PrescQIPP
Community Interest Company

Constipation

This bulletin reviews the treatment of short term and chronic constipation in adults (over 18 years). The current annual cost of all laxative preparations across England and Wales is over £98 million (NHSBSA Feb-Apr20). In line with the National Institute of Health and Care Excellence (NICE) Key therapeutic topic (KTT1), guidance is provided to review and if appropriate, revise prescribing of laxatives for adults to ensure that they are prescribed routinely only for the short-term treatment of constipation when dietary and lifestyle measures have proven unsuccessful or if there is an immediate clinical need.[1] Cost-effective treatment alternatives are also reviewed. This bulletin does not cover the treatment of children (<18 years), constipation in pregnancy and breastfeeding or the use of devices in the treatment of constipation. Laxatives should be prescribed for treating children and young people with constipation in line with the NICE Clinical Guideline (CG99).[2] Newer products for the treatment of constipation are discussed.

Recommendations

- Ensure a clear diagnosis of constipation before considering a laxative, and that the constipation is not secondary to an underlying undiagnosed complaint. Bowel habit can vary considerably in frequency without the patient suffering any harm.
- Adopt a stepwise approach to the management of constipation, starting with diet and lifestyle factors.
- Avoid or adjust drugs that cause constipation if possible, for example opioids or tricyclic antidepressant drugs.
- Review and, if appropriate, revise prescribing of laxatives for adults to ensure that they are prescribed routinely only for the short-term treatment of constipation when dietary and lifestyle measures have proven unsuccessful or if there is an immediate clinical need.
- Over the counter (OTC) laxatives can be recommended for short-term, infrequent constipation caused by changes in lifestyle or diet such as inadequate hydration or exercise.
- Be aware that evidence for the efficacy and safety of some of the older laxatives from well-designed trials is limited, as there is a lack of head-to-head comparative studies to determine whether one laxative class is superior to another.
- Stimulant laxatives should only be used short term. They should only be added to acute prescribing systems and not to repeat medication records. Bisacodyl and senna tablets are the least costly stimulant oral preparations.
- Review the continued need for laxatives after discharge from secondary care, e.g. where they were prescribed with opioids post-surgery and intended for short term use.
- For opioid induced constipation, do not use bulk forming laxatives. Offer a stimulant laxative and an osmotic laxative (or docusate which has stool-softening properties).
- If an osmotic laxative is appropriate, a macrogol prescribed generically, e.g. macrogol compound oral powder sachets sugar free, or the lowest cost brands, currently Cosmocol® or Laxido®, are the preferred options.

Recommendations

- Avoid using two drugs in the same class together, e.g. lactulose plus a macrogol.
- Laxatives can be slowly withdrawn when regular bowel movements occur without difficulty. If more than one laxative has been used, reduce one laxative at a time.
- Ensure that the NICE recommendations are followed for prucalopride, naloxegol and linaclotide.
- Prucalopride should only be prescribed by a clinician with experience of treating chronic constipation who has carefully reviewed the woman's previous courses of laxative treatments.
- Care homes should have a robust ordering system and checking process in place to ensure that laxatives and other medicines are only ordered if they are needed. Refer to PrescQIPP bulletin 93: Reducing medicines waste in care homes: information for care home staff
- Ensure laxatives for the short-term treatment of constipation are included in homely remedies policies in care homes. Refer to PrescQIPP Bulletin 72: Care homes-homely remedies

Background

Constipation is defaecation that is unsatisfactory because of infrequent stools, difficult stool passage, or seemingly incomplete defaecation. Stools are often dry and hard and may be abnormally large or abnormally small.[3] It is important that people who complain of constipation understand that bowel habit can vary considerably in frequency without doing harm. Misconceptions about bowel habits have led to excessive laxative use. Stimulant laxatives are associated with metabolic problems, atonic, non-functioning colon or diarrhoea. Laxative abuse may lead to hypokalaemia.[4]

New onset constipation, especially in patients over 50 years of age, or accompanying symptoms such as anaemia, abdominal pain, weight loss, or overt or occult blood in the stool should provoke urgent investigation because of the risk of malignancy or other serious bowel disorder.[4]

Because different definitions of chronic constipation are in use, attempts continue to be made to develop and agree more objective criteria for the definition of chronic constipation, most notably by the Rome IV criteria.[5] The Rome IV criteria categorises disorders of chronic constipation into four subtypes: functional constipation; irritable bowel syndrome with constipation; opioid-induced constipation and functional defaecation disorders.

