

Utilisation and Safety of Polyethylene Glycol 3350 With Electrolytes in Children Under 2 Years—A Retrospective Cohort

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ABSTRACT

Objectives: In the UK, Movicol paediatric plain (polyethylene glycol 3350 with electrolytes [PEG 3350+E], Norgine, UK), is licensed for chronic constipation in children 2–11 years of age and faecal impaction (FI) from 5 years. This study aimed to investigate usage and characterise the risk profile in children under 2 years of age using PEG 3350+E in the UK.

Methods: Retrospective, single exposure cohort study, with patients identified from Clinical Practice Research Datalink (CPRD) GOLD. Patients first prescribed PEG 3350+E under 2 years of age for the treatment of constipation or FI, between September 2003 and July 2019, were included.

Results: There were 13,235 patients with a constipation indication and 40 patients with FI. For the constipation cohort: median age of PEG 3350+E first prescription was 1.2 years [interquartile range (IQR) 0.9, 1.6] and 68.4% had one treatment episode (TE). The mean duration of exposure, in the first TE, was 88.9 days. The most common total daily dose was one sachet (6.9 g). In terms of incident events on treatment, 0.5% of patients had abdominal pain, 3.0% had diarrhoea (may be attributed to treatment) and 4.1% had vomiting. 2.0% had signs/symptoms which could (in extreme cases) be associated with electrolyte disturbance, however, none had abnormal electrolyte values.

Discussion: The safety aspect of this study did not identify any signals of concern in the constipation cohort. The number of patients in the FI cohort were too small for robust conclusions. If information were available, then a safety study would ideally assess treatment intake per kilogram, including electrolyte intake, before reaching safety conclusions. Nevertheless, these data contribute to real-world evidence on the use of PEG 3350+E in this population.

Key Words: Constipation, clinical practice research datalink GOLD, faecal impaction, osmotic laxative, pharmacovigilance

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What Is Known

- Polyethylene glycol 3350 with electrolytes (PEG 3350+E), an osmotic laxative, is used worldwide to treat chronic constipation in children aged 2 years and over.
- Treatment with polyethylene glycols (PEGs) in children over 2 years of age is well understood and has been extensively studied.

What Is New

- This real-world cohort study, using the Clinical Practice Research Datalink GOLD database, has identified off-label prescribing of PEG 3350+E in >13,000 children under 2 years of age for the treatment of constipation in UK primary care
- No safety signals of concern were identified for PEG 3350+E in the treatment of constipation in children under 2 years of age.

Childhood constipation is common worldwide and non-pharmacological and pharmacological interventions are available (1–3). Treatment of childhood constipation with polyethylene glycols (PEGs) is well understood and extensively studied (4–38).

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Movicol paediatric plain (polyethylene glycol 3350 with electrolytes [PEG 3350+E], Norgine, UK), an osmotic laxative, is used for constipation in children aged 2 years and over in many countries. In the UK, it is licensed for chronic constipation in children 2–11 years of age and faecal impaction (refractory constipation with faecal loading of rectum and/or colon) from the age of 5 years (39).

Certain adverse events occur at known frequencies in populations taking PEG 3350+E and are listed in the summary of product characteristics (SmPC) and package leaflet (PL). Common adverse events are gastrointestinal in nature, such as abdominal pain, borborygmi, diarrhoea, vomiting, nausea and anorectal discomfort (39).

Real-world studies, in children aged under 2 years, have been conducted with limited sample sizes (40,41). These studies confirmed the efficacy of PEG with electrolytes for chronic constipation and did not identify safety signals with use (40,41). A systematic review among children ages 0–18 years suggested that PEG preparations may be superior to placebo, lactulose and milk of magnesia for constipation, though conclude that further research is warranted (42).

Therefore, the primary objective of this study was to examine the utilisation and safety of PEG 3350+E in children under 2 years of age. The secondary objective was to assess the impact of confounding by indication, posology and treatment duration on adverse events identified.

METHODS

Setting

A single exposure retrospective observational cohort study design was used. Patients were identified from the Clinical Practice Research Datalink (CPRD) GOLD database, covering England, Scotland, Wales and Northern Ireland and contain routinely-collected data from over 800 UK primary care practices (GP) using the Vision[®] electronic health record software.

