sterculia)

How do bulk-forming laxatives work?

Bulk-forming laxatives relieve constipation by increasing faecal mass which stimulates peristalsis. During treatment with bulk-forming laxatives, adequate fluid intake must be maintained to avoid intestinal obstruction.^{2,36} Proprietary preparations containing a bulking agent are often difficult to administer to children.³⁶

Is there any evidence for the use of bulk-forming laxatives?

There is a lack of high-quality data demonstrating the efficacy of bulk-forming laxatives. A systematic review found that ispaghula husk increased stool frequency; however, there were insufficient data on methylcellulose to provide evidence-based recommendations for its use in chronic constipation.¹¹ Despite the lack of data, substantial clinical experience supports the use of these agents as a first-line intervention.

How quickly do bulk-forming laxatives work?

Patients and/or carers should be advised that the full effect of bulk-forming laxatives may take some 2-3 days to develop.^{2,36} If after 2-3 days the patient reports no relief of their constipation, the dosage and frequency should be increased to the maximum recommended before adding in/switching to another laxative.¹⁶

In which patients are bulk-forming laxatives particularly useful?

Bulk-forming laxatives are of particular value in those with small hard stools. Bulk-forming laxatives are also useful in the management of patients with colostomy, ileostomy, haemorrhoids, anal fissure, chronic diarrhoea associated with diverticular disease, irritable bowel syndrome, and as adjuncts in ulcerative colitis.²

Bulk-forming laxatives are not appropriate for rapid relief of constipation, but are a good option for long-term control.³

Are there any situations in which prescribing a bulk-forming laxative would be contra-indicated?

Bulk-forming laxatives are contra-indicated in patients with difficulty in swallowing, intestinal obstruction, colonic atony, faecal impaction.²

Maintaining an adequate intake of fluids is important to avoid the possibility of intestinal obstruction. However, this may be difficult for some people (e.g. the frail or elderly).³

What are the side-effects of bulk-forming laxatives?

There is often initial discomfort and abdominal distension upon initiation of therapy with a bulk-forming laxative.³⁷ With continued use, these effects usually decrease, particularly if the agent is started at a low dose and gradually increased.

Alternatively, patients with substantial bloating might benefit from using methylcellulose, an inorganic bulking agent that is not fermentable.¹¹

Rarely, side-effects including obstruction of the oesophagus or colon have been reported.^{38,39}

Ispaghula husk (Fibrelief®, Fybogel®, Isogel®, Ispagel Orange®, Regulan®)

Ispaghula husk is a commonly used bulking agent in the UK. There is published evidence of its effectiveness in the short-term treatment of constipation (up to eight weeks), but limited evidence of its role in the long-term.²⁸ Nevertheless, clinical experience suggests that it remains effective even with long-term use.²⁸

Methylcellulose (Celevac® 500mg tablets)

In adults and children over the age of 12 years, 3-6 tablets should be taken twice daily. Tablets should be taken with at least 300 ml of liquid. The dose may be reduced as normal bowel function is restored. In children aged 7-12 years, 2 tablets should be taken twice daily.^{2,36}



Caution: Celevac® tablets should be broken in the mouth before swallowing. Celevac® tablets swell in contact with water and should therefore be swallowed carefully.

Sterculia

Normacol® (sterculia) and Normacol Plus® (sterculia plus frangula*) are in the form of granules. In adults, 1 or 2 sachets or 1-2 heaped 5ml spoonfuls, once or twice daily after meals. In children aged 6-12 years, give half this amount. The granules should be placed dry on the tongue and without chewing or crushing, swallowed immediately with plenty of water or a cool drink. The granules may also be sprinkled onto soft food such as yoghurt, followed by plenty of liquid.^{2,36} (* Frangula acts as a mild peristaltic stimulant and aids the evacuation of the softened faecal mass).

Prescribing Notes: Bulk-forming laxatives²

- ▶ Adequate fluid intake must be maintained to avoid intestinal obstruction.
- ▶ Preparations that swell in contact with liquid should always be carefully swallowed with water and should not be taken immediately before going to bed.

Osmotic laxatives

(lactulose, macrogols)

Action

Osmotic laxatives include:⁴⁰

- poorly absorbed sugars (lactulose, sorbitol)
- macrogols (also known as polyethylene glycol preparations (PEG))
- magnesium salts

Through their osmotic actions, these agents retain water in the intestinal lumen, which leads to softer stools with a larger volume and improved propulsion.⁴⁰

How long do osmotic laxatives take to have their effect?

- Osmotic laxatives may take a few days to take effect and are not suitable for rapid relief of constipation. They may be given in divided doses throughout the day. Adequate fluid intake should be encouraged.³

Adverse effects

Osmotic laxatives may cause flatulence, bloating, abdominal cramping, nausea and diarrhoea with higher doses.^{16,41}

Lactulose is degraded by colonic bacteria to low-molecular weight acids that increase stool acidity and osmolality and lead to the accumulation of fluid in the colon. Macrogols are less likely than lactulose to produce bloating and flatulence, as macrogols are inert and not degraded by colonic bacteria.⁴²

Are there any patient groups in which osmotic laxatives may be inappropriate?

- Osmotic laxatives may lead to electrolyte disturbance and fluid overload, they should be used with caution in patients with renal impairment or cardiac failure.⁴³
- Osmotic laxatives may be counterproductive in patients with constipation associated with irritable bowel syndrome and in patients with severe bloating and fullness.⁴²

Evidence

The best-studied osmotic laxatives are the macrogols and lactulose, and there are well-designed RCTs supporting their effectiveness in treating chronic constipation.^{44,45} While both have been found to be effective, macrogols have been found to be superior to lactulose for increasing stool frequency and reducing straining.⁴⁵

Lactulose

Lactulose has been used for over 30 years and is one of the most commonly used laxatives. Lactulose is a semi-synthetic disaccharide which is not absorbed from the gastro-intestinal tract. Lactulose can cause nausea, but this can be minimised by administering lactulose with water, fruit juice or a meal. Long term use of lactulose possibly enhances anticoagulant effect of coumarins.²

Trials have demonstrated that lactulose is safe and is more effective than placebo^{11,46} but less effective than macrogols.⁴⁷

Macrogols (Table TWO)

Macrogols are inert, non-absorbable, non-metabolisable polymers of ethylene glycol.^{2,36,48} Daily doses of macrogols are effective in chronic constipation by:

- normalising frequency of bowel movements (NNT=2.4)
- decreasing straining (NNT=3.2)
- improving stool consistency (NNT=3 to 4)

In addition, daily macrogols facilitate discontinuing other laxatives (NNT=3.1).⁴⁹

Compared with lactulose, macrogols are more effective in improving symptoms of chronic constipation; they have a better tolerability profile (due to reduced electrolyte disturbance) and are associated with a reduced need for rescue medication.^{45,47} In patients with refractory constipation taking macrogols daily, a stimulant laxative may be added every second or third day to improve treatment efficacy.⁵⁰

Macrogols have been suggested to be more cost-effective than lactulose.⁵¹ **Macrogols are the first line choice of osmotic laxative in the Northern Ireland Formulary.**¹¹²

Prescribing Notes: Macrogols

- ▶ Movicol® Liquid must not be taken undiluted and may only be diluted in water – see SmPC for further details.
- ▶ Multi-ingredient products, such as macrogols, should be prescribed by brand.⁵²

Stimulant laxatives

(bisacodyl, dantron, docusate sodium, glycerol, senna, sodium picosulfate)

Stimulant laxatives include bisacodyl, sodium picosulfate, and members of the anthraquinone group, senna and dantron. Docusate sodium probably acts both as a stimulant and as a softening agent. This group also includes glycerol suppositories.

