Real-world, European study evaluating naloxegol in opioid-induced constipation in patients with cancer – The NACASY* study

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RESPONSIBLE USAGE

MOVENTIG (naloxegol) is indicated for the treatment of opioid-induced constipation (OIC) in adult patients who have had an inadequate response to laxative(s). For advice on the responsible use of opioids to treat pain, please click here

*Naloxegol Cancer Study

KKI/INT/MOV/0142 Date of preparation: July 2023.

Grünenthal Meds

NACASY: study introduction

- **PAMORAs** bind and **block the μ-opioid receptors of the gastrointestinal tract**, without crossing the blood-brain barrier and **interfering with the CNS opioid receptors**[1]
- **Naloxegol** was the **first oral PAMORA** indicated for treatment of OIC in adult patients who have had an inadequate response to laxative(s)[1,2]
- Two recent, single-country, real-world studies (**KYONAL, MovE**) investigated the **efficacy and safety of naloxegol in cancer patients with OIC** up to 1 year[3,4]
- The objective of the **NACASY study**, a multinational, European study, was to evaluate the **safety and efficacy of naloxegol in a real-world setting** in patients with cancer pain diagnosed with OIC, during a 4-week follow-up period[1]

NACASY, Naloxegol Cancer Study; CNS, central nervous system; PAMORA, peripherally acting μ-opioid receptor antagonist; OIC, opioid-induced constipation; SmPC, summary of product characteristics

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128; 2. **MOVENTIG** Summary of Product Characteristics.
3. Cobo, Dols M, *et al*. *BMJ Support Palliat Care* 2021 Mar 11; bmjspcare-2020-002816; 4. Lemaire, A, *et al. Support Care Cancer* 2021;29:7577–7586.

NACASY[1]

cancers

MDPI

Article

A Prospective, Real-World, Multinational Study of Naloxegol for Patients with Cancer Pain Diagnosed with Opioid-Induced Constipation—The NACASY Study

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Citation: Davies, A.; Cinieri, S.; Dupoiron, D.; España Fernandez, S.; Leclerc, J.; Montesarchio, V.;

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: study summary[1] (1/2)

- Four-week, real-world study in adult patients with cancer and OIC in 26 centres across 10 countries (pain units, oncology units, palliative care units)

- **Primary safety endpoint**: incidence of adverse events leading to discontinuation

- **Primary efficacy endpoint**: Response rate during the 4 weeks of treatment (proportion of patients reporting ≥3 bowel movements [without the use of rescue laxative treatment in the previous 24 h] per week and an increase of ≥1 bowel movements per week over baseline)
  - Two efficacy analyses were performed:
    Efficacy Population 1 – patients who had completed both 4 weeks of treatment and 28 days of the diary
    Efficacy Population 2 – patients who had completed ≥21 days of the diary and were not study discontinuations
  - All study data obtained from routine clinical records, diaries provided to enrolled patients, or from selected study questionnaires

- **170** patients were **included** and treated in **routine clinical practice** according to the naloxegol SmPC, with the recommendation to stop all currently used maintenance laxative therapy

OIC, opioid induced constipation; SmPC, summary of product characteristics

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: study summary[1] (2/2)

Secondary endpoints:*

- Proportion of patients who had a change in the Bowel Function Index score of ≥12 points at the end of study treatment (4 weeks)**
- Proportion of patients who had a Bowel Function Index score of <30 at the end of the study†
- Time to first post-dose bowel movement
- Change in stool consistency, according to the Bristol Stool Scale
- Change in PAC-QOL and the four subscales (physical discomfort, psychosocial discomfort, worries and concerns, and satisfaction)
- Incidence of overall adverse events, including serious adverse events
- Analgesic treatment interruptions and dose adjustments
- Naloxegol treatment interruptions and dose adjustments
- Patient satisfaction assessed via the PGI-I

*All study data obtained from routine clinical records, diaries provided to enrolled patients, or from selected study questionnaires.
**Constitutes a clinically important improvement in OIC[2]; †Constitutes well-controlled OIC
OIC, opioid induced constipation; PAC-QOL, Patient Assessment of Constipation – Quality of Life Questionnaire;
PGI-I, Patient Global Impression for Improvement Questionnaire

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128;
2. Rentz, AM, *et al. J Med Economics* 2009;12:371–383

NACASY: study questionnaires[1]

- **Bowel Function Index**: a physician-administered questionnaire consisting of 3-item patient-assessment scale (ease of defaecation, feeling of incomplete bowel evacuation, and personal judgement of constipation
- **Bristol Stool Scale**: stool consistency at time of every single bowel movement, classifying them into 7 categories (from 1 indicating small, hard, lumpy stool, to 7 denoting watery stool)
- **Straining perception**: evaluated by mean of a single closed (yes/no) question in the patient's diary and rated according to a 5-point Likert scale (not at all, a little bit, a moderate amount, a great deal and an extreme amount) and completeness of stool evacuation sensation
- **PAC-QOL**: 28-item self-reported questionnaire designed to evaluate the burden of constipation on patients' everyday HRQoL, covering the specific constipation-related domains of worries and concerns, physical discomfort, psychosocial discomfort and satisfaction; each symptom's severity is referred to the 2 previous weeks and scored on a 5-point Likert scale (0 – not at all, to 4 – extremely)
- **PGI-I**: one question for the overall self-assessment of constipation improvement using a 7-point Likert scale (1 – very much better, to 7 – very much worse)

HRQoL: health-related quality of life; PAC-QOL, Patient Assessment of Constipation – Quality of Life Questionnaire; PGI-I, Patient Global Impression for Improvement Questionnaire

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: inclusion criteria[1]