Patients were identified, from CPRD GOLD, based on prescriptions issued for PEG 3350+E. One product name (“Movicol Paediatric Plain oral powder 6.9 g sachets”) and associated CPRD product code (6599) was used to identify relevant prescriptions. PEG 3350+E was first licensed in the UK in September 2003, and so the study period was September 2003 to July 2019.

Subjects

PEG 3350+E naïve patients, aged under 2 years, prescribed PEG 3350+E for the treatment of constipation or faecal impaction were identified. Patients were stratified into two cohorts according to indication; constipation and faecal impaction and analysed separately. Indication for prescribing was derived from Read code terms, for reasons for consultations, in the 30-day period before starting treatment. A faecal impaction event in this period would ensure enrolment into the faecal impaction cohort, regardless of constipation events in the same period. Patients with other indications were summarised by counts and excluded from further analyses. Patients were further stratified to three age groups for analysis purposes: 0–<6 months, 6–<12 months and 12–<24 months. Due to the small sample size, the faecal impaction cohort was not stratified by age.

Variables

The outcomes of interest were reasons for consultations, number of prescriptions, duration of continuous treatment, dose,

number of treatment episodes (TEs), test results during treatment and patient demographics.

All adverse events on treatment were identified (using reasons for consultations) at any time during the treatment exposure period following a prescription for PEG 3350+E. Pre-specified adverse events of interest, listed on the SmPC, were examined using reasons for consultations. These included abdominal pain, peripheral oedema, diarrhoea, vomiting and electrolyte disturbance. For abdominal pain, peripheral oedema, diarrhoea and vomiting, events were derived from synonymous Read code terms.

However, there were no synonymous Read code terms reported for electrolyte disturbance. Therefore, signs and symptoms which a patient may have presented with (if experiencing electrolyte disturbance) were used as a proxy to identify potential cases (for example, seizures, muscle twitching, fatigue). Potential electrolyte disturbance events were identified by a clinician and defined as any Read codes which met the criteria for the following signs/symptoms: confusion/agitation, seizures/loss of consciousness, hypoaesthesia/paraesthesia, muscle twitching/spasms, oedema, fatigue, shortness of breath and/or dehydration. It is important to note that these Read codes are not specific for electrolyte disturbance; clinically, the frequency for some of the events of electrolyte disturbance was uncommon or rare.

Discontinuation, interruption and resumption of treatment was characterised with the identification of TEs. A TE was defined as a time period containing consecutive PEG 3350+E prescriptions with ≤ 60 days between prescriptions. The final prescription in a TE was assumed to have a duration of 60 days, unless otherwise stated, as most chronic medication prescriptions in the UK are for 2 months' supply. Within a TE the duration of a prescription was assumed to end when the next prescription was issued.

If the time period between prescriptions was more than 60 days then this indicated start of a new TE. One-off prescriptions were assumed to form their own TE with a duration of 60 days.

Covariates of interest included weight (baseline and at end of the first TE), prior events (reasons for consultations in the 3-month period before first starting PEG 3350+E) and prior medications (in the 3-month period before first starting PEG 3350+E). Patient exposure to other prescribed medications during and between TEs were characterised to explore switching patterns, add-on therapy and concomitant medications.

The complete date of birth is not provided in the CPRD GOLD database. Year of birth is provided and for patients, under 16 years of age, the month of birth may be available. Where the month of the birth was missing, these patients were excluded ($n = 31$). For all patients, the date of birth was assumed to be the midpoint of the month (15th).

Analysis

Results were summarised using mean/median values and the range or interquartile range (IQR) was used to measure dispersion. Frequencies and respective percentages were used to summarise count data.

Prior events included events occurring on the first ever (index) PEG 3350+E prescription date. Cumulative incidence risk estimates for adverse events following the index prescription date were calculated (incident events). Incident events on treatment could not occur at the start of TEs (as this could be the reason for prescribing PEG 3350+E).

Reasons for consultations were also collected in the 30-day period after the last prescription exposure period (last prescription date + 60 days), if treatment stopped for patients who had only one TE.

Concomitant medications included medications prescribed at the start of TEs. Prior medications (in the 90-day period before first ever PEG 3350+E prescription) did not include medications prescribed on the first ever PEG 3350+E index date.

Sensitivity Analyses

As prescription duration information is often missing, a sensitivity analysis was performed using the median duration of exposure (MDE), which was based on time periods between consecutive prescriptions within TEs. The MDE of the specific TE was used as the exposure for the final prescription of the respective TE, instead of the 60-day period. This was performed for incident events on treatment only.