How do stimulant laxatives work?

Stimulant laxatives increase intestinal motility by stimulating the colonic myenteric plexus on their contact with the colonic mucosa, and by inhibiting water absorption, thereby inducing passage of stools.^{17,39,46,48,53}

These agents usually produce an effect within 6 to 12 hours of ingestion and so are commonly administered at bedtime to produce an effect in the morning.¹⁶

Rectal preparations (suppositories/enemas containing phosphates or sodium citrate) can be used effectively to produce rapid evacuation (within 30 minutes) but should be used with caution in the elderly and debilitated.² Glycerol suppositories act as a rectal stimulant by virtue of the mildly irritant action of glycerol.^{2,36} Both bisacodyl and sodium picosulfate are prodrugs that are converted in the gut into the same active metabolite, which causes the desired laxative effect.

Is there an evidence-base for the use of stimulant laxatives?

Although widely used, there is a limited evidence base supporting the use of stimulants in chronic constipation. The clinical data supporting the use of stimulant laxatives in chronic constipation are derived from studies which were often done in specific subsets of patient populations and had ill-defined endpoints.⁵⁴⁻⁶¹ Placebo-controlled trials show that bisacodyl and picosulfate are more effective than placebo, but most trials are of short duration and quality is variable.^{17,39,46} In a recent 4-week placebo-controlled trial, picosulfate improved bowel function, symptoms and quality of life.⁶² Practically speaking, however, many patients report clinically relevant benefits from these agents and symptom recurrence upon discontinuation.

What adverse effects are associated with using stimulant laxatives?

Gastrointestinal adverse effects

Stimulant laxatives are generally well tolerated, but may induce

abdominal pain.^{17,39,46,63} This can often be managed by dose titration.⁶² Stools should be softened by increasing dietary fibre and liquid or with an osmotic laxative before giving a stimulant laxative.^{2,36} Stimulant laxatives should be avoided in intestinal obstruction.^{2,36}

Melanosis coli

Senna products may discolour the urine, and chronic use may cause melanosis coli, a brown-black pigmentation of the colonic mucosa. This condition does not lead to colon cancer and is reversible over time after discontinuation of use.

Tolerance/ intestinal atony

Stimulant laxatives are only licensed for short-term use,³ but long-term use is common and is justifiable in some circumstances. For example, in children with chronic constipation, especially where withholding of stool occurs, additional doses of a stimulant laxative may be required and long-term use of stimulant laxatives is sometimes necessary.

Historically, there have been concerns that long-term use of stimulant laxatives may cause a "cathartic colon" marked by diminished motility from a "burned out" myenteric plexus.^{64,65} However, this has not been confirmed in experimental studies nor in clinical practice.^{53,64,66,67} When used appropriately, stimulant laxatives are not harmful and are often both efficacious and cost-effective in many patients with occasional or chronic constipation.⁴²

Why are the indications for using dantron limited?

The indications for dantron are limited by its potential carcinogenicity (based on *rodent* carcinogenicity studies) and evidence of genotoxicity. Dantron should only be used to manage constipation in **terminally ill** patients (of all ages).^{2,36}

Faecal softeners (arachis oil, liquid paraffin)

Action

Faecal softeners are surface-acting agents that function primarily as detergents, that is, they allow water to interact more effectively with solid stool, thereby softening the stool.⁴⁸

Evidence

Laxatives which mainly soften or lubricate stools appear to be more effective than placebo in increasing the frequency of bowel movements and in overall symptoms improvement, but data are limited.⁶⁸

Problems

Although faecal softeners are relatively inexpensive and well tolerated, in patients with severe symptoms, or in patients in whom other forms of therapy have failed, it is unlikely that stool softeners *alone* will be adequate.

Prolonged use of liquid paraffin should be avoided because of anal seepage of paraffin and consequent anal irritation after prolonged use. Prolonged use has also been associated with granulomatous reactions caused by absorption of small quantities of liquid paraffin (especially from the emulsion), lipid pneumonia,⁶⁹ and interference with the absorption of fat-soluble vitamins. Liquid paraffin is contra-indicated in children under 3 years.



Caution: Arachis oil

Do not use arachis oil in a patient with a peanut allergy

NI Formulary choices

For recommended choices of laxatives, see [NI Formulary Section 1.6](#)



Newer Agents (updated 2016)

Newer agents for the management of constipation have emerged on to the market in recent years. They have different mechanisms of action and different indications. They are significantly more expensive than traditional laxatives. As such, national bodies such as NICE have set out specific prescribing criteria for their use. To date there have been no head to head studies comparing the relative efficacy of these newer agents.¹⁰⁸

5-HT₄-receptor agonists (prucalopride)

What is the mechanism of action?

Serotonin (also known as 5-hydroxytryptamine or 5-HT) is a key regulator of GI motility, sensitivity and secretion. Through 5-HT₄ receptors, 5-HT triggers and co-ordinates intestinal peristalsis.^{72,73} Prucalopride (Resolor®) is the first selective, high affinity 5-HT₄ receptor agonist to undergo clinical development.⁷⁴ Prucalopride has been shown to enhance colonic transit in healthy controls and in patients with chronic constipation.^{75,76}

What are the licensed indication(s) for prucalopride?

Prucalopride is indicated for the treatment of chronic constipation in adults, when other laxatives have failed to provide an adequate response.²

Dosage and administration

The recommended dosage in adults is 2mg administered orally once daily; exceeding this dosage is not expected to increase efficacy.⁷⁷ The recommended starting dosage of prucalopride in *people aged > 65 years* is 1mg once daily; thereafter, the

dosage can be increased to 2mg once daily, if needed. Prucalopride does not require dosage adjustment in those with mild or moderate renal or hepatic impairment. However, the recommended dosage in those with severe renal or hepatic impairment is 1mg once daily.

Importantly, most people who will benefit from treatment with prucalopride respond **within four weeks**. If the intake of once-daily prucalopride is not effective after four weeks of treatment, the person should be re-examined and the benefit of continuing treatment reconsidered.^{77,78}

The evidence-base for prucalopride

In three identical pivotal trials, 1974 patients with chronic constipation (predominantly women) were treated for 12 weeks with placebo, prucalopride 2mg or prucalopride 4mg once daily (NB: 4mg daily is not a licensed dose).^{68,79,80} Both doses of prucalopride resulted in an average of three spontaneous complete bowel movements (SCBMs) per week in approximately 20% of patients, compared with 10% of patients receiving placebo. Both active doses of prucalopride generated similar response rates.

Of note regarding these trials:³⁵

- trials were short (lasting up to 12 weeks) compared with the chronic nature of constipation
- trials did not compare the drug with existing treatments
- trials did not specify previous laxative-use as an inclusion criterion.

