



# Macrogol – guideline-based treatment for constipation

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An increase in stool frequency and an improvement in stool consistency play a decisive role in the relief of constipation. International as well as national guidelines recognise the positive effect of macrogol in relation to both parameters, with a high level of evidence. It is considered well-tolerated and safe. Some guidelines recommend the stimulant laxatives bisacodyl and sodium picosulfate with the same degree of recommendation.

Constipation is a subject that no-one readily talks about. Those affected are reluctant to speak of it because one's own bowel movements are not something to be discussed publicly! Pharmacists and even doctors often fail to adequately classify it as a relevant health problem, and constipation is frequently dismissed as a minor complaint with no disease status [1, 2]. That should set alarm bells ringing because after all, between 3 and 27% of the general population suffer from constipation, which in the majority of cases is chronic and for which sufferers all too often receive inadequate help [3].

International guidelines agree that therapy should start with general measures (more fibre, fluids and exercise) in order to compensate for any deficiency. Interestingly, there is generally no indication in patients that dietary fibre, fluid intake or exercise are insufficient. In such cases, guidelines refrain from making a recommendation and after general measures have proved inadequate, the focus shifts to symptomatic treatment with drugs.

Nevertheless, the general measures described above are tried out before the first consultation in the pharmacy or doctor's practice – often quite excessively – because they are frequently promoted in the lay press. The lack of success or the undesirable effects that occur, such as flatulence, eventually motivate people to finally talk about the troublesome taboo subject and seek expert advice [4, 5].

According to the international guidelines, the osmotic laxative macrogol is an established member of the repertoire of constipation treatments throughout the world (see **Table**). Macrogol is classed as well-tolerated and safe, which explains why this drug is also recommended and used in particularly sensitive groups such as children and pregnant or breast-

feeding women [1, 3, 6]. Guidelines often also recommend the stimulant laxatives bisacodyl or sodium picosulfate on an equal footing with macrogol [1]. Numerous studies have confirmed the efficacy and tolerability of the drug compared to placebo and other treatments [7, 8, 9]. In comparison, lactulose or anthraquinones such as senna are assessed as moderately effective and moderately well-tolerated [3].

## Conclusions

International guidelines all agree: macrogol brings effective and well-tolerated relief to patients with constipation. Something else that pharmacies and medical practices can do when advising patients is to tackle the topic of constipation head-on, and deal with the anxieties and feelings of guilt of those affected. The scientific data shows that, in the vast majority of cases, lifestyle is not the problem and laxatives such as macrogol may be used with a clear conscience.

## Literature

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Table: Summary of macrogol in international and national guidelines on the treatment of constipation [selection]