A further sensitivity analysis examined patients who were less than 2 years of age when initiating PEG 3350+E but for whom a prescription overlapped with them turning 2 years of age. This sensitivity analysis was performed for incident events on treatment only and the exposure period only included the period after the child had turned 2 years of age (for the last prescription issued under 2 years of age). In contrast, for the main analysis, events were censored when patients had reached the age of 2 years.

RESULTS

Participants

A total of 20,861 patients aged under 2 years of age who were prescribed PEG 3350+E, between September 2003 and July 2019, were initially identified. From this initial identification, 13,235 patients were identified with the indication of constipation and 40 patients identified with the indication of faecal impaction who had at least one PEG 3350+E prescription.

Furthermore, from the initial identification, 7586 patients were excluded from analysis as their reasons for consultation in the 30 days before prescription did not specify constipation or faecal impaction. It is possible that the child presented with constipation which was not recorded by the GP in the consultation record when prescribing, or that the prescription related to a reason for consultation recorded after prescribing or >30 days before prescribing.

For the constipation cohort; cohort characteristics are presented in Table 1 and incident events of interest are presented in Table 2. Due to small numbers for the FI cohort (n=40), only cohort characteristics are presented in Table 3.

Constipation Cohort

Among children with constipation, 9380 patients (70.9%) were aged between 12 and <24 months, with a further 3855 patients (29.1%) aged <12 months. Specifically, PEG 3350+E was used in 477 patients (3.6%) who were <6 months of age. In total, 7512 patients (56.8%) were female. Where reported, the median weight at index was 9.3 kg (IQR 7.4, 11.0; n = 445) and the median weight at the end of the first TE, for those with weight reported at index, was 9.3 kg (IQR 8.4, 10.9; n = 34).

Total daily dose (TDD) was explored across all prescriptions in TEs. In total, 9325 patients (70.5% cohort) with constipation had a TDD of one sachet. Other common doses were 1.5 sachets (n = 1845, 13.9%) and two sachets (n = 2021, 15.3%). Stratification by age group revealed that a higher proportion of those aged 0–<6 months had a TDD of <1 sachet (85.1%) or one sachet (71.5%) across all prescriptions in TEs.

Constipation and related symptoms [a composite outcome of multiple Read terms relating to constipation; including, for example, constipation, constipation not otherwise specified (NOS), constipation symptom] were the most commonly reported incident

events on treatment in the constipation cohort (n = 3340, 25.2% cohort). Of these, there were 1535 reports of constipation and related symptoms on treatment in patients with concomitant laxative use (50.9% of concomitant laxative users). In the 30 days after stopping the first TE (in those with one TE only), the frequency of constipation and related symptoms was low (n = 164, 1.8% of those who only had one TE).

Further stratification of incident events by TDD at index and first TE duration was undertaken. General patterns of incident events on treatment remained the same after these further stratifications (data not presented).

For the other events of interest, 63 patients (0.5% cohort) had abdominal pain, 401 patients (3.0%) experienced diarrhoea and 537 patients (4.1%) experienced vomiting. There were no reports of peripheral oedema on treatment. Table 2 presents the numbers of these events, stratified by age at index.

Further examination of the incident events on treatment revealed that 263 patients (2.0% cohort) had a Read code term which may be suggestive of a potential presentation of electrolyte disturbance (though as stated previously, this is an unlikely possibility); however, when laboratory test results were evaluated during the first 90 days after PEG 3350+E treatment (for those who also had a baseline test results; n < 5) none were identified as having an electrolyte disturbance.

A sensitivity analysis was undertaken to investigate the use of the MDE instead of the 60-day treatment exposure period for the final prescription in a TE. There was no change in the most frequently reported events between the main analysis and the sensitivity analysis (data not shown). Constipation and related symptoms were the most frequently reported events in the constipation cohort when using the MDE (n = 3268, 24.7% cohort).

A further sensitivity analysis was conducted to examine events in patients who were aged under 2 years when a PEG 3350+E prescription was issued but had turned 2 years of age during the 60 day exposure period (n = 1131). As a result, the exposure period for this sensitivity analysis covered the period of the overlapping prescription after the child had turned 2 years of age and as such, event counts are limited. In the constipation cohort, the most frequently reported events were constipation and related symptoms (n = 201, 1.5% cohort). Events of interest reported on treatment in these patients were: abdominal pain (n = 13, 1.1%), diarrhoea (n = 30, 2.7%) and vomiting (n = 40, 3.5%).

