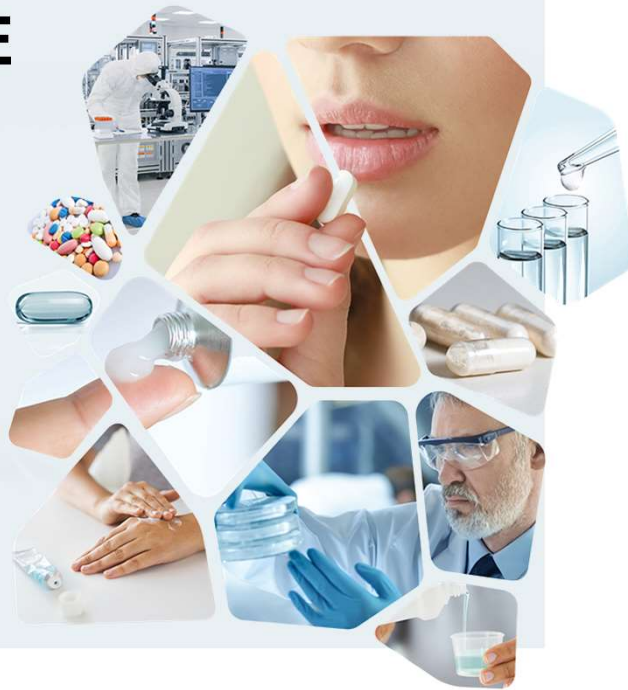


# Polyethylene Glycol: Use as API for Laxative Formulations

## HEALTH CARE



**CLARIANT** 

Confidential

Industrial and Consumer Specialties  
Health Care

what is precious to you?

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- Constipation – some background facts
- Laxatives – Advantages and Disadvantages
- PEG as laxative
- Clariant's offering in API Polyethylene glycols



# Clariant ICS Health Care

## CONSTIPATION

- Some Background Facts



## What is constipation?

**A healthy frequency of a bowel movement are 3 bowel movements per day to 3 per week.**

A constipation is chronic if two of the following symptoms appear for more than three months<sup>[1]</sup> :

- Strong pressing
- Lumpy or hard stool
- Incomplete emptying
- Manual support for bowel movements
- Less than 3 bowel movements per week

Chronic constipation might have a big impact on people's lives with an influence in life quality<sup>[2]</sup> and can be a cause for hemorrhoidal disease.



1. Longstreth, G.F., et al., *Functional bowel disorders*. Gastroenterology, 2006. **130**(5): p. 1480-91

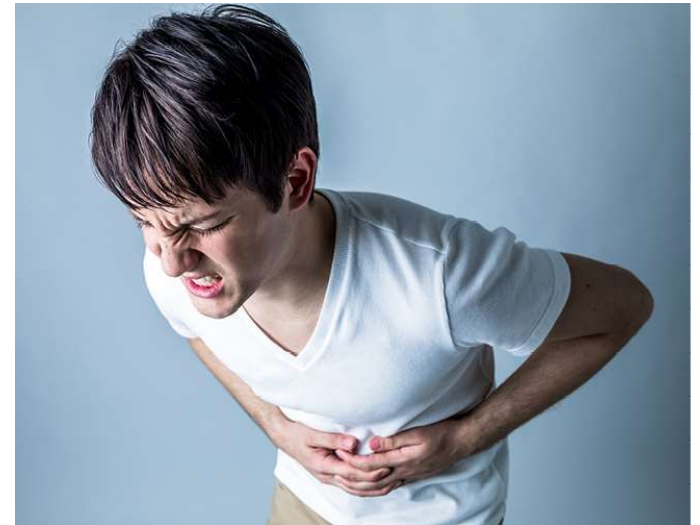
2. Sun, S.X., et al., Impact of chronic constipation on health-related quality of life, work productivity, and healthcare resource use: an analysis of the National Health and Wellness Survey. *Dig Dis Sci*, 2011. **56**(9): p. 2688-95

## Talking about... constipation

**5 – 15 % of the German population suffers from chronic constipation. The frequency increases with age and women are more affected than men [3,4].**

Common reasons for constipation:

- stress, travelling (different food or time change)
- low fiber diet
- suppression of the bowel movement
- long colon transit
- hormone conversion during pregnancy or menopause
- Side-effect of certain diseases (e.g. multiple sclerosis, irritable colon, Parkinson's disease) and medicaments



3. Suares, N.C. and A.C. Ford, *Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis*. Am J Gastroenterol, 2011. **106**(9): p. 1582-91.