Area of validity [year of publication] Publisher/Title of guideline	Recommendations and instructions about macrogol (PEG) Quotations: (Note: All reference numbers within the quotations are those used in the list of references in the quoted original publication.)	Reference
<p><b>Europe [2020] ESNM:</b> European Society of Neurogastroenterology and Motility guidelines on functional constipation in adults</p>	<p>Statement 41: Saline laxatives, especially polyethylene glycol (PEG), <b>are effective in treating symptoms of constipation in patients with chronic constipation</b>; Level of evidence: Strong; Recommendation: Strong; Level of agreement: 100%; <i>Current evidence and literature: The evidence supporting the usefulness of saline laxatives, especially polyethylene glycol (PEG), is strong.</i> There are several large, high-quality trials supporting the fact that PEG is superior to placebo in improving symptoms in patients with chronic constipation, with a NNT of 3 (95% CI 2–4)<sup>5,172–180</sup>. Moreover, a Cochrane analysis also concluded that <b>PEG is superior to lactulose in patients with chronic constipation, resulting in more frequent stools, looser stools, and less abdominal pain.</b> PEG also increases the number of spontaneous complete bowel movements, improves stool consistency, and reduces severity of straining, without clearly affecting abdominal pain, in patients with IBS-C, further supporting its usefulness to treat constipation. The most common side effects with PEG are diarrhoea and abdominal pain, but not all trials find these to be more common in patients treated with PEG compared to the placebo group.</p>	[3]
<p><b>Germany [2013] DGNM/DGVS:</b> S2k-Guideline Chronic Constipation: Definition, pathophysiology, diagnosis and therapy</p>	<p>Statement 5-1; Conventional drug treatment (conventional “laxatives”) (Strong consensus) <b>Macrogols</b>, sodium picosulfate and bisacodyl should be used as first-line medication. There is no justification for limiting their period of use. They can also be used in <b>pregnancy</b>. <i>Comment:</i> Macrogol, bisacodyl and sodium picosulfate are effective and safe in acute functional and chronic constipation and are among the agents of first choice. This also applies to pregnancy. In chronic constipation, the dosage and frequency of ingestion are governed by individual requirements. The choice with regard to the form of administration (coated tablets, drops, soluble (oral) powder) and taste, is based on patient preference. The <b>efficacy and safety of macrogol</b> (=PEG=polyethylene glycol 3350 or 4000) in chronic constipation <b>has been demonstrated in numerous studies.</b> A meta-analysis [79] concluded that in terms of stool frequency and consistency, relief of abdominal pain and need for ingestion of laxatives, PEG is superior to lactulose (better efficacy with fewer side effects). In a comparative study, macrogol was more effective than the partial 5-HT<sub>4</sub>-agonist tegaserod [80]. Although pregnant women were excluded from the controlled studies, there are no reservations regarding use during pregnancy [81]. PEG undergoes only minimal absorption and is excreted in the urine unchanged [82]. The addition of electrolytes when PEG is used as laxative is unnecessary, only with intestinal lavage or in the treatment of coprostitas. Electrolyte-free preparations taste better [83].</p>	[1]
<p><b>France [2018] FNSC:</b> Clinical practice guidelines from the French National Society of Coloproctology in treating chronic constipation</p>	<p>First-line laxatives Osmotic and bulk laxatives remain the first-line laxative treatment for treating chronic constipation (CC), including during pregnancy (Expert Recommendation). Osmotic laxatives are recommended as a first-line treatment for constipation on the basis of their efficacy and good tolerance with the dietetic rules or as a complement to them (Level II, Grade B). They are more effective than a placebo with an increase of 2–3 stools per week and a two-fold higher success (≥3 stools/week) (Level I, Grade A). Among osmotic laxatives, polyethylene glycol is more effective than lactulose in improving the stool frequency and consistency as well as for abdominal pain (Level I, Grade A) [15–20]. Bulk laxatives can be soluble (psyllium, ispaghula, etc.) or insoluble fibres (wheat bran). These are organic polysaccharides that retain water in the intestinal lumen. They should be ingested with sufficient quantities of water [13,21,22]. They are also a first-line laxative option (Level II, Grade B). Moreover, they can improve the frequency and consistency of faeces as well as the symptoms of dyschezia. Their main side effects are meteorism and flatulence. Bulk laxatives are contraindicated in cases of intestinal stenosis, faecal impaction or inflammatory colitis.</p>	[10]
<p><b>Italy [2012] AIGO/SICCR:</b> Consensus statement AIGO/SICCR diagnosis and treatment of chronic constipation and obstructed defecation (part II: treatment)</p>	<p>Medical treatment in chronic constipation → Polyethylene glycol: level of evidence I; grade of recommendation: A <i>Placebo-controlled trial of PEG:</i> PEG is an organic polymer that is not degraded by the intestinal flora. The effectiveness of PEG has been documented in numerous trials [40–44]. PEG increased the stool frequency (P &lt; 0.01) while improving the stool consistency [40,41,43] and reducing other symptoms of constipation [41,43]. Iso-osmotic or hypo-osmotic solutions of PEG consistently improved the frequency of bowel movements compared with the frequency before treatment (P &lt; 0.001) [45]. PEG was well tolerated, and side effects (abdominal cramps, flatulence, nausea) were rare. <i>Trials of PEG vs other laxatives:</i> PEG is more effective than lactulose [31,32] in increasing the stool frequency and improving the stool’s consistency. In patients treated with PEG, there are also lower rates of rescue medication use and flatulence. One trial showed that PEG was more effective than tegaserod [46]. PEG is a pillar in the treatment of chronic idiopathic constipation because of its high efficacy. There is evidence that PEG provides significant benefits compared with placebos and other laxatives. Furthermore, retrospective studies show that PEG remains effective for up to two years of treatment [46,47]. <b>The use of PEG is supported by Level I evidence, Grade A recommendation.</b></p>	[11]
<p><b>UK [2019] HERPC:</b> Guideline on Management of Constipation approved by HERPC</p>	<p><b>RECOMMENDED TREATMENT OF CONSTIPATION IN ADULTS:</b> 2nd line: OSMOTIC LAXATIVE: Macrogols 1 – 3 sachets daily in divided doses +/- STIMULANT Laxative <i>Treatment of faecal impaction:</i> 1st line (Oral): Macrogols 8 sachets daily in divided doses</p>	[12]
<p><b>Global [2011] WGO:</b> World Gastro-enterology Organization Global Guideline Constipation—A Global Perspective</p>	<p>The second step in the graded approach is to add osmotic laxatives. <b>The best evidence is for the use of polyethylene glycol</b>, but there is also good evidence for lactulose.</p>	[13]