The use of the Bristol Stool Chart can provide an objective record of the person's stool form.[2]

Functional constipation is chronic constipation without a known cause and is also known as primary or idiopathic constipation.

Secondary (organic) constipation is constipation caused by a medicine or medical condition.[3]

Table 1 overleaf lists medical conditions predisposing to constipation and table 2 lists medicines that commonly cause constipation.

Table 1. Medical conditions predisposing to constipation[3]

In adults with no drug cause for their constipation, consider the following medical conditions predisposing to constipation:
• Endocrine and metabolic diseases:
» Diabetes mellitus (with autonomic myopathy)
» Hypercalcaemia
» Hypokalaemia
» Hyperparathyroidism
» Hypothyroidism (severe)
» Uraemia
• Myopathic conditions:
» Amyloidosis
» Myotonic dystrophy
» Scleroderma
• Neurologic diseases:
» Autonomic neuropathy
» Cerebrovascular disease
» Hirschsprung's disease
» Multiple sclerosis
» Parkinson's disease
» Spinal cord injury, tumours
• Structural abnormalities:
» Anal fissures, strictures
» Haemorrhoids
» Colonic strictures (following diverticulitis, ischaemia, surgery)
» Inflammatory bowel disease
» Obstructive colonic mass lesions (for example colorectal cancer) — careful examination can usually distinguish a faecal mass from a tumour or cyst: firm pressure exerted by a finger will leave a palpable indentation in hard faeces
» Rectal prolapse or rectocele
» Postnatal damage to pelvic floor or third degree tear
• Other:
» Irritable bowel syndrome
» Colonic inertia
» Pelvic or anal dyssynergia

Table 2. Medicines that commonly cause constipation[3,4]

Medicines that commonly cause constipation
Aluminium-containing antacids
Antimuscarinics (such as procyclidine, oxybutynin)
Antidepressants (most commonly tricyclic antidepressants, but others may cause constipation in some individuals)
Some antiepileptics (for example carbamazepine, gabapentin, oxcarbazepine, pregabalin, phenytoin)
Sedating antihistamines
Antipsychotics such as amisulpiride, clozapine* (See MHRA warning[6]) or quetiapine
Antispasmodics (such as dicycloverine, hyoscine)
Calcium-channel blockers such as verapamil
Calcium supplements
Diuretics such as furosemide
Iron supplements
NSAIDs
Opioids

Clozapine

When prescribing clozapine, particular care should be taken in patients at risk of constipation, including those receiving medications known to cause constipation (especially those with anticholinergic properties such as some antipsychotics, antidepressants and antiparkinsonian treatments); with a history of colonic disease or a history of lower abdominal surgery; aged 60 years and older

- Advise patients that if they develop constipation, they should tell their doctor immediately before taking the next dose of clozapine.
- It is vital that constipation is recognised early and actively treated.
- Refer to the full summary product of characteristics for a complete list of warnings and recommendations for clozapine.[6]

Management

The management of constipation is described below and a summary pathway for chronic constipation in adults is included in attachment 1. Prescribing choice mainly depends on the presenting symptoms, the person's preference, and cost.

It is recommended that the dose, choice and combination of laxatives are tailored to symptoms, the speed with which relief is required, response to treatment, and individual preference.

The dose of laxative should be adjusted gradually to produce one or two soft, formed stools per day. The use of multiple laxatives should be avoided unless necessary, titrating individual doses to the maximum before adding an additional laxative.[3]

While many preparations are taken orally, rectal preparations if needed, are easy to use if administered correctly. Timing of effect may be more predictable than with oral laxatives; suppositories may be best given after breakfast to synchronise the effect of the gastro-colic response. Some people find them undignified and unpleasant to use. All are unlicensed uses for the treatment of faecal loading/impaction except Relaxit® micro-enema and arachis oil retention enema.[3]

Tables 3 and 4 on pages 7 and 15 highlight the different laxatives available within different drug classes.