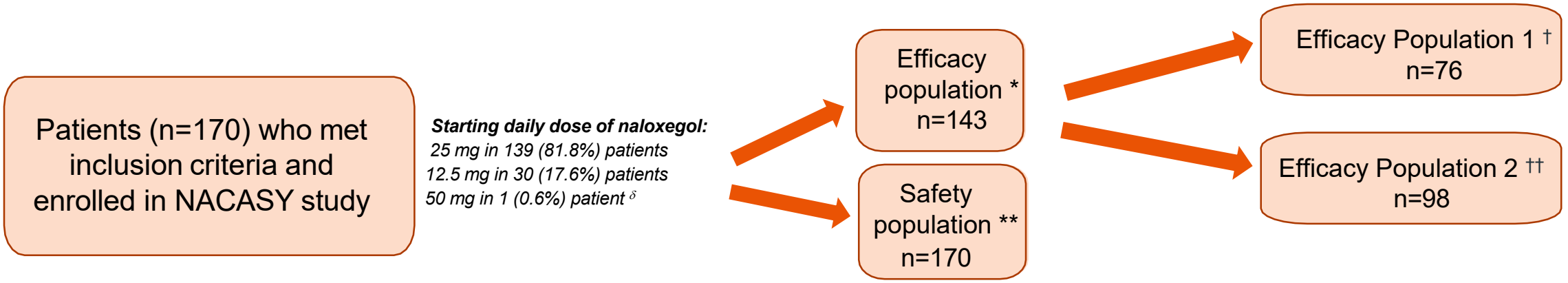
- Patients >18 years old with cancer pain
- Opioid treatment for ≥4 weeks (expected to remain on opioids for duration of study)
- Diagnosed with OIC*
- ≥2 of the following symptoms in ≥25% of bowel movements during that period:
  - lumpy (Type 2) or hard stools (Type 1) stools according to Bristol Stool Scale; straining; sensation of incomplete bowel movement; sensation of anorectal obstruction or blockage; need for manual manoeuvres to facilitate bowel movements; loose stools rarely present without use of laxatives

* <3 documented spontaneous bowel movements per week on average within previous 2 weeks
OIC, opioid induced constipation

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: study design[1]

- NACASY was a 4-week, single-arm, open-label, prospective real-world observational follow-up study



Follow-up visits at Week 2 and Week 4

Categorical variables were compared using the Chi-square or Fisher's exact test; quantitative variables were compared using the paired-sample T-test. Association between different study variables were analysed using either the T-test for equality of means or the ANOVA test.

δ 1/170 initiated at unlicensed dose 50mg
* Patients who had met all selection criteria, had received at least one dose of naloxegol, and had least one post-baseline efficacy assessment;
** Patients who met all selection criteria and had received at least 1 dose of naloxegol;
† 4 weeks of treatment + 28 days of diary completed;
†† 21 days of diary completed + no study discontinuation;

ANOVA, analysis of variance; OIC, opioid induced constipation

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: selected baseline demographics[1] (1/2)

Most frequent **primary tumour** locations: **lung 24.5%** (n=35), **breast 22.4%** (n=32); **69.2%** of patients (n=99) had **metastases**

46.2% of patients (n=66) **receiving chemotherapy** treatment at study entry

72.7% of patients (n=104) **receiving laxative** treatment at study entry

Most commonly used **opioids at inclusion: fentanyl 26.6%** (n=38); **oxycodone 25.2%** (n=36), **morphine 11.2%** (n=16)

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: selected baseline demographics[1] (2/2)

Demographics	n=143
Age, years, median (IQR)	66.0 (58.0; 72.0)
Gender, female, N (%)	78 (54.5)
Race, Caucasian, N (%)	116 (81.1)
Height, cm, median (IQR)	165.5 (160.0; 171.0)
Weight, kg, median (IQR)	66.0 (58.0; 78.0)

IQR, interquartile range

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: baseline treatment[1] (1/2)

		N (%)
Opioids administered for the treatment of pain	Fentanyl	38 (26.6)
	Oxycodone	36 (25.2)
	Morphine	16 (11.2)
	Codeine*	11 (7.7)
	Oxycodone/Naloxone	10 (7.0)
	Hydromorphone	8 (5.6)
	Methadone	7 (4.9)
	Tramadol	6 (4.2)
	Fentanyl + Morphine	2 (1.4)
	Tramadol/paracetamol	2 (1.4)
	Tapentadol	1 (0.7)
	Other	6 (4.2)
Previous laxative treatments for OIC**	Osmotic	83 (79.8)
	Stimulant	32 (30.8)
	Stool softeners	12 (11.5)
	Bulking agents	4 (3.8)
	Linaclotide	1 (1.0)
	Other	19 (18.3)

*Includes combination of codeine plus paracetamol with or without caffeine; **Percentages have been calculated over the total number of patients with previous laxative treatment (n=104). Patients could receive more than one laxative treatment.

OIC, opioid induced constipation

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: baseline treatment[1] (2/2)

Opioids

- **Week 2 baseline opioid treatment** was modified in 31/140 (22.1%) patients, with dose increase, dose reduction, and opioid treatment change in 20, 8 and 3 patients, respectively

- **Week 4 baseline opioid treatment** was modified in 22/118 (18.6%) patients, with dose increase, dose reduction, and opioid treatment change in 14, 4 and 4 patients, respectively

Previous laxatives

- At baseline, 104/143 patients (72.7%) patients were receiving **conventional laxatives**, and proportions at Weeks 2 and 4 were 105/140 (75%) and 43/118 (36.4%), respectively

- **Osmotic and stimulant laxatives** were the most frequently used at every study visit

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Primary safety endpoint: study discontinuations due to adverse events[1] (1/2)