Faecal Impaction Cohort

The size of the faecal impaction cohort was very small; however, the line of demarcation between the diagnosis of constipation and FI in real-world clinical practice is blurred (43,44). In total, seven patients (17.5% cohort) with FI had a TDD of two sachets. Other doses were one sachet (n = 5, 12.5%), 1.5 sachets (n < 5) and 0.5 sachets (n < 5). Constipation and related symptoms, was the most commonly reported incident event on treatment in the faecal impaction cohort (n = 12, 30.0% cohort). Frequency of events of interest was low; with only diarrhoea reported on treatment (n < 5).

DISCUSSION

This real-world, utilisation and safety study was conducted to provide additional data on off-label use of PEG 3350+E in patients under 2 years of age.

Constipation Cohort

PEG 3350+E was most frequently prescribed for children aged 12–<24 months with a median age of 1.2 years at first TE. The

TABLE 1. Constipation cohort characteristics

	Age at index											
	Total cohort (N = 13,235)			Age 0- <6 months (N = 477)			Age 6- <12 months (N = 3378)			Age 12- <24 months (N = 9380)		
	n	Median (IQR)*	Mean (range)	n	Median (IQR)*	Mean (range)	n	Median (IQR)*	Mean (range)	n	Median (IQR)*	Mean (range)
Age at start of treatment episode one (years)	13,235	1.23 (0.94, 1.61)	477	0.35 (0.20, 0.44)	3378	0.78 (0.65, 0.90)	9380	1.45 (1.19, 1.83)				
Weight at first prescription (index) (kg)	445	9.3 (7.4, 11.0)	86	5.2 (4.6, 5.9)	119	8.4 (7.4, 9.3)	240	10.6 (9.5, 12.0)				
Weight at end of first treatment episode (kg)	34	9.3 (8.4, 10.9)	8	8.2 (7.3, 9.3)	14	9.2 (8.4, 11.1)	12	9.6 (9.1, 11.2)				
Duration between treatment episodes one and two (days)	4176	33.0 (12.0, 88.0)	380	88.5 (27.0, 224.0)	1407	44.0 (15.0, 114.0)	2389	26.0 (10.0, 66.0)				
	n	Mean (range)	n	Mean (range)	n	Mean (range)	n	Mean (range)	n	Mean (range)	n	Mean (range)
Number of prescriptions in treatment episode one	13,235	1.9 (1.0, 31.0)	477	2.3 (1.0, 22.0)	3378	2.0 (1.0, 31.0)	9380	1.9 (1.0, 19.0)				
Duration of continuous treatment in treatment episode one (days)	13,235	88.9 (60.0, 691.0)	477	100.1 (60.0, 691.0)	3378	91.8 (60.0, 571.0)	9380	87.4 (60.0, 418.0)				
Total daily dose in treatment episode one (sachets)	6268	1.21 (0.25, 28.0)	201	0.87 (0.5, 3.0)	1376	1.07 (0.25, 4.0)	4691	1.27 (0.43, 28.0)				
	n	%	n	%	n	%	n	%	n	%	n	%
Number of treatment episodes												
1	9059	68.4	97	20.3	1971	58.3	6991	74.5				
2	2759	20.8	208	43.6	781	23.1	1770	18.9				
>3	1417	10.7	172	36.1	626	18.5	619	6.6				
Total daily dose across all treatment episodes (sachets)												
<1	1871	14.1	406	85.1	1023	30.3	442	4.7				
1	9325	70.5	341	71.5	2190	64.8	6794	72.4				
1.5	1845	13.9	66	13.8	332	9.8	1447	15.4				
2	2021	15.3	93	19.5	551	16.3	1377	14.7				
>2	450	3.4	9	1.9	88	2.6	353	3.8				
Prior use of osmotic laxatives	4220	31.9	173	36.3	1139	33.7	2908	31.0				
Prior use of stimulant laxatives	934	7.1	42	8.8	221	6.5	671	7.2				
Most common events before starting treatment												
Cough (any)	2087	15.8	64	13.4	690	20.4	1333	14.2				
Upper respiratory tract infection	2081	15.7	59	12.4	632	18.7	1574	16.8				
Concomitant use of osmotic laxatives	2079	15.7	129	27.0	569	16.8	1381	14.7				
Concomitant use of stimulant laxatives	1532	11.6	86	18.0	410	12.1	1036	11.0				

*IQR = interquartile range.