Short term constipation[3]

1. Adjust any constipating medication, if possible. See table 1 - medicines that commonly cause constipation.
2. Advise the person about increasing dietary fibre, drinking an adequate fluid intake, and exercise. Further information is found in attachment 2 which is a patient information leaflet about constipation.
   - Aim for a balanced diet containing whole grains, fruits and vegetables.
   - Increase fibre intake gradually (to minimise flatulence and bloating) and continue as part of a normal diet.
   - Adults should aim to consume 18-30g of fibre per day, e.g. one medium sized bowl of All Bran cereal contains 7.2g of fibre.
   - Although the effects of a high fibre diet may be seen in a few days, it may take up to four weeks.
   - Adequate fluid intake is important (particularly with a high fibre diet or fibre supplements), but can be difficult for some people, e.g. people with frailty or older adults who may be unlikely to be able to drink the required volume of fluid.
   - Fruits high in fibre and sorbitol (natural occurring sugar), and fruit juices high in sorbitol, can help prevent and treat constipation, these include apples, apricots, grapes (and raisins), peaches, pears, plums (and prunes), raspberries and strawberries. The concentration of sorbitol is about 5-10 times higher in dried fruit. This is however cautioned in patients with diabetes.
3. Offer oral laxatives if dietary measures are ineffective, or while waiting for them to take effect.
   - Start treatment with a bulk-forming laxative (adequate fluid intake is important).
   - 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.[3]

NHS England OTC guidance recommends that constipation can be effectively managed with a change in diet or lifestyle. Pharmacists can help if diet and lifestyle changes aren't helping; they can suggest an over the counter laxative for short term, infrequent constipation caused by changes in lifestyle or diet such as lack of water or movement or changes in diet. The OTC guidance does not recommend laxatives for children unless they are prescribed by a GP.[7]

Chronic constipation in adults[4]

1. Begin by relieving faecal loading/impaction, if present.
2. Set realistic expectations for the results of treatment of chronic constipation.
3. Advise people about lifestyle measures — increasing dietary fibre (including the importance of regular meals), drinking an adequate fluid intake, and exercise. See attachment 2, a patient information leaflet.
4. Adjust any constipating medication, if possible. See table 1.
5. 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.
6. If laxative treatment is indicated:
   - Start 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. people with frailty or older adults who may be unlikely to be able to drink the required volume of fluid).
   - If stools remain hard, switch to or add an osmotic laxative.

- Use macrogols as first choice of an osmotic laxative.
- Use lactulose if macrogols are not effective, or not tolerated.
- If stools are soft but the person still finds them difficult to pass or complains of inadequate emptying, add a stimulant laxative.
- Prucalopride, prescribed by a clinician with experience in treating chronic constipation may be considered.
    - Ensure that NICE recommendations have been fulfilled before prescribing prucalopride; use of at least two laxatives (from different classes) at the highest tolerated recommended doses for at least six months.

Opioid-induced constipation[4]

1. Advise the person to increase the intake of fluid and fruit and vegetables if necessary.
2. Avoid bulk-forming laxatives as their mode of action is to distend the colon and stimulate peristalsis, but opioids prevent the colon responding with propulsive action. This may cause abdominal colic and rarely bowel obstruction.
3. Use an osmotic laxative (or docusate which also softens stools) and a stimulant laxative.
4. Adjust the laxative dose to optimise the response.
5. Advise the person that laxatives can be stopped once the stools become soft and easily passed again.
6. The NICE clinical guideline on the use of strong opioids in palliative care in adults advises that laxatives should be prescribed for everyone initiating 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.[16]
7. Naloxegol may be considered if NICE criteria are fulfilled in adult patients who have had an inadequate response to laxatives.[8]

Laxative abuse

Prescribers should be aware of potential laxative abuse. Laxative abuse occurs when a person attempts to eliminate unwanted calories, lose weight, "feel thin," or "feel empty" through the repeated, frequent use of laxatives.[10]

The Royal College of Psychiatrists state that studies consistently show that over half of patients with eating disorders have misused laxatives at some point in their illness. Constipation is common in anorexia nervosa as only small amounts of food are ingested and gastric motility subsequently slows down. Patients often struggle with the sensation of food in their bodies and subsequently take laxatives to relieve this feeling. They seem to favour stimulant laxatives as they come in tablets and are more powerful than bulk forming or osmotic laxatives. Their use varies from occasional, just over the recommended guidelines to those sufferers who take 100+ tablets per day.[11]

Table 3: Laxatives for constipation and cost of 28 days treatment. Refer to individual SPCs for additional information.