- Overall, 56 of 170 patients discontinued the study
- **20 of 170 patients** (11.8%; 95% CI 6.9–16.6) **discontinued** study due to **adverse events**
- **12 of 170 patients** (7.1%; 95% CI 3.2–10.9%) **discontinued** study due to **naloxegol-related adverse events**
  - Mainly gastrointestinal side effects, including 8 cases of abdominal pain, 2 cases of diarrhoea, 1 due to intestinal perforation and 1 due to fatigue

CI, confidence interval

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Primary safety endpoint: study discontinuations due to adverse events[1] (2/2)

Reason for study discontinuation	N (%)
Naloxegol adverse reaction	12 (21.4)
Patient decision	10 (17.9)
Adverse event	8 (14.3)
Death	7 (12.5)
Loss to follow-up	7 (12.5)
Investigator decision	6 (10.7)
Consent withdrawn	6 (10.7)
TOTAL	**56 (100)**

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Primary efficacy endpoint: Response rate during the 4 weeks of treatment[1] (1/2)

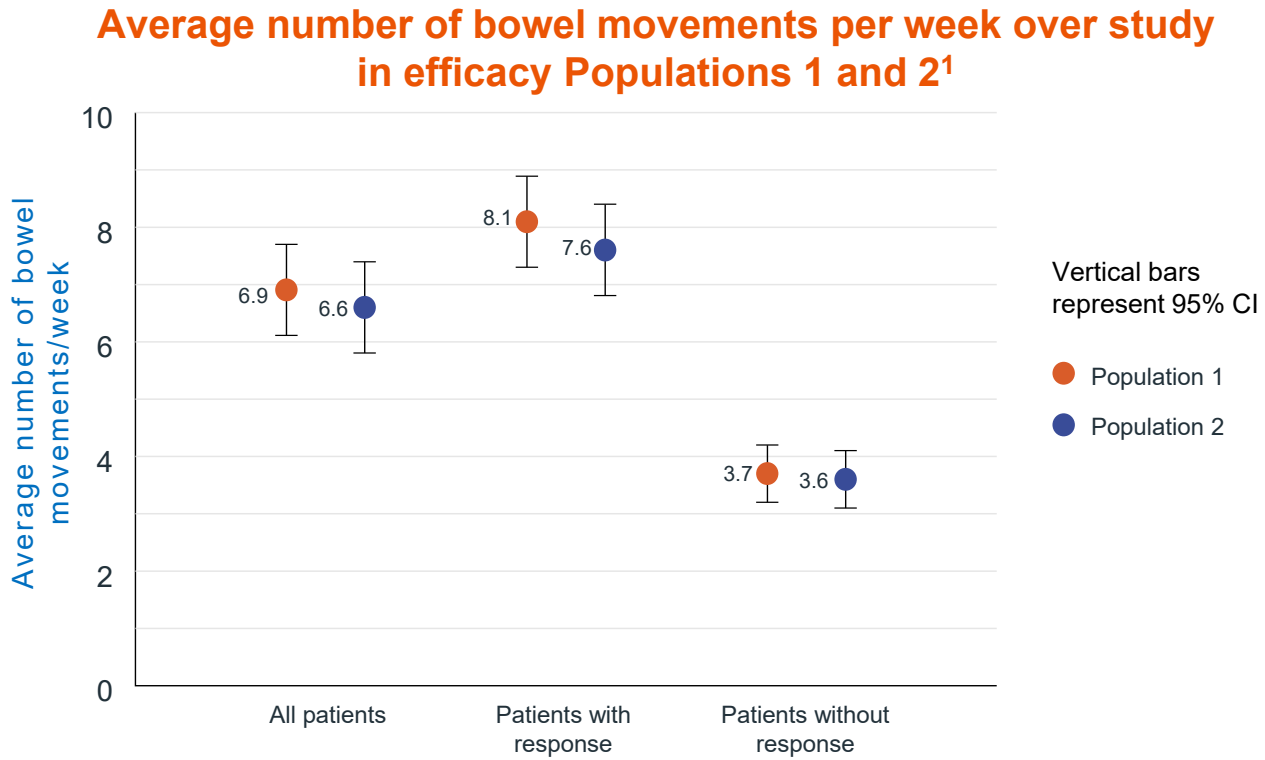
- 55 patients (**72.4%;** 95% CI 62.3%–82.4%) from Population 1* (N=76) met primary efficacy endpoint after the 4-week study follow-up period, and were **regarded as responders† to naloxegol treatment**
- 74 patients (**75.5%**; 95% CI 67.0%–84.0%) from Population 2** (N=98) **responded to naloxegol** treatment
- **Response to naloxegol** was **mainly** observed within the **first week** of treatment
- Mean number (SD) **of bowel movements per week increased** from <3 at baseline to 7.6 (5.0) and 7.3 (4.8) at Week 1 in Populations 1 and 2, respectively
- Average number of weekly bowel movements was sustained between Weeks 1 and 4 in both populations

*Population 1: Patients who completed both 4 weeks of treatment + 28 days of diary. **Population 2: Patients who completed ≥21 days of diary and were not study discontinuations.
† Proportion of patients reporting ≥3 bowel movements (without the use of rescue laxative treatment in the previous 24 h) per week and an increase of ≥1 bowel movements over baseline.