Long-term open-label follow-up studies involving patients who had previously participated in the original trials have shown that satisfaction with bowel movement was maintained for up to 18 months of treatment. A total of 20% of patients discontinued

treatment during the course of the studies due to insufficient response.⁸¹

Why was prucalopride previously only licensed in women?

The drug company's initial proposed therapeutic indication for prucalopride was for the treatment of adults (both women and men) with chronic constipation in whom laxatives fail to provide adequate relief.³⁵ However, most of the participants in the key trials were women, and subgroup analysis showed that the drug might not have a statistically significant effect in male participants. The Committee for Medicinal Products for Human Use noted that the efficacy had not been demonstrated sufficiently in men and therefore recommended that it should be licensed for use only in women when prucalopride was first brought to the market.

Why is prucalopride now licensed in men?

The approval of prucalopride in women in 2009 was on the condition that follow-up controlled study data was provided for use of prucalopride in men in the future. A 12 week, multicentre, randomised, double-blind, placebo controlled phase III trial which involved 374 men with a history of constipation was carried out.

Men were randomised to receive prucalopride 1-2mg or placebo. After 12 weeks, more men in the prucalopride group reported an average of three or more SCBMs per week (37.9%) compared with placebo (17.7%; $p < 0.0001$). The proportion achieving more than three SCBMs was greater in the prucalopride group compared with placebo at 1 to 4 weeks (29.9% vs. 14.9%, $p < 0.005$), 5 to 8 weeks (41.2% vs. 23.2%, $p < 0.0001$) and 9 to 12 weeks (39% vs. 23.8%, $p < 0.005$).^{86,116}

What are the adverse effects of prucalopride?

In initial clinical trials, the adverse effects which were experienced more frequently by patients treated with prucalopride versus placebo include:

- headache
- nausea
- diarrhoea
- abdominal pain

These effects resolved within a few days of continued treatment. Other unwanted effects included abnormal bowel sounds, anorexia, dizziness, dyspepsia, fatigue, fever, flatulence, frequent urination, malaise, palpitations, rectal haemorrhage, tremors and vomiting.

During long-term follow-up studies, the most frequent adverse effects which resulted in study discontinuation were abdominal pain, diarrhoea, headache and nausea.⁸¹

Is there a risk of arrhythmia with 5-HT₄-receptor agonists?

Cisapride, a drug in the same class, was withdrawn from the UK market in July 2000 because it prolonged the Q-T_c interval. However, prucalopride has been reported to be more selective than cisapride; clinical trials on prucalopride found the incidence of QT interval prolongation to be low and similar to that with placebo.^{68,79,80} Additionally, extensive cardiovascular safety assessments, including a study in elderly institutionalised patients, showed no arrhythmogenic potential for prucalopride.⁸³

The SmPC advises prucalopride should be used with caution in patients with a history of arrhythmias or ischaemic cardiovascular disease.⁸²

What do national guidelines say for prucalopride?

NICE have, to date, only reviewed the use of prucalopride in **women**. This is covered in the 2010 NICE Technology Appraisal of prucalopride, that recommends:⁸⁴

- prucalopride is an option for symptomatic treatment for chronic constipation in **women** who have had inadequate relief with **at least two laxatives** (from **different classes**, at the **highest tolerated recommended doses** for at least **6 months**) and for whom **invasive treatment for constipation is being considered**
- prucalopride should be prescribed only by a "**clinician with experience of treating chronic constipation**", and only after the clinician has **carefully reviewed the woman's previous laxative treatments**
- if treatment with prucalopride is not effective after **4 weeks**, the woman should be re-examined and the benefit of continuing treatment reconsidered.

Chloride channel activators

(lubiprostone)

What is the mechanism of action?

Lubiprostone is a prostone (a bicyclic fatty acid compound) derived from prostaglandin E1. It activates chloride channel type-2 (ClC-2) in epithelial cells of the intestine so increasing the chloride concentration of intestinal fluid. This is followed by a passive secretion of sodium ions and water, which results in increased isotonic fluid in the lumen, which in turn promotes small bowel and colonic transit.^{96,97}

What are the licensed indication(s)?

Lubiprostone (*Amitiza*®▼) is indicated for the treatment of chronic idiopathic constipation in adults when response to diet and other non-drug measures (e.g. education, physical activity) are inadequate.⁹⁶

Dosage and administration

The dose is one capsule (24 microgram) twice daily. The SmPC states that a course of treatment with lubiprostone is 2 to 4 weeks, but does not specify how frequently treatment can be repeated.⁹⁴ Treatment with lubiprostone should be stopped if there is no response after at least 2 weeks.⁹⁶

The evidence-base for lubiprostone

The results of RCTs in adults suggest that one week of treatment with lubiprostone resulted in an additional two SCBMs movements compared with placebo.⁹⁵

What are the adverse effects?

The most common adverse effects are nausea (~24%), diarrhoea (~8%), chest tightness and/or difficulty taking a breath (usually within 30-60 minutes of taking the first dose and resolving within a few hours) (~2%). Other common adverse effects include other abdominal effects (distension, flatulence, discomfort, pain and dyspepsia), palpitations, oedema, headache, dizziness, hyperhidrosis and hot flushes (~1-10%).^{95,96}

What do national guidelines say for lubiprostone?

NICE advise that lubiprostone is recommended as an option for treating chronic idiopathic constipation, that is, for adults in whom treatment with at least 2 laxatives from different classes, at the highest tolerated recommended doses for at least 6 months, has failed to provide adequate relief and for whom invasive treatment for constipation is being considered.

- ▶ If treatment with lubiprostone is not effective after 2 weeks, the person should be re-examined and the benefit of continuing treatment reconsidered.
- ▶ Lubiprostone should only be prescribed by a clinician with experience of treating chronic idiopathic constipation, who has carefully reviewed the person's previous courses of laxative treatments.⁹⁷

Guanylate Cyclase-C Receptor Agonists (linaclotide)

What is the mechanism of action?

Linaclotide is an oral guanylate cyclase-C receptor agonist. Stimulation of guanylate-cyclase-subtype-C (GC-C) receptors on the luminal surface of the intestinal epithelium, leads to higher levels of intra- and extracellular cyclic guanosine monophosphate (cGMP).¹⁰² The increase in intracellular cGMP leads to secretion of chloride and bicarbonate into the intestinal lumen, increased intestinal fluid secretion and accelerated transit. The increase in extracellular cGMP has been shown to reduce visceral hypersensitivity in animal models,¹⁰³ and is believed to result in decreased sensitivity to nociceptive stimuli thereby reducing the sensation of pain.¹⁰⁴

What are the licensed indication(s)?

Linaclotide 290microgram capsules (Constella[®]▼) are indicated for the symptomatic treatment of moderate to severe irritable bowel syndrome with constipation (IBS-C) in adults.¹⁰²

Dosage and administration

The dose is one capsule (290 micrograms) once daily. If patients have not experienced improvement in their symptoms after 4 weeks of treatment, the patient should be re-examined and the benefit and risks of continuing treatment reconsidered.¹⁰²

The evidence-base for linaclotide

In trials (lasting 12 and 26 weeks), linaclotide produced a statistically significant increase in the number of patients reporting relief of symptoms (constipation, abdominal pain and discomfort, and bloating) compared with placebo. However, only a third of patients responded to linaclotide and the clinical significance of the improvement in symptoms is not clear.¹⁰⁰ Longer term comparative studies are required for linaclotide.¹⁰⁰

What are the adverse effects?