Laxative class/formulation		Dose[4]	Onset of action[4,19]	Contra-indications[4]	Other information[4]	Cost/28 days at max dose unless specified[4,12]	OTC (branded) preparations/ OTC availability
Bulk forming preparation to increase faecal mass- stimulates peristalsis	Ispaghula sachets 3.5g	One sachet 1-3 times daily	2-3 days	Faecal impaction Intestinal obstruction Swallowing difficulty Colonic atony Palliative patients (due to long onset of action)	Adequate fluid intake is important to prevent obstruction (6-8 cups per day) and do not take immediately before bed. Not suitable for people with frailty and older adults patients who are unlikely to be able to drink the required volume of fluid. Note: when mixed with water, the resulting mixture is quite thick and should be taken as soon as possible as it gets thicker on standing.	£7.92 (Ispagel most cost effective brand £6.86)	Fybogel Hi-Fibre
	Sterculia granules	1-2 spoonfuls daily or twice daily	2-3 days	Intestinal obstruction Faecal impaction Total atony of the colon	-	£7.92 (500g)	Normacol
	Methylcellulose 500mg	3-6 tablets twice daily	2-3 days	Imminent or threatened intestinal obstruction Faecal impaction Patients who have difficulty in swallowing Colonic atony Infective bowel disease Severe dehydration	-	£9.66	Celevac

Laxative class/formulation		Dose[4]	Onset of action[4,19]	Contra-indications[4]	Other information[4]	Cost/28 days at max dose unless specified[4,12]	OTC (branded) preparations/ OTC availability
Osmotic oral preparation to increase the amount of water in the large bowel	Macrogol compound oral powder sachets sugar free	Severe constipation dose: Initially 1 to 3 sachets daily in divided doses usually for up to 2 weeks. Maintenance, 1 to 2 sachets daily. Faecal impaction dose: 4 sachets on first day then increased in steps of 2 sachets daily up to max. of 8 sachets per day. Total daily dose to be drunk within 6 hour period.	2-3 days	Intestinal obstruction Paralytic ileus Severe inflammatory conditions of the intestinal tract	For patients with faecal impaction and severe constipation only. Ensure that patient is capable of drinking the required volume. Patients may adjust dose according to stool consistency. Warn patient to seek advice if diarrhoea starts and advise faecally impacted patients that faecal overflow may occur before impaction is resolved and they should seek further advice if unsure. Patients with cardiovascular impairment should not take more than 2 sachets in any 1 hour. Dissolve each sachet in half a glass of water (approx. 125ml). Solution to be kept in fridge once made (discard if unused after 6 hours).	Lowest cost: Generic - £7.73 (1 sachet twice daily) Cosmocol® - £7.37 Laxido® - £7.65 More costly brand: Movicol® - £15.14	All OTC
	Macrogol liquid	Maintenance 25ml once to twice daily	2-3 days		Dissolve or mix with water before taking	£15.15	OTC
	Macrogol Ready to take sachets	Maintenance: 1-2 sachets daily	2-3 days		Dissolve or mix with water before taking	£14.41	OTC
	Lactulose	15ml twice daily	Up to 2 days	Intestinal obstruction	Contra-indicated in galactosaemia, intolerant to lactose	£6.60	OTC