CI, confidence intervals; SD, standard deviation

1. Davies, A, *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

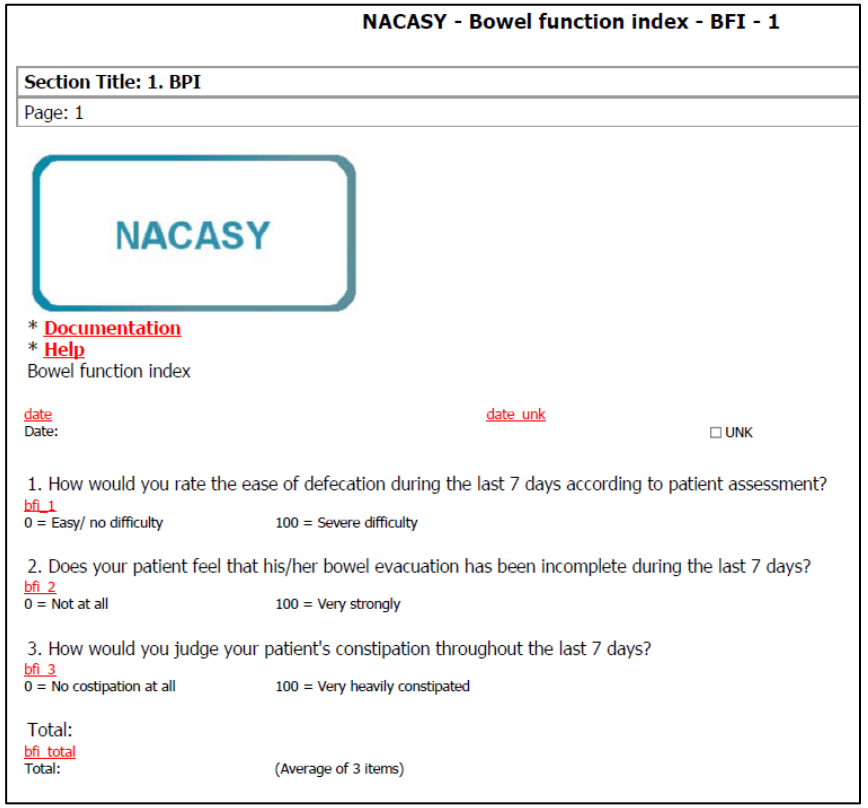
Primary efficacy endpoint: Response rate during the 4 weeks of treatment[1] (2/2)



1. Davies, A, *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Clinically important improvement in bowel function[1]

64.1% (75/117) of patients (95% CI 55.4–72.8%) had **Bowel Function Index score change of ≥12 points*** at end of study



NACASY - Bowel function index - BFI - 1

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Bowel function index

date
Date:

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1. How would you rate the ease of defecation during the last 7 days according to patient assessment?
bfi_1
0 = Easy/ no difficulty 100 = Severe difficulty

2. Does your patient feel that his/her bowel evacuation has been incomplete during the last 7 days?
bfi_2
0 = Not at all 100 = Very strongly

3. How would you judge your patient's constipation throughout the last 7 days?
bfi_3
0 = No constipation at all 100 = Very heavily constipated

Total:
bfi_total
Total: (Average of 3 items)

Adapted from approved eCRF "KYO229007 (NACASY) - eCRF version 3.0 21/JUN/2019 (Annotated CRF)"

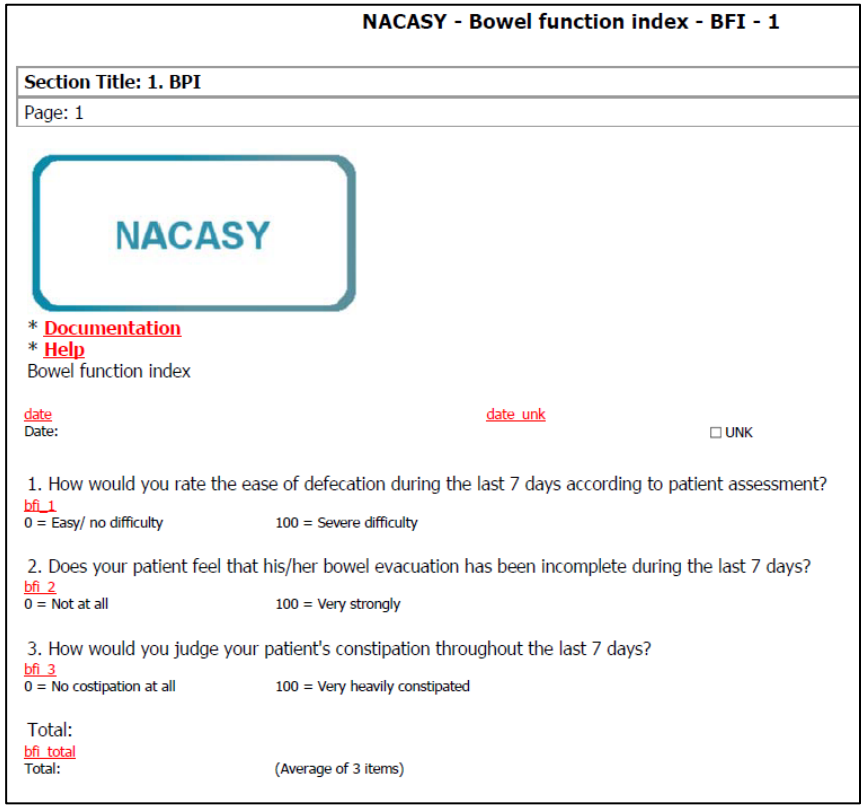
*Constitutes a clinically important improvement in OIC;[2] rating scale 0 (no difficulty/not at all) to 100 (severe difficulty/very strong)[2]

CI, confidence intervals; OIC, opioid induced constipation

1. Davies, A, *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128;
2. Rentz, AM, *et al*. *J Med Economics* 2009;12:371–383

Well-controlled OIC[1]

36.8% of patients (43/117; 95% CI 28.1–45.5%) had **Bowel Function Index score of <30 points*** at end of study