The most commonly reported adverse effect is diarrhoea, consistent with the pharmacological action of linaclotide (~20%).^{102,109} Other common adverse reactions (>1%) include abdominal pain, abdominal distension and flatulence.^{100,102}

What do national guidelines say for linaclotide?

In the NICE Clinical Guideline for IBS in adults, NICE advise:

- ▶ Consider linaclotide for people with IBS only if:
 - optimal or maximum tolerated doses of previous laxatives from different classes have not helped and
 - they have had constipation for at least 12 months.
- ▶ Follow up people taking linaclotide after 3 months.¹⁰¹

Peripheral opioid-receptor antagonists (methylnaltrexone bromide and naloxegol)

Methylnaltrexone bromide (Relistor[®])

What is the mechanism of action?

Methylnaltrexone bromide is a peripherally acting opioid-receptor antagonist.

What are the licensed indication(s)?

Methylnaltrexone bromide (Relistor[®]) is indicated for the treatment of opioid-induced constipation when response to laxative therapy has not been sufficient in adult patients, aged 18 years and older.⁸² Methylnaltrexone bromide does not alter the central analgesic effect of opioids.^{70,71}

Dosage and administration

Opioid-induced constipation in adult patients with chronic pain (except palliative care patients with advanced illness):

12mg subcutaneously, as needed, given as at least 4 doses weekly, up to once daily (7 doses weekly).⁸²

Opioid-induced constipation in adult patients with advanced illness (palliative care patients): 8mg subcutaneously for patients weighing 38-61 kg or 12mg subcutaneously for patients weighing 62-114 kg. The usual administration schedule is one single dose every other day

What are the adverse effects?

The most common adverse effects are abdominal cramping (~28%), flatulence (~13%), nausea (~11%), and dizziness (~7%). Long-term use of methylnaltrexone bromide has not been evaluated.⁴⁸

What do national guidelines say for methylnaltrexone?

NICE were unable to make an appraisal for methylnaltrexone for treating opioid-induced bowel dysfunction in people with advanced illness receiving palliative care as no evidence submission was received from the pharmaceutical company.¹¹³

Naloxegol (Movalting[®]▼)

What is the mechanism of action?

Naloxegol is a peripherally acting mu-opioid receptor antagonist. It is a derivative of naloxone to which has been added a polyethylene glycol group (PEGylation) to reduce permeability across the blood-brain barrier. This allows the drug to reduce the peripheral gastrointestinal effects of opioids without affecting centrally activated analgesia.^{93,94}

What are the licensed indication(s)?

Naloxegol (Movalting[®]▼) is licensed for the treatment of opioid-induced constipation in adults who have had an inadequate response to laxative treatment.⁸⁸

An inadequate response is defined as opioid-induced constipation symptoms of at least moderate severity in at least 1 of the 4 stool symptom domains (that is, incomplete bowel movement, hard stools, straining or false alarms) while taking at least 1 laxative class for at least 4 days during the prior 2 weeks.^{88,89}

Dosage and administration

The dose is 25mg orally once daily. When naloxegol therapy is initiated, it is recommended that all currently used maintenance laxative therapy is stopped, until clinical effect of naloxegol is determined.¹¹⁰

The evidence-base for naloxegol?

At a dose of 25mg, naloxegol produced a small but statistically significant increase in response rate over 12 weeks in two trials of patients with non-cancer related pain and opioid-induced constipation. However, the effect size was smaller than anticipated and in one study did not reach statistical significance with the 12.5mg dose. Overall, the response rate was greater in patients who were defined as having had an inadequate response to laxative treatment, and the product licence is restricted to use in such patients.⁹⁰

There is limited clinical experience of using naloxegol in opioid-induced constipation in patients with cancer-related pain.⁹⁰

Patients with opioid-induced constipation should be reviewed and their laxative regime optimised.⁹⁰

What are the adverse effects?

The most commonly reported adverse effects were abdominal pain and diarrhoea (>10%). Other common side effects include nausea, flatulence and vomiting (1-10%).¹¹⁰

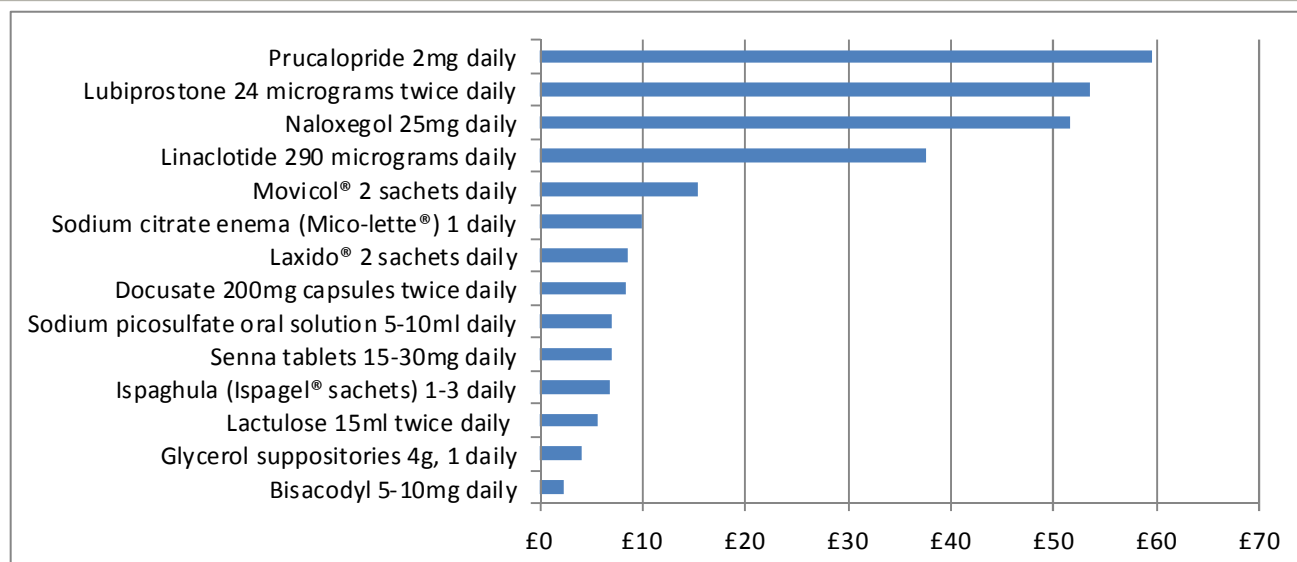
What do national guidelines say for naloxegol?