Laxative class/formulation		Dose[4]	Onset of action[4,19]	Contra-indications[4]	Other information[4]	Cost/28 days at max dose unless specified[4,12]	OTC (branded) preparations/ OTC availability
Stimulant to increase intestinal motility (1)	Bisacodyl tablets 5mg	5 to 10mg at night, increased if necessary to max. 20mg at night	8-12 hours	Intestinal obstruction Recent abdominal surgery Acute inflammatory bowel disease	Initial dose should be low then gradually increased.	£4.85	Dulcolax 5mg gastro-resistant tablets
	Senna tablets or liquid	15mg to 30mg daily, usually at night, but dose can be divided	8-12 hours	Atony; intestinal obstruction; undiagnosed abdominal pain.	Initial dose should be low then gradually increased. Senna liquid has a strong taste that may be disliked by some.	£4.31 - tabs £6.70 - liquid	Senokot tablets Senokot Max Strength Senokot 7.5mg/5ml liquid
	Sodium picosulphate elixir	5-10mg night	10-14 hours	Intestinal obstruction Recent abdominal surgery Acute inflammatory bowel disease	Initial dose should be low then gradually increased.	£7.54 - liquid	Dulcolax Pico liquid

Laxative class/formulation		Dose[4]	Onset of action[4,19]	Contra-indications[4]	Other information[4]	Cost/28 days at max dose unless specified[4,12]	OTC (branded) preparations/ OTC availability
Stimulant to increase intestinal motility (2)	Dantron in codanthramer 25/200 (with poloxamer 188) suspension	5-10ml at night	6-12 hours	Acute abdominal conditions; acute inflammatory bowel disease; intestinal obstruction; severe dehydration.	Restricted for patients with terminal disease, but not generally recommended due to risk of dantron burns (see below) if patient's mobility deteriorates. Control can usually be achieved with alternative laxatives. Avoid in patients with urine or faecal incontinence- prolonged contact with the skin can cause a dantron burn — an erythematous rash with a sharply demarcated border. May colour urine red. Stimulant at higher doses. Note: capsules now discontinued. Liquid taste may be unacceptable to some patients.	£168 - suspension	No
	Dantron in codranthrusate (50/60 with docusate sodium) suspension	5-15ml at night	6-12 hours	Acute abdominal conditions; acute inflammatory bowel disease; intestinal obstruction; severe dehydration.	Use is limited to constipation in terminally ill patients because of potential carcinogenicity (based on animal studies) and evidence of genotoxicity.	£425.25 - suspension	No
Stool softener and weak stimulant increases intestinal motility and softens stools	Docusate sodium capsules 100mg Liquid 50mg/5ml	Up to 500mg per day in divided doses	1-2 days	Intestinal obstruction	Liquid taste may be unacceptable to some patients	200mg bd - £7.80 - caps £34.31 - liquid	DulcoEase

Laxative class/formulation		Dose[4]	Onset of action[4,19]	Contra-indications[4]	Other information[4]	Cost/28 days at max dose unless specified[4,12]	OTC (branded) preparations/ OTC availability
Rectal (1)	Glycerol suppository (lubricant and weakly stimulant)	1 x 4g moistened with water before use when required	15-30 minutes	-	Can be used for hard or soft stools. Licensed for occasional use only. Suppositories must be placed alongside the bowel wall so that body heat causes them to dissolve and distribute around the rectum. Suppositories should be moistened before use to aid insertion. They are hygroscopic and also act as a lubricant.	£3.01 for 30 suppositories £0.11/ suppository	Glycerin suppositories
	Bisacodyl suppositories (stimulant)	10mg once daily in the morning	20 to 60 minutes	Acute abdominal conditions; acute inflammatory bowel disease; intestinal obstruction; severe dehydration.	Avoid if large, hard stools, as no softening effect. Use for soft stools.	£0.29/ suppository	Dulcolax suppository
	Bisacodyl 10mg/30ml enemas	-	-	Acute abdominal conditions; acute inflammatory bowel disease; intestinal obstruction; severe dehydration.	Unlicensed.	Cost per item £545.36 [NHSBSA June 19 - May 20]	Not available OTC
	Docusate sodium 120mg/10g enema (softener and weak stimulant)	The contents of one enema	15-30 minutes	-	Can be used for hard or soft stools. Correct administration important to prevent damage to rectal mucosa.	£4.67/enema	Norgalax 120mg/10g enema