NACASY - Bowel function index - BFI - 1

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NACASY

* Documentation
* Help

Bowel function index

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*Constitutes well-controlled OIC;[1] rating scale 0 (no difficulty/not at all) to 100 (severe difficulty/very strong)[2]

CI, confidence intervals; OIC, opioid induced constipation

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2. Rentz, AM, *et al. J Med Economics* 2009;12:371–383

Time to first post-dose bowel movement[1]

Mean (SD) **time** to **first post-dose bowel movement** was **1.9 (1.7) days**

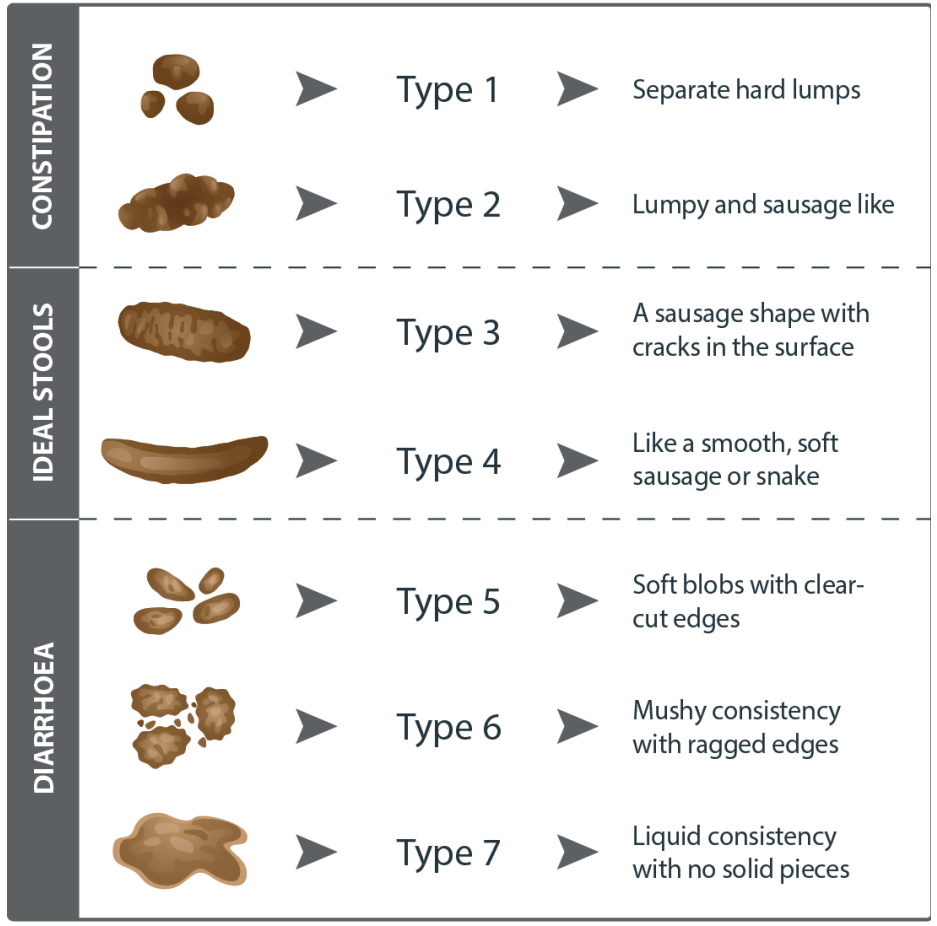
SD, standard deviation

1. Davies, A, *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Significant improvement in stool consistency from baseline to Week 4 ($p<0.001$)[1]

Stool consistency increased by mean (SD) of **0.8 (1.8) points by Week 2** and **0.9 (1.8) points by Week 4**, as assessed by Bristol Stool Scale*

Pairwise comparison showed **significant improvement in Bristol Stool Scale score from baseline to Week 4 ($p<0.001$)**



Bristol Stool Scale[2]*

Adapted from Chumpitazi BP, *et al. Neurogast Motil* 2016;28(3):443-8. Bristol Stool Form Scale Reliability.[2]

*7-point scale that describes shape and consistency (from 1 indicating small, hard, lumpy stool, to 7 denoting watery stool)[2]

SD, standard deviation

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128
2. Chumpitazi BP, *et al. Motil* 2016;28(3):443-8. Bristol Stool Form Scale Reliability.

Improvement in total PAC-QOL and its four subscales[1]

PAC-QOL changes throughout NACASY study[1]

- **PAC-QOL*** total score and its four subscales **improved** from baseline to 4 weeks of follow-up
- **37.1%** (n=124) of patients had **clinically relevant improvement** in total PAC-QOL score
- All changes in PAC-QOL scores reached statistical significance in pairwise comparisons

*Measures impact of constipation on daily life over past 2 weeks, using 28 items forming four subscales (physical discomfort, psychosocial discomfort, worries and concerns and satisfaction, where 0 – not at all, to 4 – extremely)

CI, confidence intervals; PAC-QOL, Patient Assessment of Constipation — Quality of Life Questionnaire;

1. Davies, A *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Adverse events (1/2)[1]

- Overall, 89 of 170 patients (**52.4%**) reported **at least one adverse event**, and 38 (22.4%) were serious adverse events
- **Adverse events** considered to be related to **naloxegol** were reported in 23 patients (**13.5%**)
- **Treatment-related adverse events** were **mainly gastrointestinal**, with abdominal pain being the most frequently reported (n=14, 8.2%) and diarrhoea (n=5, 2.9%)
  - Two-treatment related adverse events were considered serious adverse reactions: a case of Grade 5 intestinal perforation and a case of Grade 2 diarrhoea
  - Two cases of withdrawal syndrome were categorised as Grade 1

1. Davies, A, *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Adverse events (2/2)[1]

Adverse reactions to naloxegol (according to CTCAE v4.03)