4. Wald, A., et al., *A multinational survey of prevalence and patterns of laxative use among adults with self-defined constipation*. Aliment Pharmacol Ther, 2008. **28**(7): p. 917-30.

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## LAXATIVES

- Advantages and disadvantages



## Common Laxatives types against constipation and how they work

NATURAL LAXATIVES		STIMULANT LAXATIVES	OSMOTIC LAXATIVES
<b>Fibres</b> e.g. <b>Psyllium fibres</b>	<b>Leaves &amp; blossoms</b> e.g. <b>Senna plants</b>	e.g. <b>Bisacodyl &amp; Sodium Pico sulphate</b>	e.g. <b>Lactulose &amp; PEG</b>
<ul style="list-style-type: none"> <li>– containing Polysaccharide<sup>[5]</sup>, build a gel with water in the colon</li> <li>– By this the stool is enlarged and softens</li> </ul>	<ul style="list-style-type: none"> <li>– containing Anthraquinone, which stimulate the mobility of the colon</li> <li>–</li> <li>– Stimulate the secretion which leads to a softer stool</li> </ul>	<ul style="list-style-type: none"> <li>– Directly attracting the nerves in the colon and stimulate the mobility of the colon (peristalsis) by this</li> <li>– Inhibit water resorption in the colon and stimulate secretion which leads to softer stool</li> </ul>	<ul style="list-style-type: none"> <li>– Attract water, enhance the stool volume and soften the stool</li> </ul>

5. [www.mucofalk.de/html](http://www.mucofalk.de/html) (01.06.2021)

## Common Laxative types: Advantages & Disadvantages

	NATURAL LAXATIVES		STIMULANT LAXATIVES	OSMOTIC LAXATIVES	
	Fibres e.g. Psyllium fibres	Leaves & blossoms e.g. Senna plants	e.g. Sodium Pico sulphate	Lactulose	PEG <sup>[7]</sup>
Advantages	<ul style="list-style-type: none"> <li>✓ Suitable for long term therapy</li> </ul>	<ul style="list-style-type: none"> <li>✓ More effective than Lactulose<sup>[6]</sup></li> </ul>	<ul style="list-style-type: none"> <li>✓ Possible to be taken while breastfeeding</li> <li>✓ Easy dosage</li> <li>✓ Possible use starting from 4 years old</li> </ul>	<ul style="list-style-type: none"> <li>✓ Recommended during pregnancy.</li> </ul>	<ul style="list-style-type: none"> <li>✓ Low resorption from the body</li> <li>✓ Recommended during pregnancy<sup>[6]</sup></li> <li>✓ More effective and less side effects than Lactulose<sup>[9]</sup></li> <li>✓ Possible use starting from 2 years old**<sup>[8]</sup></li> <li>✓ Low gastrointestinal side effects</li> <li>✓ Suitable for long-term therapy</li> <li>✓ Aroma free types suitable for diabetic<sup>[8]</sup></li> </ul>
Disadvantages	<ul style="list-style-type: none"> <li>– Not recommended to use in combination with other medicine as adsorption could be delayed or prevented by the gel<sup>[5]</sup></li> <li>– Not recommended below the age of 12 years</li> <li>– side effects include gas and bloating</li> </ul>	<ul style="list-style-type: none"> <li>– Not recommended below the age of 12 years</li> <li>– Cramping is often observed</li> <li>– Not recommended for long term use in combination with other medicine such as diuretics, cortisone, cardiac glycosides</li> <li>– No data for long time use available</li> <li>– Can cause allergic reaction</li> </ul>	<ul style="list-style-type: none"> <li>– Cramping is often observed</li> <li>– Sudden urgency might occur</li> <li>– Fast reaction time might lead to unpredictable situations.</li> <li>– Habituation effect is noticed in some cases</li> <li>– No data for use during pregnancy</li> <li>– Not suitable for long-term therapy</li> </ul>	<ul style="list-style-type: none"> <li>– Might contain fructose, which might cause allergies.</li> <li>– Partially resorbed by the body</li> <li>– Could lead to gas in the colon.</li> <li>– Less effective for long colon transit times<sup>[6]</sup></li> <li>– Not recommended below the age of 14 years</li> </ul>	