Laxative class/formulation		Dose[4]	Onset of action[4,19]	Contra-indications[4]	Other information[4]	Cost/28 days at max dose unless specified[4,12]	OTC (branded) preparations/ OTC availability
Rectal (2)	Sodium citrate enema (osmotic)	The contents of one micro enema	5-15 minutes	Acute gastrointestinal conditions	Smaller volume (5 mL) than a phosphate enema (130 mL). Useful to remove hard, impacted stools. Correct administration is important to prevent damage to rectal mucosa. Licensed for occasional use only. Use with caution in individuals susceptible to sodium and water retention or debilitated adult patients.	£0.38/enema (Micolette) £0.41/enema (Micralax) £0.43/enema (Relaxit)	Micolette® microenema
	Sodium Phosphate enema® (osmotic) e.g. Cleen Ready-to-use enema 133ml	The contents of one enema	2-5 minutes	Acute gastrointestinal conditions (including gastro-intestinal obstruction, inflammatory bowel disease, and conditions associated with increased colonic absorption) Use of phosphate enemas are contraindicated in people who have signs of dehydration or significant renal impairment, as there is an increased risk of hypernatraemia, hyperphosphataemia, hypocalcaemia and hypokalaemia.	Useful to remove hard, impacted stools. Correct administration important to prevent damage to rectal mucosa. Licensed for occasional use only. Risk of rectal gangrene in people who are systemically unwell with a history of haemorrhoids. Can cause electrolyte disturbance and local irritation.	£1.95/133ml Ready to use enema 128ml long tube and standard tube (£27.93 each)	OTC

Laxative class/formulation		Dose[4]	Onset of action[4,19]	Contra-indications[4]	Other information[4]	Cost/28 days at max dose unless specified[4,12]	OTC (branded) preparations/ OTC availability
Rectal (3)	Arachis oil enema (softener)	The contents of one enema	Retention enema used overnight and warmed before use	Should not be used in people with peanut allergy.	Useful for hard, impacted stools.	£47.50/enema	OTC

Newer treatments

A number of new drugs have been introduced for the treatment of chronic constipation, opioid induced constipation or irritable bowel syndrome (IBS) with constipation. They are significantly more costly than older laxatives. These newer treatments are discussed together with their place in the constipation treatment pathway to ensure cost effective use.

Chronic constipation

Prucalopride

Prucalopride is licensed for the symptomatic treatment of chronic constipation in adults (both men and women) in whom laxatives fail to provide adequate relief.[13] The NICE technology appraisal (TA211) recommends prucalopride as a possible treatment for chronic constipation only in women for whom treatment with at least two laxatives from different classes, taken at the highest tolerated recommended doses for at least six months, has failed to provide adequate relief and invasive treatment for constipation is being considered.[14] Prucalopride should only be prescribed by a clinician with experience in treating chronic constipation. If treatment is not effective after four weeks, the patient should be reassessed and the benefit in continuing prucalopride reconsidered.[14]

Opioid induced constipation

Naloxegol

Naloxegol is licensed for the treatment of opioid-induced constipation in adult patients who have had an inadequate response to laxative(s).[15] Naloxegol is a form of naloxol which has been pegylated (that is, attached to a molecule of polyethylene glycol, or PEG). In this form, it selectively antagonises peripheral opioid receptors to relieve constipation. NICE TA345 recommends naloxegol, 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 one of the four stool symptom domains (that is, incomplete bowel movement, hard stools, straining or false alarms) while taking at least one laxative class for at least four days during the prior two weeks.[9] The SPC also recommends that all currently used maintenance laxative therapy should be halted, until clinical effect of naloxegol is determined.[15]

Naloxegol should be taken on an empty stomach at least 30 minutes prior to the first meal of the day or 2 hours after the first meal of the day. The dose should be taken in the morning to avoid bowel movements in the middle of the night.[15]

Cases of opioid withdrawal syndrome have been seen with naloxegol. Opioid withdrawal syndrome typically develops within minutes to several days following administration of an opioid antagonist.[15]