Adverse reaction	Grade 1-3 N (%)	Grade 4-5 N (%)	Grade NA N (%)
Abdominal pain	10 (5.9)	0 (0.0)	4 (2.4)
Diarrhoea	4 (2.4)	0 (0.0)	1 (0.6)
Fatigue	1 (0.6)	0 (0.0)	0 (0.0)
Flatulence	2 (1.2)	0 (0.0)	0 (0.0)
Gastrointestinal pain	1 (0.6)	0 (0.0)	0 (0.0)
Intestinal perforation	0 (0.0)	1 (0.6)	0 (0.0)
Nausea	2 (1.2)	0 (0.0)	0 (0.0)
Pollakiuria	1 (0.6)	0 (0.0)	0 (0.0)
Vertigo	1 (0.6)	0 (0.0)	0 (0.0)
Withdrawal syndrome	1 (0.6)	0 (0.0)	0 (0.0)

Grade 1: Mild; asymptomatic or mild symptoms; Grade 2: Moderate; minimal, local, or noninvasive; intervention indicated; Grade 3: Severe or medically significant but not immediately life-threatening; Grade 4: Life-threatening consequences; urgent intervention indicated; Grade 5: Death delated to adverse event

CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events.

1. Davies, A *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Opioid treatment modifications during the study[1]

		Week 2 N (%)	Week 4 N (%)
Treatment modified	Yes	31 (22.1)	22 (18.6)
	Total	140 (100)	118 (100)
Opioid treatment change	Dose increase	20 (64.5)	14 (63.6)
	Change of opioid	8 (5.8)	4 (18.2)
	Dose reduction	3 (9.7)	4 (18.2)
	TOTAL	**31 (100)**	**22 (100)**

1. Davies, A, *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Naloxegol treatment interruptions and dose adjustments[1]

Initial naloxegol dose at baseline: 169/170† patients

Dose	% of patients (n)
12.5 mg	17.6% (30)
25 mg	81.8% (139)

† 1/170 initiated at unlicensed dose 50mg

Week 2: 140 patients

Dose	% of patients (n)
Treatment interruptions	10.0% (14)
Dose increase	2.8% (4)

Week 4: 118 patients

Dose	% of patients (n)
Treatment interruptions	7.8% (11)
Dose adjustments*	4.3% (6)

* 5 patients had a dose increase, while sixth patient had both an increased and a reduced dose adjustment

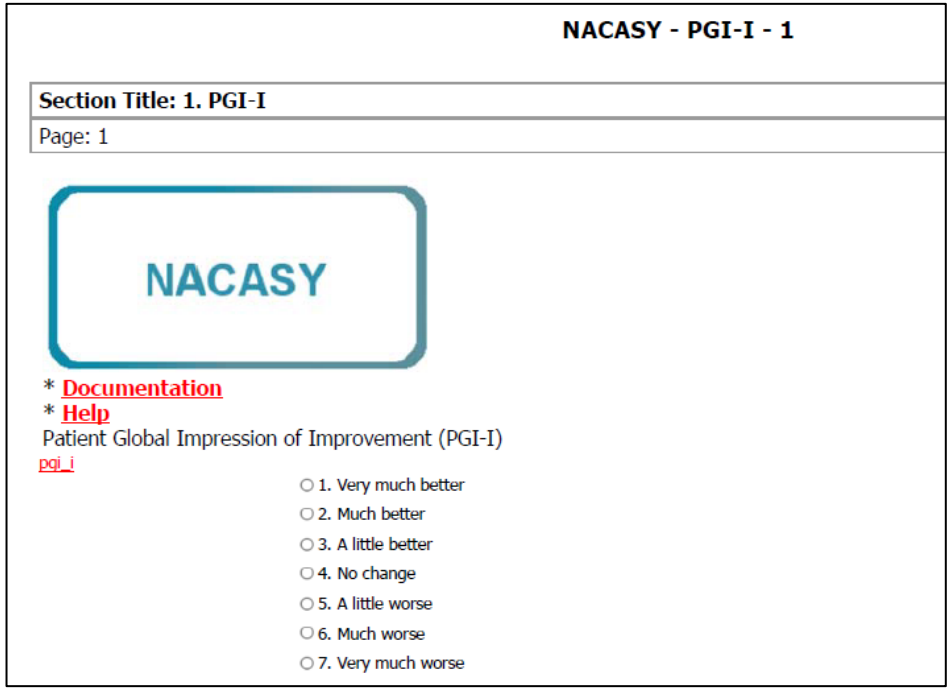
1. Davies, A *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Total of 75.0% of patients reported improvement in constipation[1]

75.0% of patients (n=118; 95% CI 67.2–82.8%) reported **improvement in constipation**, according to PGI-I questionnaire*, after 4 weeks of treatment

43.2% (51) were "**much better**" or "**very much better**"

Direct association between responses to HrQoL, PAC-QOL (total score) and PGI-I (p<0.001)


NACASY - PGI-I - 1

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NACASY

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Patient Global Impression of Improvement (PGI-I)

pgi_i

- 1. Very much better
- 2. Much better
- 3. A little better
- 4. No change
- 5. A little worse
- 6. Much worse
- 7. Very much worse

Adapted from approved eCRF "KYO229007 (NACASY) - eCRF version 3.0 21/JUN/2019 (Annotated CRF)"

*Condition rated on 7-point scale from 1 – very much better to 7 – very much worse

CI, confidence interval; HrQOL, health-related quality of life; PAC-QOL, Patient Assessment of Constipation – Quality of Life Questionnaire; PGI-I, Patient Global Impression for Improvement Questionnaire