The NICE clinical guideline on the use of strong opioids in palliative care in adults advises that laxatives should be prescribed for everyone commencing strong opioids. It recommends that laxatives should be taken regularly at an effective dose and that people should be informed of the importance of medicines adherence.⁹²

Naloxegol

NICE advise that naloxegol is recommended, within its marketing authorisation, as an option for treating opioid induced constipation in adults whose constipation has not adequately responded to laxatives. An inadequate response is defined as opioid-induced constipation symptoms of at least moderate severity in at least 1 of the 4 stool symptom domains (that is, incomplete bowel movement, hard stools, straining or false alarms) while taking at least 1 laxative class for at least 4 days during the prior 2 weeks.⁸⁹

Figure ONE: Cost comparison chart for laxatives and newer agents (30 days treatment) ^{2,85,91}



Constipation in pregnancy and lactation

How should constipation in a pregnant or breastfeeding woman be managed?

Constipation is quite common during pregnancy. For pregnant and breastfeeding women the emphasis lies in first-line use of dietary and lifestyle measures. The use of laxatives should only be considered if these measures fail.³

Using laxatives in pregnancy

If dietary and lifestyle changes fail to control constipation in pregnancy or breastfeeding, moderate doses of poorly absorbed laxatives may be used. Consider a bulk-forming laxative first. If stools remain hard, add or switch to lactulose or a macrogol. If stools are soft but the person still finds them difficult to pass or complains of inadequate emptying, consider a short course of bisacodyl or senna.⁴ Occasional use of glycerol or bisacodyl suppositories is also an option.

- **Bulk-forming laxatives, lactulose and macrogols** are not absorbed from the gastrointestinal tract and are therefore suitable for use during pregnancy
- **Bisacodyl** is poorly absorbed from the gastrointestinal tract (only about 5%). It has not been reported to cause teratogenic or fetotoxic effects and is therefore suitable for use during pregnancy.

- **Senna** is partially absorbed from the gastrointestinal tract but does not appear to be teratogenic. Concerns have been raised that senna should be avoided in the third trimester because a stimulating effect on uterine contractions has been reported with *other* anthraquinone derivatives. However, this has not been reported with senna.
- **Glycerol suppositories** are also suitable for use during pregnancy

Laxatives that are not recommended:

- **Docusate** is less preferred because there is a single case report of neonatal hypomagnesaemia after maternal overuse of oral docusate sodium. However, docusate could be considered in low doses if the recommended laxatives (above) are unsuccessful
- **Sodium picosulfate**: there is less experience with its use in pregnancy, so it is therefore not recommended
- **Sodium citrate and sodium phosphate enemas** should be avoided if possible during pregnancy, because they may cause fluid and electrolyte imbalances.