TABLE 2. Events of interest on treatment in the constipation cohort

Event of interest*	Age at index							
	Total cohort (N = 13,235)		0–<6 months (N = 477)		6–<12 months (N = 3378)		12–<24 months (N = 9380)	
	n	%	n	%	n	%	n	%
Potential electrolyte disturbance	263	2.0	34	7.1	82	2.4	147	1.6
Specified potential electrolyte disturbance events†								
Confusion/Agitation	12	4.6	<5	n/a	<5	n/a	6	4.1
Seizures/Loss of consciousness	35	13.3	<5	n/a	11	13.4	22	15.0
Hypoesthesia/paraesthesia	0	0.0	0	0.0	0	0.0	0	0.0
Muscle twitching/spasms	<5	0.8	<5	n/a	0	0.0	0	0.0
Oedema	7	2.7	<5	n/a	<5	n/a	<5	n/a
Fatigue	163	62.0	21	61.8	49	59.8	93	63.3
Shortness of breath	61	23.2	9	26.5	26	31.7	26	17.7
Dehydration	20	7.6	<5	n/a	<5	n/a	14	9.5
Abdominal pain	63	0.5	11	2.3	19	0.6	33	0.4
Diarrhoea	401	3.0	50	10.5	145	4.3	206	2.2
Vomiting	537	4.1	54	11.3	171	5.1	312	3.3

*Patient or event counts less than five have been suppressed as part of Clinical Practice Research Datalink patient confidentiality guidelines and as such percentages have not been shown (n/a).

†Patients may have had more than one type of specified potential electrolyte disturbance event, so figures for specified events represent event counts rather than patient numbers, and percentage of patients with a potential electrolyte disturbance event.

median weight at index was 9.3 kg (IQR 7.4, 11.0) which corresponds to the median age of patients, relative to UK-WHO growth charts (45). In addition, patients with weight reported at baseline and the end of the first TE (n = 34, 7.6% of patients with weight reported at index), showed no decrease in median weight, although this finding was based on a small sample and should be interpreted with caution.

68.4% of the constipation cohort had a single TE, with 20.8% having two TEs and 10.7% having three or more TEs.

Discontinuation of treatment after one TE could reflect the improvement of symptoms, initiation of alternative treatments or discontinuation due to tolerability issues. In the 30 days after stopping the first TE (patients with one TE only), the frequency of constipation and related symptoms was low which suggests an improvement in symptoms and no further need for treatment. In addition, since the majority of patients received a mean of 1.9–2.2 prescriptions in the first TE, this may reflect acceptable tolerability and adherence. This observation is consistent with former studies

TABLE 3. Faecal impaction cohort characteristics

	Total cohort (N = 40)	
	n	Median (IQR)*
Age at start of treatment episode one (years)	40	1.52 (1.08, 1.73)
Duration between treatment episodes one and two (days)	14	31.0 (10.0, 162.0)
Number of prescriptions in treatment episode one	n	Mean (range)
Duration of continuous treatment in treatment episode one (days)	40	2.17 (1.0, 10.0)
Total daily dose in treatment episode one (sachets)	40	90.5 (60.0, 307.0)
	n	%
Number of treatment episodes		
1	26	65.0
>2	14	35.0
Total daily dose across all treatment episodes (sachets)		
1	5	12.5
2	7	17.5
Other	5	12.5
Prior use of osmotic laxatives	15	37.5
Prior use of stimulant laxatives	5	12.5
Most common events before starting treatment		
Constipation and related symptoms	23	57.5
Concomitant use of osmotic laxatives	9	22.5
Concomitant use of stimulant laxatives	12	30.0

*IQR = interquartile range.

that have shown that PEG-based treatments are well tolerated in children aged 2 years and over (46,47); however, the investigation of tolerability-related issues (eg, palatability) and adherence were not objectives of this study as there would likely be under-reporting of these outcomes in an electronic healthcare record database, especially in children under 2 years of age. Future studies, utilising primary data collection methods (eg, parent/patient-based surveys) to collect information on tolerability-related issues and adherence, would be required to investigate this comprehensively.