Naldemedine

Naldemedine is licensed for the treatment of opioid-induced constipation in adult patients who have previously been treated with a laxative.[16] Naldemedine is in the same class of laxative as naloxegol, a peripherally acting opioid receptor antagonist. The NICE technology appraisal on naldemedine for treating opioid-induced constipation [TA651] recommends the use of naldemedine within its marketing authorisation as an option for treating opioid-induced constipation in adults who have had laxative treatment.[17] The Scottish Medicines Consortium (SMC) accepted its use in Scotland for the licensed use as naldemedine compared to placebo significantly improved the spontaneous bowel movement response rate in patients with opioid induced constipation in either non-cancer or cancer pain.[18] Naldemedine may be taken at any time of day, but it is recommended to be taken at the same time every day. Naldemedine can be taken with or after food.[16]

Irritable Bowel Syndrome (IBS) with constipation and linaclotide

NICE guidance CG61 recommends self-help as a key component of the management of IBS and advises that people should receive general information on lifestyle, physical activity and diet. If a person's IBS symptoms persist while following general lifestyle and dietary advice, offer advice on further dietary management. Such advice should include single food avoidance and exclusion diets (for example, a low FODMAP [fermentable oligosaccharides, disaccharides, monosaccharides and polyols] diet) and only be given by a healthcare professional with expertise in dietary management.[20]

Pharmacological management may be considered, with the choice of agent(s) depending on the predominant symptom(s). Treatments include antispasmodic agents for abdominal pain and laxatives or antimotility agents, depending on the presence of constipation or diarrhoea. People with IBS should be advised how to adjust their doses of laxative or antimotility agent according to clinical response. A tricyclic antidepressant or a selective serotonin reuptake inhibitor (off label) may be considered if laxatives and antispasmodics are ineffective. Referral for psychological interventions may be considered for people with IBS who do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile.[20]

Lincaclotide

Linaclotide is a first-in-class, oral, once-daily guanylate cyclase-C receptor agonist (GCCA), licensed for the symptomatic treatment of moderate-to-severe irritable bowel syndrome with constipation (IBS-C) in adults.[21] The NICE medicines evidence summary (ESNM16) reports on two short-term placebo-controlled randomised trials that showed linaclotide was more effective than placebo in composite outcomes relating to abdominal discomfort and bowel movements.[21] There is no data comparing linaclotide with other treatments for IBS with constipation, e.g. laxatives, or antispasmodics, or antidepressants. There are no long-term data for the efficacy of this treatment beyond 12 or 26 weeks. NICE ESNM16 states that local decision makers will need to consider the place of linaclotide alongside existing treatments that may be used to manage symptoms of IBS-C, such as the concomitant use of antispasmodics and laxatives.[21] As recommended in the SPC, patients receiving linaclotide should be reviewed for improvement of symptoms after the first four weeks of treatment and at regular intervals thereafter, and treatment discontinued if improvement is not sustained.[22] NICE CG61 recommends to 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. The update also recommends to follow up people taking linaclotide after three months.[20]

Table 4: Summary of newer laxative treatments

Drug	Indication and class	Dose[4]	Cost/28 days[4,12]
Prucalopride (Resolor®)	Chronic constipation - Dihydrobenzofuran-carboxamide and selective, high affinity serotonin (5-HT4) receptor agonist	2mg once daily (1mg daily in women > 65 years)	£59.52 (for 2mg tablets)
Linaclotide (Constella®)	Irritable Bowel Syndrome - guanylate cyclase-C receptor agonist	290 micrograms once daily	£37.56

Drug	Indication and class	Dose[4]	Cost/28 days[4,12]
Naloxegol (Moventig®)	Opioid induced constipation - peripherally acting opioid receptor antagonist	25mg daily or 12.5mg daily in people with renal insufficiency	£51.52 (25mg or 12.5mg dose)
Naldemedine (Rizmoic®)	Opioid induced constipation - peripherally acting opioid receptor antagonist	200 micrograms once daily	£41.72

Medicine optimisation priorities

Review laxative treatment in chronic constipation. This will include medication reviews as part of structured medication reviews, polypharmacy or STOMP reviews.