6. Andresen V et al; AWMF S2k-Leitlinie Chronische Obstipation: Definition, Pathophysiologie, Diagnostik und Therapie, 2013, p. 23-26

7. DiPalma JA et al. South Med J. 2007;100:1085-1090 8. [www.movicol.de/patientenratgeber](http://www.movicol.de/patientenratgeber) Inside Health 2018 p.6-8

9. Pare P, Fedorak RN. Can J Gastroenterol Hepatol. 2014;28:549-557

\*\* special products for Children available with prescription



## Common Laxative types: Side effects are much lower with PEGs

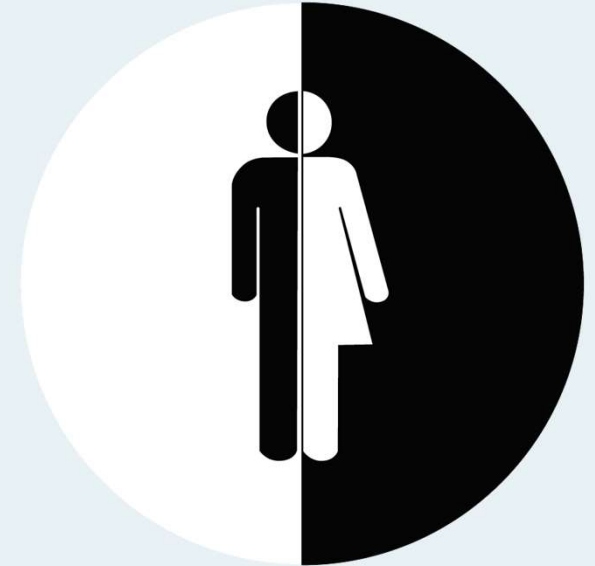
SIDE EFFECTS*	PSYLLIUM FIBRES <sup>[5]</sup> (NATURAL LAXATIVES)	SENNA PLANTS <sup>[10]</sup> (NATURAL LAXATIVES)	STIMULANT LAXATIVES (E.G. SODIUM PICOSULPHATE <sup>[11]</sup> )	LACTULOSE <sup>[12]</sup> (OSMOTIC LAXATIVE)	PEG <sup>[7,13]</sup> (OSMOTIC LAXATIVE)
<b>Bloating</b>	Incidental			Oftentimes	
<b>Cramping</b>		Possible	Oftentimes	Oftentimes	
<b>Stomach indisposition</b>			Oftentimes	Oftentimes	
<b>Nausea</b>			Incidental		
<b>Diarrhoea</b>		Possible	Very often	Very often	
<b>Dizziness</b>			Incidental		
<b>Habituation effect</b>			Possible		
<b>Absorption &amp; Metabolism</b>			Yes	Yes	

\* [Categories of side effects](#)

10. [Abführtee mit Sennesblättern bei gelegentlicher Verstopfung - Sidroga](#) 11. [dulcolax-np-tropfen-beipackzettel.pdf](#) / (30.06.2021)  
12. [2016-12\\_50064085\\_GI\\_160x520.indd \(hexal.biz\)](#) / (06.06.2021) 13. [Patient Resources | MiraLAX® HCP](#) / (30.06.2021)