References

- Mihaylov, S., Stark, C., McColl, E., et al. Stepped treatment of older adults on laxatives. The STOOL trial. *Health Technol. Assess.* 2008; 12: iii-139.
- RPSGB/BMA. British National Formulary. June, 2016
- MeReC. The management of constipation. *MeReC Bulletin* 2011; 21: 1-8.
- NICE. Constipation in children and young people. Diagnosis and management of idiopathic childhood constipation in primary and secondary care. NICE Clinical Guideline 99 2010;
- Peppas, G., Alexiou, V. G., Mourtzoukou, E., et al. Epidemiology of constipation in Europe and Oceania: a systematic review. *BMC.Gastroenterol.* 2008; 8: 5.
- Heaton, K. W., Radvan, J., Cripps, H., et al. Defecation frequency and timing, and stool form in the general population: a prospective study. *Gut* 1992; 33: 818-824.
- Walter, S. A., Kjellstrom, L., Nyhlin, H., et al. Assessment of normal bowel habits in the general adult population: the Popcol study. *Scand.J.Gastroenterol.* 2010; 45: 556-566.
- Herz, M. J., Kahan, E., Zalevski, S., et al. Constipation: a different entity for patients and doctors. *Fam.Pract.* 1996; 13: 156-159.
- Pare, P., Ferrazzi, S., Thompson, W. G., et al. An epidemiological survey of constipation in Canada: definitions, rates, demographics, and predictors of health care seeking. *Am.J.Gastroenterol.* 2001; 96: 3130-3137.
- Longstreth, G. F., Thompson, W. G., Chey, W. D., et al. Functional bowel disorders. *Gastroenterology* 2006; 130: 1480-1491.
- Brandt, L. J., Prather, C. M., Quigley, E. M., et al. Systematic review on the management of chronic constipation in North America. *Am.J.Gastroenterol.* 2005; 100 Suppl 1: S5-S21.
- Dennison, C., Prasad, M., Lloyd, A., et al. The health-related quality of life and economic burden of constipation. *Pharmacoeconomics.* 2005; 23: 461-476.
- Stewart, W. F., Liberman, J. N., Sandler, R. S., et al. Epidemiology of constipation (EPOC) study in the United States: relation of clinical subtypes to sociodemographic features. *Am.J.Gastroenterol.* 1999; 94: 3530-3540.
- Higgins, P. D. and Johanson, J. F. Epidemiology of constipation in North America: a systematic review. *Am.J.Gastroenterol.* 2004; 99: 750-759.
- Gallagher, P. F., O'Mahony, D. and Quigley, E. M. Management of chronic constipation in the elderly. *Drugs Aging* 2008; 25: 807-821.
- Eoff, J. C. Optimal treatment of chronic constipation in managed care: review and roundtable discussion. *J.Manag.Care Pharm.* 2008; 14: 1-15.
- Tack, J. and Muller-Lissner, S. Treatment of chronic constipation: current pharmacologic approaches and future directions. *Clin.Gastroenterol.Hepatol.* 2009; 7: 502-508.
- McCallum, I. J., Ong, S. and Mercer-Jones, M. Chronic constipation in adults. *BMJ* 2009; 338: b831.
- Rao, S. S., Seaton, K., Miller, M. J., et al. Psychological profiles and quality of life differ between patients with dysynergia and those with slow transit constipation. *J.Psychosom.Res.* 2007; 63: 441-449.
- Johanson, J. F. Review of the treatment options for chronic constipation. *MedGenMed.* 2007; 9: 25.
- Wald, A., Scarpignato, C., Kamm, M. A., et al. The burden of constipation on quality of life: results of a multinational survey. *Aliment.Pharmacol.Ther.* 2007; 26: 227-236.
- Dennison, C., Prasad, M., Lloyd, A., et al. The health-related quality of life and economic burden of constipation. *Pharmacoeconomics.* 2005; 23: 461-476.
- Heaton, K. W. and O'Donnell, L. J. An office guide to whole-gut transit time. Patients' recollection of their stool form. *J.Clin.Gastroenterol.* 1994; 19: 28-30.
- Lewis, S. J. and Heaton, K. W. Stool form scale as a useful guide to intestinal transit time. *Scand.J.Gastroenterol.* 1997; 32: 920-924.
- Badiali, D., Corazzari, E., Habib, F. I., et al. Effect of wheat bran in treatment of chronic nonorganic constipation. A double-blind controlled trial. *Dig.Dis.Sci.* 1995; 40: 349-356.
- Ashraf, W., Park, F., Lof, J., et al. Effects of psyllium therapy on stool characteristics, colon transit and anorectal function in chronic idiopathic constipation. *Aliment.Pharmacol.Ther.* 1995; 9: 639-647.
- Pare, P., Bridges, R., Champion, M. C., et al. Recommendations on chronic constipation (including constipation associated with irritable bowel syndrome) treatment. *Can.J.Gastroenterol.* 2007; 21 Suppl B: 3B-22B.
- Petticrew, M., Watt, I. and Sheldon, T. Systematic review of the effectiveness of laxatives in the elderly. *Health Technol. Assess.* 1997; 1: i-52.
- Annelis, M. and Koch, T. Constipation and the preached trio: diet, fluid intake, exercise. *Int.J.Nurs.Stud.* 2003; 40: 843-852.
- Chung, B. D., Parekh, U. and Sellin, J. H. Effect of increased fluid intake on stool output in normal healthy volunteers. *J.Clin.Gastroenterol.* 1999; 28: 29-32.
- Dukas, L., Willett, W. C. and Giovannucci, E. L. Association between physical activity, fiber intake, and other lifestyle variables and constipation in a study of women. *Am.J.Gastroenterol.* 2003; 98: 1790-1796.
- Meshkinpour, H., Selod, S., Movahedi, H., et al. Effects of regular exercise in management of chronic idiopathic constipation. *Dig.Dis.Sci.* 1998; 43: 2379-2383.
- Schiller, L. R. Review article: the therapy of constipation. *Aliment.Pharmacol.Ther.* 2001; 15: 749-763.
- Johanson, J. F. and Kralstein, J. Chronic constipation: a survey of the patient perspective. *Aliment.Pharmacol.Ther.* 2007; 25: 599-608.
- What role for prucalopride in constipation? *Drug Ther.Bull.* 2011; 49: 93-96.
- RPSGB/BMA. BNF for children, June 2016
- Doughty, D. B. When fiber is not enough: current thinking on constipation management. *Ostomy.Wound.Manage.* 2002; 48: 30-41.
- Jones, M. P., Talley, N. J., Nuyts, G., et al. Lack of objective evidence of efficacy of laxatives in chronic constipation. *Dig.Dis.Sci.* 2002; 47: 2222-2230.
- Tramonte, S. M., Brand, M. B., Mulrow, C. D., et al. The treatment of chronic constipation in adults. A systematic review. *J.Gen.Intern.Med.* 1997; 12: 15-24.
- Tack, J. Current and future therapies for chronic constipation. *Best.Pract.Res.Clin.Gastroenterol.* 2011; 25: 151-158.
- Borum, M. L. Constipation: evaluation and management. *Prim.Care* 2001; 28: 577-90, vi.
- Wald, A. Chronic constipation: advances in management. *Neurogastroenterol.Motil.* 2007; 19: 4-10.
- Lembo, A. and Camilleri, M. Chronic constipation. *N.Engl.J.Med.* 2003; 349: 1360-1368.
- DiPalma, J. A., Cleveland, M. V., McGowan, J., et al. A randomized, multicenter, placebo-controlled trial of polyethylene glycol laxative for chronic treatment of chronic constipation. *Am.J.Gastroenterol.* 2007; 102: 1436-1441.
- Attar, A., Lemann, M., Ferguson, A., et al. Comparison of a low dose polyethylene glycol electrolyte solution with lactulose for treatment of chronic constipation. *Gut* 1999; 44: 226-230.
- Ramkumar, D. and Rao, S. S. Efficacy and safety of traditional medical therapies for chronic constipation: systematic review. *Am.J.Gastroenterol.* 2005; 100: 936-971.
- Lee-Robichaud, H., Thomas, K., Morgan, J., et al. Lactulose versus Polyethylene Glycol for Chronic Constipation. *Cochrane.Database.Syst.Rev.* 2010; CD007570.
- Singh, S. and Rao, S. S. Pharmacologic management of chronic constipation. *Gastroenterol.Clin.North Am.* 2010; 39: 509-527.
- Corazzari, E., Badiali, D., Habib, F. I., et al. Small volume isosmotic polyethylene glycol electrolyte balanced solution (PMF-100) in treatment of chronic nonorganic constipation. *Dig.Dis.Sci.* 1996; 41: 1636-1642.
- Blaker P and Wilkinson M. Chronic constipation: diagnosis and current treatment options. *Prescriber* 2010; 21: 30-45.
- Guest, J. F., Clegg, J. P. and Helter, M. T. Cost-effectiveness of macrogol 4000 compared to lactulose in the treatment of chronic functional constipation in the UK. *Curr.Med.Res.Opin.* 2008; 24: 1841-1852.
- Ni Health and Social Care Board. Items Unsuitable for Generic Prescribing. http://primarycare.hscni.net/pdf/Generic_Exception_List_Nov2011.pdf 2011;
- Geboes, K., Nijs, G., Mengs, U., et al. Effects of 'contact laxatives' on intestinal and colonic epithelial cell proliferation. *Pharmacology* 1993; 47 Suppl 1: 187-195.
- Stern, F. H. Constipation—an omnipresent symptom: effect of a preparation containing prune concentrate and cascarn. *J.Am.Geriatr.Soc.* 1966; 14: 1153-1155.
- Kinnunen, O., Winblad, I., Koistinen, P., et al. Safety and efficacy of a bulk laxative containing senna versus lactulose in the treatment of chronic constipation in geriatric patients. *Pharmacology* 1993; 47 Suppl 1: 253-255.
- Williamson, J., Coll, M. and Connolly, M. A comparative trial of a new laxative. *Nurs.Times* 1975; 71: 1705-1707.
- Odes, H. S. and Madar, Z. A double-blind trial of a celandin, aloe vera and psyllium laxative preparation in adult patients with constipation. *Digestion* 1991; 49: 65-71.
- KASDON, S. C. and MORENTIN, B. O. The management of puerperal constipation with a senna preparation. *J.Int.Coll.Surg.* 1959; 31: 455-458.
- Corman, M. L. Management of postoperative constipation in anorectal surgery. *Dis.Colon.Rectum* 1979; 22: 149-151.
- Connolly, P., Hughes, I. W. and Ryan, G. Comparison of "Duphalac" and "irritant" laxatives during and after treatment of chronic constipation: a preliminary study. *Curr.Med.Res.Opin.* 1974; 2: 620-625.
- MacLennan, W. J. and Pooler, A. F. W. M. A comparison of sodium picosulphate ("Laxoberal") with standardised senna ("Senokot") in geriatric patients. *Curr.Med.Res.Opin.* 1974; 2: 641-647.
- Mueller-Lissner, S., Kamm, M. A., Wald, A., et al. Multicenter, 4-week, double-blind, randomized, placebo-controlled trial of sodium picosulfate in patients with chronic constipation. *Am.J.Gastroenterol.* 2010; 105: 897-903.
- Kienzle-Horn, S., Vix, J. M., Schuijt, C., et al. Comparison of bisacodyl and sodium picosulfate in the treatment of chronic constipation. *Curr.Med.Res.Opin.* 2007; 23: 691-699.
- Wald, A. Is chronic use of stimulant laxatives harmful to the colon? *J.Clin.Gastroenterol.* 2003; 36: 386-389.
- Joo, J. S., Ehrenpreis, E. D., Gonzalez, L., et al. Alterations in colonic anatomy induced by chronic stimulant laxatives: the cathartic colon revisited. *J.Clin.Gastroenterol.* 1998; 26: 283-286.
- Mueller-Lissner, S. A., Kamm, M. A., Scarpignato, C., et al. Myths and misconceptions about chronic constipation. *Am.J.Gastroenterol.* 2005; 100: 232-242.
- Xing, J. H. and Soffer, E. E. Adverse effects of laxatives. *Dis.Colon.Rectum* 2001; 44: 1201-1209.
- Quigley, E. M., Vandeplasche, L., Kerstens, R., et al. Clinical trial: the efficacy, impact on quality of life, and safety and tolerability of prucalopride in severe chronic constipation—a 12-week, randomized, double-blind, placebo-controlled study. *Aliment.Pharmacol.Ther.* 2009; 29: 315-328.
- Laurent, F., Philippe, J. C., Vergier, B., et al. Exogenous lipid pneumonia: HRCT, MR, and pathologic findings. *Eur.Radiol.* 1999; 9: 1190-1196.
- Becker, G. and Blum, H. E. Novel opioid antagonists for opioid-induced bowel dysfunction and postoperative ileus. *Lancet* 2009; 373: 1198-1206.
- McNicol, E. D., Boyce, D., Schumann, R., et al. Mu-opioid antagonists for opioid-induced bowel dysfunction. *Cochrane.Database.Syst.Rev.* 2008; CD006332.
- Gershon, M. D. and Tack, J. The serotonin signaling system: from basic understanding to drug development for functional GI disorders. *Gastroenterology* 2007; 132: 397-414.
- Cash, B. D. and Chey, W. D. Review article: The role of serotonergic agents in the treatment of patients with primary chronic constipation. *Aliment.Pharmacol.Ther.* 2005; 22: 1047-1060.
- De Maeyer, J. H., Lefebvre, R. A. and Schuurkes, J. A. 5-HT₄ receptor agonists: similar but not the same. *Neurogastroenterol.Motil.* 2008; 20: 99-112.
- Bouras, E. P., Camilleri, M., Burton, D. D., et al. Selective stimulation of colonic transit by the benzofuran 5HT₄ agonist, prucalopride, in healthy humans. *Gut* 1999; 44: 682-686.
- Bouras, E. P., Camilleri, M., Burton, D. D., et al. Prucalopride accelerates gastrointestinal and colonic transit in patients with constipation without a rectal evacuation disorder. *Gastroenterology* 2001; 120: 354-360.
- Frampton, J. E. Prucalopride. *Drugs* 2009; 69: 2463-2476.
- Emmanuel, A. and Kerr, S. Prucalopride. *Prescriber (Supplement)* 2011;
- Camilleri, M., Kerstens, R., Ryck, A., et al. A placebo-controlled trial of prucalopride for severe chronic constipation. *N.Engl.J.Med.* 2008; 358: 2344-2354.
- Tack, J., van, Outryve M., Beyens, G., et al. Prucalopride (Resolor) in the treatment of severe chronic constipation in patients dissatisfied with laxatives. *Gut* 2009; 58: 357-365.
- Camilleri, M., Van Outryve, M. J., Beyens, G., et al. Clinical trial: the efficacy of open-label prucalopride treatment in patients with chronic constipation - follow-up of patients from the pivotal studies. *Aliment.Pharmacol.Ther.* 2010; 32: 1113-1123.
- Swedish Orphan Biovitrum Ltd. Resolor. Summary of Product Characteristics 2016
- Camilleri, M., Beyens, G., Kerstens, R., et al. Safety assessment of prucalopride in elderly patients with constipation: a double-blind, placebo-controlled study. *Neurogastroenterol.Motil.* 2009; 21: 1256-e117.
- NICE. Prucalopride for the treatment of chronic constipation in women. NICE Technology Appraisal 211 2010;
- Haymarket Media Group Ltd. MIMS, June 2016
- East & South East England Specialist Pharmacy Services. Prucalopride for chronic idiopathic constipation in men. Dec 2015.