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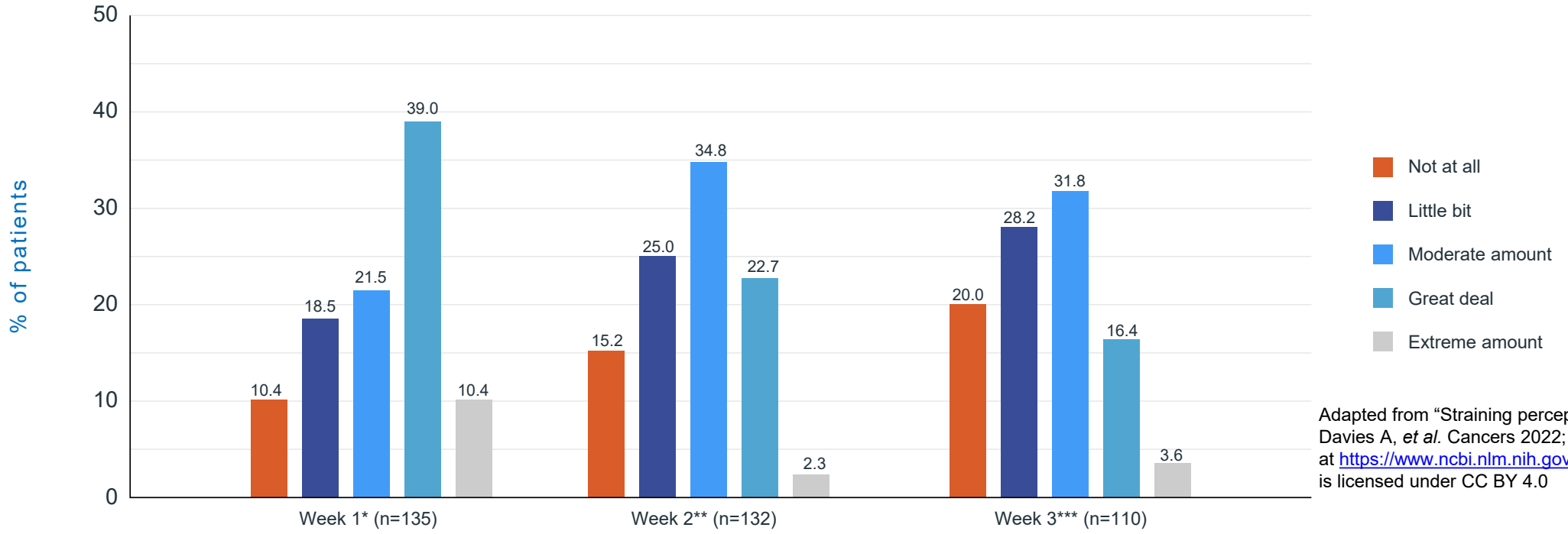
Other efficacy outcomes[1]

Straining perception† during the NACASY study[1]



* 8 missing data. ** 11 missing data. *** 9 missing data

- **Decrease** in proportion of patients with "great deal" or an "extreme amount" of **straining perception*** during bowel movement from **49.6%** (67/135) at baseline to **20.0%** (22/110) at Week 4
- **Significant improvement in self-reported** straining perception observed from baseline to Week 2 (p=<0.001) and to Week 4 (p<0.001) according to pairwise comparisons

† Measured on 5-point scale (from "Not at all" to "Extreme amount") in response to question "How much did you strain during your bowel movement?"

1. Davies, A, *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

Other efficacy outcomes[1]

Sensation of **incomplete evacuation decreased** from **79.6%** (109/137) of patients at baseline to **60.6%** (80/132) at Week 2 and **55.6%** (63/113) at Week 4

Statistically **significant difference** in proportion of patients with sensation of incomplete evacuation **between baseline** and **Week 2** (p=0.007); between **baseline and Week 4** did **not** reach **statistical significance** (p=0.089)

1. Davies, A, *et al*. *Cancers* 2022;14:1128. doi: 10.3390/cancers14051128

NACASY: conclusions

- **NACASY study** is the **first multinational European study** evaluating **naloxegol** for the treatment of OIC in cancer patients in a **real-world setting**[1]
- **Response rate of 72.4%** for naloxegol treated patients at 1 month[1]
- **Efficacy and tolerability profiles** of naloxegol were **similar** to that seen in two single-country, real-world studies (**KYONAL, MovE**)[1-3]
- **Clinically important improvement** in **bowel function** (as measured by Bowel Function Index questionnaire) and **statistically significant improvement** in **stool consistency** (evaluated by Bristol Stool Scale; $p<0.001$)[1]
- **Quality of life** of patients **improved** by study end, as reflected by changes in PAC-QOL total score and all its subscale scores[1]
- Highlights importance of **using precise and practical tools** for an efficient **OIC diagnosis** and **management** in patients with cancer[1]
- Potential occurrence of **OIC** should be **considered** from **start of opioid treatment** in cancer patients[1]

OIC, opioid induced constipation; PAC-QOL, Patient Assessment of Constipation – Quality of Life Questionnaire

1. Davies, A, *et al. Cancers* 2022;14:1128. doi: 10.3390/cancers14051128; 2. Cobo, Dols M, *et al. BMJ Support Palliat Care* 2021 Mar 11; bmjspcare-2020-002816;

Thank you.

Grünenthal
Meds

PRESCRIBING INFORMATION (prepared August 2021)
Moventig® (naloxegol oxalate) 12.5mg and 25mg film-coated tablets
Consult Summary of Product Characteristics (SmPC) before prescribing.