# Clariant ICS Health Care

## PEG AS LAXATIVES



## What is PEG?

- PEG is the abbreviation for a synthetic polymer group called Polyethylene glycol.
- Made by anionic polymerization of Ethylene oxide, it results into a polymer with the common formula  $H-(OCH_2-CH_2)_n-OH$
- Known also under its pharmaceutical name Macrogol and it is used already since decades as pharmaceutical ingredient in the Pharmaceutical industry.
- Overall, they are described in various regional and the large international pharmacopoeias such as:
  - European Pharmacopoeia (Ph. Eur.)
  - Japanese Pharmacopoeia (J. P.)
  - US Pharmacopoeia (USP-NF)
- The products with a mean molecular weight of 3350 g/mol and 4000 g/mol are known as Active Pharmaceutical Ingredients (“API”) to give relief from constipation.
- There is also a US monograph for laxative formulation with PEG 3350 available.

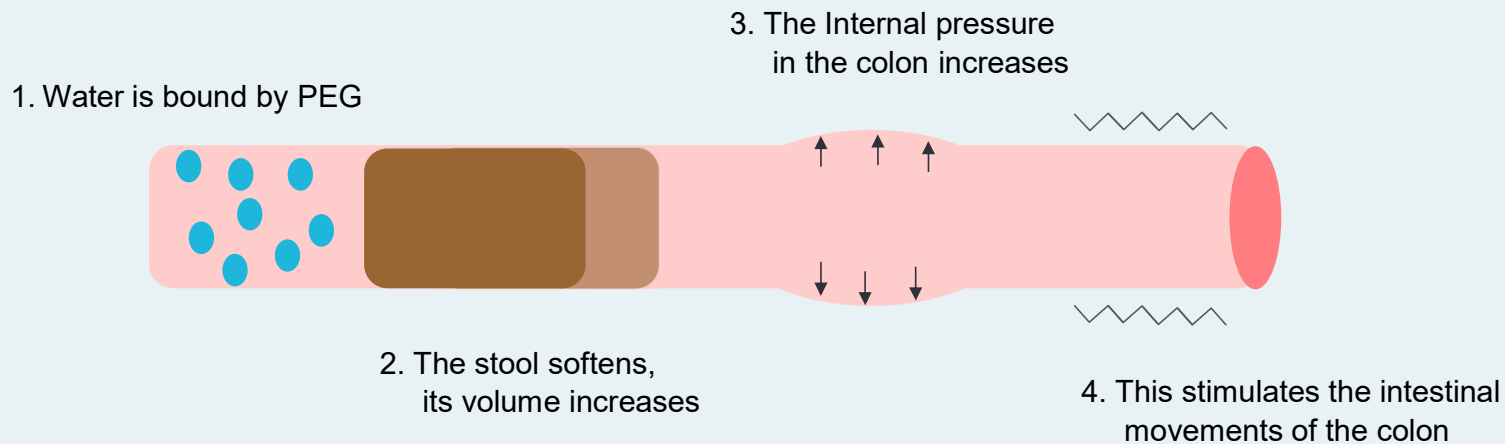
## PEG as laxative

- PEG in laxative formulations is an osmotic agent, which is very gentle to the body.
- PEG is a very hygroscopic substance and shows therefore better effectiveness than other osmotic agents.
- Due to its polymeric nature, it is showing a very low resorption to the body.
- It is excreted completely and not absorbed by the digestive tract.
- Therefore, there is no influence by this API to the patient's diet.
- Furthermore, this results into low gastrointestinal side effects.
- Formulations with PEG as API suitable for long-term therapy and recommended during pregnancy.
- In combination with salts in the formulation the electrolytic balance of the body is not affected by these laxatives.
- Special PEG formulations could be used already by children > 2 years also for long term use.<sup>[13]</sup>
- High efficacy and low side-effects of PEG makes it the golden standard for colonoscopy and pre-surgical treatment worldwide.