Laxatives need to be continued long term for:

- People taking a constipating drug that cannot be stopped such as an opioid.
- People with a medical cause of constipation.[3]

The NICE Clinical Knowledge Summary (CKS) on constipation provides pragmatic advice which can be used to support deprescribing laxatives:[3]

- Laxative medication should not be suddenly stopped. Wean gradually to minimise the risk of requiring “rescue therapy” for recurrent faecal loading and/or impaction.
- Laxatives can be slowly withdrawn when regular bowel movements occur without difficulty, e.g. two to four weeks after defaecation 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.
- If more than one laxative has been used, reduce and stop one at a time. Begin by reducing stimulant laxatives first, if possible. However, it may be necessary to also adjust the dose of the osmotic laxative to compensate.
- Advise the person that it can take several months to be successfully weaned off all laxatives.
- Relapses are common. Treat early with increased laxative doses.
- It is recommended that care homes have a robust ordering system and checking process in place to ensure that laxatives and other medicines are only ordered if they are needed. In some care homes “as required” (prn) medicines, including laxatives, are routinely ordered on a monthly basis, even if they have not been used up and this should be reviewed.

An audit and patient invitation letters for review are available in attachments 3 and 4.

Review the cost-effectiveness of prescribed laxatives

- Ensure generic prescribing of macrogols or lowest cost brands, currently Cosmocol® or Laxido®.
- Switch Fybogel®/ispaghula sachets to Ispagel® Orange sachets.
- Review patients on laxatives containing dantron (co-danthramer suspension, co-danthrusate suspension (capsules have been discontinued). This is only licensed for use in terminally ill patients due to potential carcinogenic risk.[23]
- Discuss changing stimulant laxatives to acute prescription to prompt review.
- Review the continued need of laxatives after discharge from secondary care, e.g. post surgery, when they have been prescribed for short term use when opioids were prescribed.

- Review bisacodyl enemas and switch to bisacodyl suppositories if appropriate.
- Consider a switch from naloxegol to naldemedine which is more convenient for patients as naldemedine can be taken anytime of the day (but the same time each day) and with or without food. Liaise with the specialist over the switch and take into account patient preference.

Cost and savings

Spend on laxatives is over £98 million per annum across England and Wales (NHSBSA Feb-Apr20). Savings can be generated through appropriate prescribing and through good clinical practice and review. Prescribing should be reviewed to ensure it is appropriate and treatment is effective/still required. Laxative prescribing should mostly be for short term only.

A 30% reduction in laxative prescribing could result in potential annual savings of £29.4 million across England and Wales or £46,072 per 100,000 population.

Over £8.5 million is spent on Movicol® preparations in England and Wales (NHSBSA Feb-Apr20). **A 50% switch from Movicol to generic prescribing (macrogol compound oral powder sachets sugar free), or to the lowest cost brands, Cosmocol® and Laxido® could result in potential annual savings of over £2 million or £3,367 per 100,000 patients.**

£1.3 million was spent on naloxegol across England and Wales (NHSBSA Feb-Apr20) and there was a 67.3% growth in items compared to Feb-Apr19. **Switching 50% of patients from naloxegol to naldemedine could save £126,737 per annum across England and Wales or £199 per 100,000 population.**

Summary

Ensure there is a clear diagnosis of constipation before considering a laxative and that the constipation is not secondary to an underlying undiagnosed complaint or medicines e.g. opioids. Advise on lifestyle measures such as increasing dietary fibre, fluid intake and activity levels in short-duration and chronic constipation. OTC laxatives can be considered in adults with short term, infrequent constipation caused by changes in lifestyle or diet such as lack of water or movement or changes in diet. Bulking agents can be tried first and then add or switch to an osmotic laxatives, such as a macrogol. Stimulant laxatives are not recommended for long term use. For short-term and chronic constipation, laxatives can be slowly withdrawn when regular bowel movements occur without difficulty.

Review and, if appropriate, revise prescribing of laxatives for adults to ensure that they are prescribed routinely only for the short term treatment of constipation when dietary and lifestyle measures have proven unsuccessful or if there is an immediate clinical need.

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Additional PrescQIPP resources

Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-272-constipation/
Implementation tools	https://www.prescqipp.info/our-resources/bulletins/bulletin-272-constipation/
Data pack	https://data.prescqipp.info/#/views/B272_Constipation/FrontPage?:iid=1

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