For children aged 2–6 years, the recommended starting dose for chronic constipation is one sachet daily, and two sachets daily for 7–11 years of age (39). Dosage can be adjusted as required, though this does not normally exceed four sachets a day (39). In this study, the most common TDD, in children under 2 years of age, was one sachet. Variability was observed in the TDD prescribed although higher doses, >4 sachets per day, were uncommon ($n = 6$, <0.1%). This variability probably reflects the clinical need to adjust the dosage to relieve constipation.

The most frequently prescribed concomitant medications were listed under the Broad-spectrum Penicillins BNF Chapter, commonly prescribed for respiratory infections, and is in keeping with the incidence of respiratory infections and cough observed during the study. Concomitant laxative use was recorded for 22.8% of the cohort, these patients had a higher incidence of constipation and related symptoms on treatment (50.9% of concomitant laxative users vs 25.2% of cohort), which may be indicative of continuing symptoms requiring additional treatment; however, osmotic laxative use (most frequently reported prior medication) decreased when examining concomitant medications.

In the SmPC for PEG 3350+E, vomiting and diarrhoea are listed as ‘common’ adverse events (3), thus findings from this study are consistent with known evidence. A lower incidence of abdominal pain was identified than the ‘very common’ incidence in the SmPC (39). This finding may be related to patients age as children <2 years of age may potentially be unlikely to communicate symptoms; however, the non-reporting of pain was not a study objective as this could not be reliably assessed in this electronic healthcare record database. There were no confirmed cases of electrolyte disturbance reported during treatment with PEG 3350+E. It is known that minor adverse events with PEG-based treatments in children are common but occur at a lower incidence than other constipation treatments (48).

A 60-day period was used as the treatment exposure for the last prescription in a TE. To assess this assumption, comparisons were made using the MDE. The potential impact of using 60 days, instead of the MDE, would be an over-estimation of treatment exposure. Overall, using the MDE made no significant impact to incident events on treatment. This may suggest that recording of events by the GP may be occurring during the course of the TE, rather than after the issue date of the last prescription in a TE. Patients may be more likely to report events when attending the primary care practice and/or receiving their prescription.

Faecal Impaction Cohort

The most frequently prescribed concomitant medications were listed under the Stimulant Laxatives BNF Chapter. This suggests that GPs are prescribing other laxatives in addition to PEG 3350+E to treat faecal impaction. Osmotic laxatives use (most frequently reported prior medication) decreased when examining concomitant medications suggesting that GPs may prescribe alternative laxatives before starting PEG 3350+E.

Stratification of prior and incident events by TDD at index and first TE duration was undertaken in both cohorts. General

patterns of prior and incident events on treatment remained the same after stratification, suggesting that results are unlikely to have been impacted by confounding by indication, posology and treatment duration.

Limitations

There may be missing information in CPRD GOLD regarding prescription information, concomitant medications and clinical events from secondary care. Adverse events occurring in secondary care may not be recorded by the GP, meaning that adverse event rates may be slightly lower than in overall clinical practice. Non-serious adverse events may not always be recorded by the GP, however, GPs are often made aware of severe adverse events occurring in secondary care. The prescribing and subsequent management of patients prescribed PEG 3350+E is expected mainly in primary care, so secondary care reporting is expected to be minimal.

Potential misclassification may arise due to patients failing to report clinical events to the GP and/or variations in the coding of diagnoses between GPs. This may vary depending on the clinical event, but it is assumed that serious events will be reported and recorded.

Finally, we assume that prescribing equates to actual medication usage, although this may not be the case for every patient. Usage depends on the parent/guardian and low treatment adherence rates have previously been reported in children with constipation (49), though adherence with PEG-based treatments may be greater than other laxatives (50). In addition, the presentation of the child to the GP and the description of symptoms depends on the parent/guardian.

CONCLUSION

This utilisation and safety study was conducted to characterise the paediatric population and use of PEG 3350+E in a cohort first prescribed treatment younger than 2 years of age. The safety aspect of this study did not identify any signals of concern in the constipation cohort. Patient numbers in the faecal impaction cohort were too small to draw robust conclusions on safety. If information were available, then a safety study would ideally assess treatment intake per kilogram, including electrolyte intake, before reaching safety conclusions. Nevertheless, findings from this study contribute to real-world evidence on the use of PEG 3350+E in this population, in countries where the product is available.

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