Area of validity [year of publication] Publisher/Title of guideline	Recommendations and instructions about macrogol (PEG) Quotations: (Note: All reference numbers within the quotations are those used in the list of references in the quoted original publication.)	Reference
USA [2013] AGA: American Gastroenterological Association Medical Position Statement on Constipation	We suggest a gradual increase in fiber intake, as both foods included in the diet and as supplements and/or an inexpensive osmotic agent, such as milk of magnesia or <b>polyethylene glycol</b> . Depending on stool consistency, the next step may be to supplement the osmotic agent with a stimulant laxative (e.g. bisacodyl or glycerol suppositories), which is preferably administered 30 minutes after a meal to synergize the pharmacologic agent with the gastrocolonic response.	[14]
South Korea [2015] Korean Society of Neurogastroenterology and Motility: Guidelines for the Diagnosis and Treatment of Chronic Functional Constipation in Korea	24. Statement: <b>Polyethylene glycol improves bowel frequency and stool consistency in patients with chronic constipation.</b> <ul style="list-style-type: none"> <li>▪ <b>Grade of recommendation: 1.; Level of evidence: A.</b></li> <li>▪ Experts' opinions: completely agree (73.1%), mostly agree (26.9%), partially agree (0%), mostly disagree (0%), completely disagree (0%), and not sure (0%).</li> </ul> 25. Statement: <b>Long-term administration of polyethylene glycol is recommended</b> because serious adverse reactions are rare. <ul style="list-style-type: none"> <li>▪ <b>Grade of recommendation: 1.; Level of evidence: A.</b></li> <li>▪ Experts' opinions: completely agree (50.0%), mostly agree (50.0%), partially agree (0%), mostly disagree (0%), completely disagree (0%), not sure (0%).</li> </ul>	[15]
Mexico [2018] Asociacion Mexicana de Gastroenterología. The Mexican consensus on chronic constipation	24. Polyethylene glycol is the most widely studied laxative in functional constipation (FC) and has been shown to increase defecation frequency and improve stool consistency. <b>Quality of evidence and strength of recommendation: A1 strong, in favour of the intervention (in complete agreement: 86%; in partial agreement: 14%).</b> Polyethylene glycol (PEG 3350) is an organic polymer whose osmotic activity is proportionate to the number of monomers that form it. It is metabolically inert, not metabolized or degraded by colonic bacteria, and interacts with water in a solution to increase osmotic pressure. There are multiple studies that demonstrate the effectiveness of PEG over placebo, lactulose, and other laxatives in the treatment of FC. <sup>113–118</sup> In a recent meta-analysis, <sup>119</sup> 19 studies were evaluated (9 with PEG alone, 8 with PEG plus electrolytes, and 2 that compared PEG vs PEG plus electrolytes), demonstrating that the administration of PEG (with and without electrolytes) increased the number of bowel movements per week and softened stool consistency. According to the 2010 Cochrane review, <sup>120</sup> PEG is superior to lactulose in increasing defecation frequency, softening stool consistency, and reducing the need for rescue laxatives. The NNT has been estimated at 3 (95% CI: 2–4) and the majority of the studies had less bias and heterogeneity than the studies on other drugs. The side effects reported were infrequent and the most common were abdominal pain and headache. Even though most of the studies had a follow-up under 6 months, PEG effectiveness did not appear to decrease after that period of time. The recommended dose is 17 g of PEG diluted in at least 250 ml of water.	[16]
Latin America [2008] Latin American Consensus on Chronic Constipation	<b>Osmotic laxatives</b> <b>Polyethylene glycol (PEG) has demonstrated effectiveness and safety in well-designed studies in patients with Chronic constipation [CC] (grade A recommendation).</b> There are no studies evaluating lactulose in the management of CC during the last 10 years and the only recent evidence suggests that it is less effective than PEG. However, given that previous studies were considered acceptable, the Consensus did not disapprove its use when required (grade C recommendation). Agents in this group include nonabsorbable sugars (lactulose), saline agents (magnesium hydroxide), and PEG. Lactulose clinical studies are old and have methodological limitations; however, they suggest that it is more effective than placebo <sup>52–56</sup> . Recent studies compared lactulose with PEG and, although it can be said that they have an intermediate methodological quality, PEG proved to be more effective than lactulose and it presented less adverse effects <sup>55,56</sup> (Table V). Some well-designed studies have shown that PEG is effective in both short-term and long-term interventions (6 months) (Table VI). The dose is 17–32 g/day, with a rapid onset time of action (0.5–1 h) and the most frequent secondary event is fecal incontinence due to its laxative potency <sup>57–59</sup> . One study even compared PEG with lactulose, and showed that PEG in doses of 13–39 g/day was more effective and better tolerated in CC <sup>56</sup> . Finally, no clinical studies have been conducted with magnesium hydroxide in CC.	[17]

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