## PEG as API – how does it work?

**PEG has an osmotic effect, that means it binds water and makes the stool become softer and easier to drain.**

This process takes place in overall 4 steps: <sup>[14]</sup>



## Typical PEG-based formulation types against constipation\*

PEG	SOLID POWDER FORMULATIONS**				LIQUID FORMULATIONS**	
	without electrolytes		with electrolytes		without electrolytes	with electrolytes
	pure	+ other ingredients				
3350	Formulation containing 100% PEG, no other ingredients, main dosage of PEG: 17 g		Formulation containing ,> 85% PEG, electrolytes, sweetener / flavour main dosage of PEG: 2,95 / 5,9 g	Formulation containing 95% PEG, electrolytes, sweetener / flavour main dosage of PEG: 13,125 g		Formulation containing appr. 50% PEG, electrolytes, purified water, sweetener / flavour, preservatives
4000	Formulation containing 100% PEG, no other ingredients, main dosage of PEG: 10 g	Formulation containing >99% PEG, with sweetener / flavour, main dosage of PEG: 10 g	Formulation containing ,> 85% PEG, electrolytes, sweetener / flavour main dosage of PEG: 7.3 g		Formulation containing appr. 50 % PEG, purified water, sweetener / flavour, preservatives	

\* concentrating on the adult formulations and disregarding the different flavour types.

\*\*composition and type of PEG depends also on the country & region

## Clariant ICS Health Care

### **CLARIANT'S OFFERING in API Polyethylene glycols**



## Clariant Polyethylene Glycols – Pharma Quality with long experience

- More than 30 years experience in producing Polyethylene glycols for the Pharmaceutical Industry
- Marketing Polyethylene glycols under the name “Polyglykol” and “VitiPure”
- Offering the whole range of possible molecular weights (200 to 35000 g/mol)
- Available excipient and API ranges.
- Offered in various physical forms (liquid, pastes, flakes (S), sprayed powders (PS), milled powders (P/PF))
- Specified according to General requirements of the 3 international pharmacopoeias (Ph. Eur., USP-NF, JP)





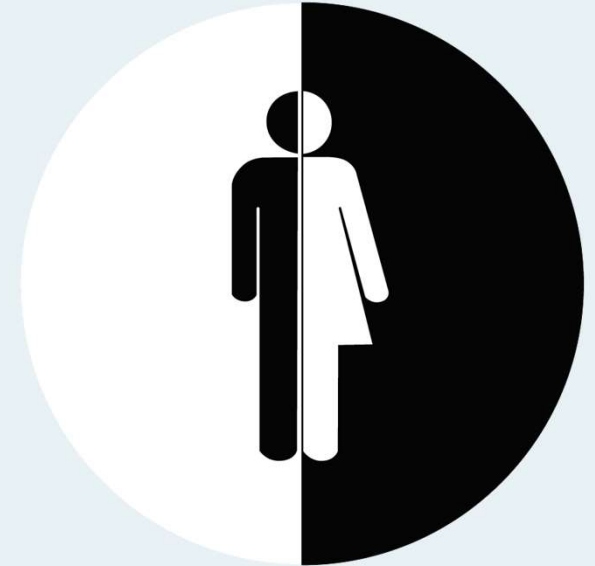
## Clariant API Polyethylene Glycols – a tool-box for the individual laxative formulation

- More than 25 years experience in producing API Polyethylene glycols.
- Available in various physical forms available suitable for your final formulation (flake, sprayed powders, milled powders)
- Specified according to General requirements of the 3 international pharmacopoeias (Ph. Eur., USP-NF, JP)
- Registered at various authorities to support your dossier (e.g. CEP, DMF, China)
- PEG dedicated reactors to avoid cross contamination.
- Audited by the authorities for GMP compliance.



# Clariant ICS Health Care

## BACKUP



## Categories of side effects

<b>CATEGORY</b>	
<b>very often</b>	More than 1 of 10 patients
<b>often</b>	1 to 10 of 100 patients
<b>incidental</b>	1 to 10 of 1.000 patients
<b>rarely</b>	1 to 10 of 10.000 patients
<b>very rarely</b>	Less than 1 of 10.000 patients
<b>not common</b>	Frequency cannot be estimated based on available data