Indication: Opioid-induced constipation (OIC) in adult patients who have had an inadequate response to laxative(s) (concurrent OIC symptoms of at least moderate severity while taking at least one laxative class for a minimum of four days during the previous 2 weeks). **Dosage and administration:** Recommended 25 mg once daily. Take on empty stomach at least 30 minutes prior to first meal of day or 2 hours after first meal of day. Crushed tablets can be mixed with water (120ml) and drunk immediately or administered via a nasogastric tube (CH8 or greater). **Renal impairment:** Moderate or severe renal impairment starting dose 12.5mg. Discontinue if side effects impact tolerability. Increase to 25mg if well tolerated. **Hepatic impairment:** Use in severe hepatic impairment not recommended. **Moderate CYP3A4 inhibitors:** Starting dose 12.5mg, can be increased to 25mg if well tolerated. **Paediatric population (<18 years):** Safety and efficacy not yet established. **Adverse effects:** Consult SmPC for full list of side effects. Very Common: Abdominal pain, diarrhoea. Common: Nasopharyngitis, headache, flatulence, nausea, vomiting, hyperhidrosis. Uncommon: Opioid withdrawal syndrome. Not known: Hypersensitivity, Gastrointestinal perforation. **Contraindications:** Hypersensitivity to active substance or any of the excipients or any other opioid antagonist. Patients with known or suspected gastrointestinal (GI) obstruction or patients at increased risk of recurrent obstruction. Patients with underlying cancer who are at heightened risk of GI perforation, such as those with underlying malignancies of gastrointestinal tract or peritoneum, recurrent or advanced ovarian cancer or vascular endothelial growth factor (VEGF) inhibitor treatment. Concomitant use with strong CYP3A4 inhibitors. **Warnings and precautions:** Cases of gastrointestinal perforation have been reported in the post-marketing setting, including fatal cases when naloxegol was used in patients who wereat an increased risk of gastrointestinal (GI) perforation. Naloxegol must not be used in patients with known or suspected gastrointestinal obstruction or in patients at increased risk of recurrent obstruction. Use with caution in patients with any condition which might result in impaired integrity of the gastrointestinal tract wall. Advise patients to discontinue therapy and promptly report if unusually severe or persistent abdominal pain develops. Use with caution in patients with clinically important disruptions to the blood brain barrier and observe for potential CNS effects. Discontinue if interference with opioid- mediated analgesia or opioid withdrawal syndrome occurs. Use with caution in patients taking methadone. If opioid withdrawal syndrome is suspected the patient should discontinue Moventig and contact their physician. Use with caution in patients with a recent history of myocardial infarction, symptomatic congestive heart failure, overt cardiovascular (CV) disease or with a QT interval of ≥500msec. Use with caution in OIC patients with cancer-related pain. Use of naloxegol with another opioid antagonist (e.g. naltrexone, naloxone) should be avoided. **Use in pregnancy and lactation:** Not recommended. **Legal category:** POM. **Marketing Authorisation numbers:** Moventig 12.5mg and 25mg tablets (ROI: EU/1/14/962/001-011),(GB: PL GB 50262/004&5) **Further information available on request from the Marketing Authorisation holder:**Kyowa Kirin Holdings B.V., Bloemlaan 2, 2132NP Hoofddorp,The Netherlands.

For the United Kingdom:

NHS cost: Moventig 12.5mg, 30 tablets, £55.20; Moventig 25mg, 30 tablets, £55.20.

Adverse Events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse Events should also be reported to Kyowa Kirin Ltd. on +44(0)1896 664000, email medinfo@kyowakirin.com

For the Republic of Ireland

Adverse Events should be reported. Information about adverse event reporting can be found at www.hpra.ie. Adverse Events should also be reported to Kyowa Kirin Ltd. on +44 (0)1896 664000, email medinfo@kyowakirin.com

General considerations for the management of pain with any medication that contains an opioid mechanism of action

The following general aspects should be considered:

- An individualized, patient-centered approach for the diagnosis and treatment of pain is essential to establish a therapeutic alliance between patient and clinician.
- Consider patient variables that may affect opioid dose for each patient prior to opioid use[1]
- In patients with acute pain e.g. post-surgery pain, the use of medication should be for the shortest necessary time[1]. All patients should be carefully selected, addiction risk factors evaluated and regular monitoring and follow-up implemented to ensure that opioids are used appropriately[3-4] and in alignment with treatment goals (pain intensity and functionality) as agreed with the patient[3-4]
- Patients should be made aware of the potential side effects of opioids and the potential for developing tolerance, dependence and addiction[3-4].
- It is important to optimally use multimodal, non-opioid approaches in acute and chronic pain before escalating to opioids or in conjunction with opioid therapy[1]
- Addiction is possible even when opioids are taken as directed. The exact prevalence of addictive disorders in patients treated with opioids for chronic pain is difficult to determine[5]
- Regular clinical reviews are required for long-term opioid treatment to assess pain control, impact on lifestyle, physical and psychological well-being, side effects and continued need for treatment[2]
- Any long term treatment with opioids should be monitored and re-evaluated regular incl. tapering down the dose or discontinuing treatment[3-4]
- Signs of opioid use disorder should be monitored and addressed[3-4]
- Patients and the general public can benefit from clear educational materials and awareness interventions to support the responsible use of opioids[6].

References:

1. DHHS Pain Management Best Practices Inter-Agency Taskforce Report May 2019
2. O'Brien T et al. Eur J Pain 2017;21:3-192
3. Faculty of Pain Medicine, Opioids Aware **https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware** Accessed September 2019
4. Kosten TR et al, Scie Pract. Perspect 2002;1:13-20
5. Rosenblum A et al Exp. Clin. Psychopharmacol. 2008;16(5):405-416
6. OECD Health Policy. Addressing Problematic opioid use in OECD Countries May 2019
   http://www.oecd.org/health/addressing-problematic-opioid-use-in-oecd-countries-a18286f0-en.htm

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