<http://www.medicinesresources.nhs.uk>

87. AWMMSG. Prucalopride (Resolor[®]), April 2016 <http://www.awmsg.org>
88. AstraZeneca. Moventig. Summary of Product Characteristics 2016.
89. NICE. Naloxegol for treating opioid-induced constipation, TA345, 2015.
90. DTB. Naloxegol for opioid-induced constipation. DTB, 2015;53(12)138-140.
91. PrescQIPP. Constipation. Bulletin 137, June 2016.
92. NICE. Palliative care for adults: strong opioids for pain relief. NICE CG140, 2012.
93. Bruner HC et al. Clinical utility of naloxegol in the treatment of opioid-induced constipation. J Pain Res 2015; 8: 289-94.94. Garnock-Jones KP. Naloxegol: a review of its use in patients with opioid-induced constipation. Drugs 2015; 75: 419-25.
95. DTB. Lubiprostone for chronic constipation in adults. DTB, 2014;52(4)42-44.
96. Takeda UK Ltd. Amitiza. Summary of Product Characteristics, 2016.
97. NICE. Lubiprostone for treating chronic idiopathic constipation. NICE TA318, July 2014.
98. Camilleri M et al. Effect of a selective chloride channel activator, lubiprostone, on gastrointestinal transit, gastric sensory, and motor functions in healthy volunteers. Am J Physiol Gastrointest Liver Physiol 2006; 290: G942-7.
99. Cuppoletti J et al. Effects of lubiprostone on human uterine smooth muscle cells. Prostaglandins Other Lipid Mediat 2008; 86: 56-60.
100. DTB. Linacotide for constipation-predominant IBS. DTB, 2013;51(11)129-132
101. NICE. Irritable bowel syndrome in adults: diagnosis and management. NICE CG61, 2008 with update 2015.
102. Allergan. Constella. Summary of Product Characteristics, 2016.
103. Malagelada JR. Clinical evidence for the role of linacotide for the treatment of irritable bowel syndrome. Clin Invest 2012; 2: 1039-46.
104. EMA. Linacotide. Constella: EPAR— Summary for the public. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002490/human_med_001597.jsp&mid=WC0b01ac058001d124
105. MHRA. Amitiza 24 microgram soft capsules PL21341/0003 UKPAR, 2012 [online]. Available: <http://www.mhra.gov.uk/home/groups/par/documents/websitesources/con205412.pdf>
106. FDA. Amitiza (lubiprostone) capsules label [online], 2012. Available: http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/021908s010lbl.pdf
107. Panas RM et al. PTH-195 Lubiprostone treatment improves constipation and related symptoms in patients refractory to other constipation therapies. Gut 2013; 62: A291.
108. Wilson N and Schey R. Lubiprostone in constipation: clinical evidence and place in therapy. Ther Adv Chronic Dis. 2015 Mar; 6(2): 40–50.
109. Sayuk GS. Linacotide: promising IBS-C efficacy in an era of provisional study endpoints. Am J Gastroenterol 2012; 107: 1726-9.
110. AstraZeneca. Moventig. Summary of Product Characteristics, 2016.
111. NICE. Methylnaltrexone for treating opioid-induced bowel dysfunction in people with advanced illness receiving palliative care (terminated appraisal), NICE TA277, 2013.
112. HSC. Northern Ireland Formulary. <http://niformulary.hscni.net> [accessed 1/8/2016]
113. NICE. Methylnaltrexone for treating opioid-induced bowel dysfunction in people with advanced illness receiving palliative care (terminated appraisal), NICE TA277, 2013.
114. Wald A. Etiology and evaluation of chronic constipation in adults. UpToDate. [Accessed 12/8/2016]
115. Lacy BE et al. Bowel Disorders. Gastroenterology, 2016;150:1393–1407.
116. Yiannakou Y et al. A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial to Evaluate the Efficacy, Safety, and Tolerability of Prucalopride in Men With Chronic Constipation. The American Journal of Gastroenterology. 2015;110(5):741-748.
117. NICE. Clinical Knowledge Summaries. Constipation (last revised October 2015). <http://cks.nice.org.uk>

This material was prepared on behalf of the Northern Ireland Health and Social Care Board by:

Michelle O'Prey, MPharm MSc MPS
Medicines Management Information Pharmacist
COMPASS Unit
Pharmaceutical Department
NI Health and Social Care Board
2 Franklin Street, Belfast
BT2 8DQ.

Any queries should be directed to Michelle O'Prey
(e-mail Michelle.O'Prey@hscni.net, telephone 028 9536 3925).

You may re-use this material free of charge in any format or medium for private research/study, or for circulation within an organisation, provided that the source is appropriately acknowledged. The material must be re-used accurately in time and context, and must NOT be used for the purpose of advertising or promoting a particular product or service for personal or corporate gain.

Please note that every effort has been made to ensure that the content of the COMPASS Therapeutic Notes is accurate at the time of publication. Readers are reminded that it is their responsibility to keep up-to-date with any changes in practice.

With thanks to the following for kindly reviewing this document:

- Dr Brian Johnston, Consultant Gastroenterologist, Belfast Health and Social Care Trust
- Dr TCK Tham, Consultant Gastroenterologist, South Eastern Health and Social Care Trust

The Editorial Panel for this edition of COMPASS Therapeutic Notes:

- Dr Bryan Burke (General Practitioner)
- Miss Veranne Lynch (Pharmacy Advisor, HSCB)
- Dr Ursula Mason (General Practitioner)
- Miss Joanne McDermott (Pharmacy Advisor, HSCB)
- Dr Thérèse Rafferty (Medicines Management Information Analyst, HSCBSO)
- Mrs Stephanie Sloan (Community Pharmacist)

COMPASS THERAPEUTIC NOTES ASSESSMENT**Management of Chronic Constipation in Primary Care**

COMPASS Therapeutic Notes are circulated to GPs, nurses, pharmacists and others in Northern Ireland. Each issue is compiled following the review of approximately 250 papers, journal articles, guidelines and standards documents. They are written in question and answer format, with summary points and recommendations on each topic. They reflect local, national and international guidelines and standards on current best clinical practice. Each issue is reviewed and updated every three years.

Each issue of the Therapeutic Notes is accompanied by a set of assessment questions. This edition will contribute 3 hours towards your CPD/CME requirements. Submit your completed MCQs to the appropriate address (shown below) or complete online (see below). Assessment forms for each topic can be submitted in **any order** and at **any time**.

If you would like extra copies of Therapeutic Notes and MCQ forms for this and any other topic you can:

Visit the COMPASS Web site: www.medicinesni.com or www.hscbusiness.hscni.net/services/2163.htm

or

Email your requests to: compass.team@hscni.net

or

Phone the COMPASS Team on: 028 9536 3901

You can now complete your COMPASS multiple choice assessment questions and print off your completion certificate online:

- **Doctors and nurses** should submit their answers at: www.medicinesni.com
- **Pharmacists** should submit their answers at: www.nicpld.org

Are you a

Pharmacist? ☐ Community ☐ Hospital ☐ Other (please specify) _____

GP? ☐ Enter your cipher number: _____

Nurse? ☐ Enter your PIN number: _____

Title: Mr/Mrs/Miss/Ms/Dr

Surname: _____ First name: _____

Address: _____

Address _____

Postcode: _____

GPs and Nurses:

Complete the form overleaf and return to:

COMPASS Unit

Pharmaceutical Department

HSC Business Services Organisation

2 Franklin Street

Belfast

BT2 8DQ

Pharmacists:

Complete the form overleaf and return to:

Northern Ireland Centre for Pharmacy Learning & Development

FREEPOST NICPLD

Belfast BT9 7BL

COMPASS THERAPEUTIC NOTES ASSESSMENT

Management of Chronic Constipation in Primary Care

For copies of the Therapeutic Notes and assessment forms for this and any other topic please visit: www.medicinesni.com or www.hscbusiness.hscni.net/services/2163.htm

Successful completion of these assessment questions equates with **3 hours** Continuing Professional Development time. Circle your answer TRUE (T) or FALSE (F) for each question. When completed please post this form to the relevant address shown overleaf. Alternatively, you can submit your answers online:

- **Doctors and nurses** should submit their answers at: www.medicinesni.com
- **Pharmacists** should submit their answers at: www.nicpld.org

1. Constipation:

a	There is robust evidence that individuals with chronic constipation should be advised to increase dietary fibre intake in order to alleviate symptoms	T	F
b	Tricyclic antidepressants can cause constipation	T	F
c	Constipation can occur in up to 20% of elderly patients who live in an institution	T	F
d	The diagnosis of constipation is often arbitrary and is largely dependent on the patient's perception of "normal" bowel function	T	F

2. Laxatives in general:

a	There is a wealth of robust evidence that underpins the use of laxatives in chronic constipation	T	F
b	The aim of treatment with laxative agents is to produce comfortable defaecation with soft, formed stools once or twice a day	T	F
c	Consider gradually withdrawing laxatives when regular bowel movements occur without difficulty (2–4 weeks after defaecation has become comfortable and a regular bowel pattern with soft, formed stools has been established)	T	F
d	Prolonged treatment with laxatives is sometimes necessary	T	F

3. Osmotic laxatives:

a	Osmotic laxatives take around 12 hours to produce an effect	T	F
b	Macrogols are less likely than lactulose to cause bloating and flatulence	T	F
c	Lactulose is less effective than macrogols	T	F
d	Movicol® liquid should always be diluted with water before taking	T	F

4. Stimulant laxatives:

a	Stimulant laxatives usually produce an effect within 6 to 12 hours of ingestion and so are commonly administered at bedtime to produce an effect in the morning	T	F
b	Stools should be softened by increasing dietary fibre and liquid or with an osmotic laxative before giving a stimulant laxative	T	F
c	Long term use of stimulant laxatives should be avoided	T	F
d	Dantron should only be used to manage constipation in terminally ill patients	T	F

5. In regard to the newer agents used in the management of chronic constipation:

a	Methylnaltrexone is a new oral agent licensed for the treatment of opioid-induced constipation in patients receiving palliative care	T	F
b	Most people who will benefit from treatment with prucalopride respond within four weeks. If the person has not responded within four weeks he/she should be re-examined and consideration given to discontinuing prucalopride.	T	F
c	Lubiprostone should be continued indefinitely.	T	F
d	Linacotide is indicated for the treatment of chronic idiopathic constipation in adults when response to diet and other non-drug measures (e.g. education, physical activity) are inadequate.	T	F