Opioid Induced Constipation

This presentation has been developed by Grünenthal Meds

Prescribing Information and Adverse Event Reporting
Information available on slide 12 of this presentation

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

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Grünenthal Meds

Opioid-induced bowel dysfunction and opioid induced constipation

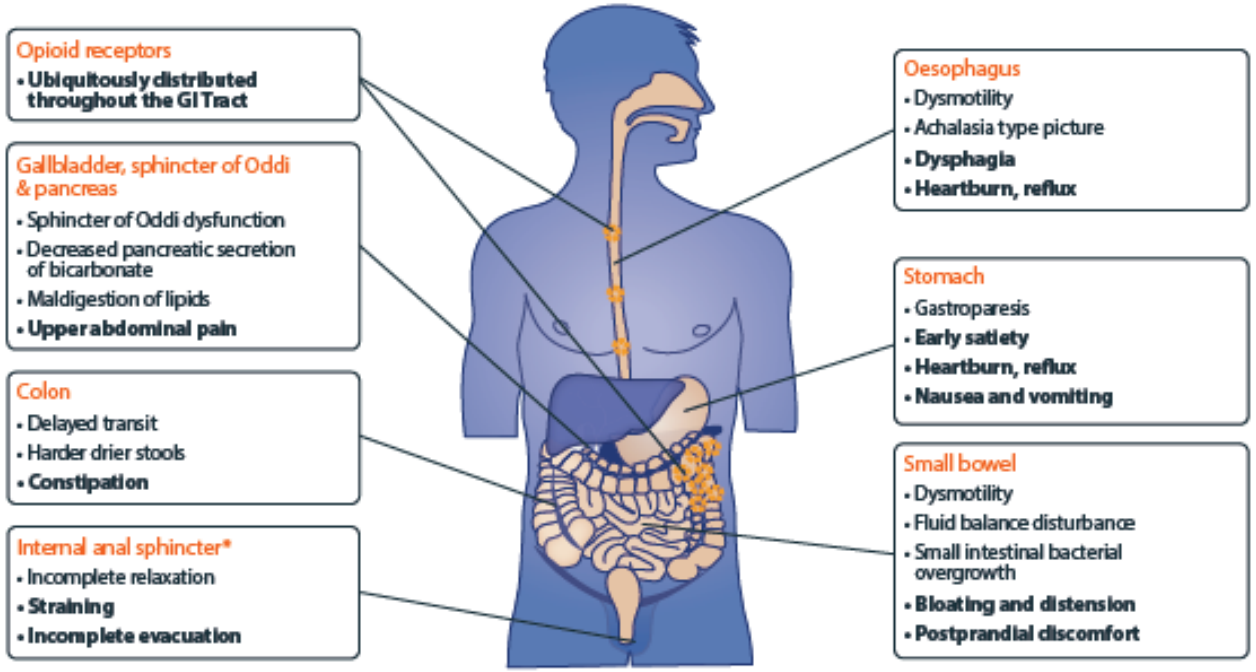
- Opioids are a class of potent analgesics, and their use has increased markedly in recent years[1]
- Opioid-induced bowel dysfunction (OIBD) encompasses a spectrum of symptoms including nausea, vomiting, bloating, gastro-oesophageal reflux-related symptoms and constipation[1]
- Opioid induced constipation (OIC) is the most common subtype of OIBD for patients receiving opioids[1]
- OIC may be associated with reduced work productivity, a decrease in quality of life and increased healthcare utilisation[1]

Opioid-induced bowel dysfunction (OIBD) occurs in **51–87% of patients** receiving opioids for **cancer pain** and between **41–57% of patients** receiving opioids for **chronic noncancer pain.**[1]

1. Farmer AD, et al. *United European Gastroenterology Journal*. 2019;7(1):7-20

Basic pathophysiology of OIBD[1]

Opioid receptors are distributed throughout the GI tract and exert a profound influence on GI function. Opioids bind to receptors and affect GI motility and secreto-absorptive function.[1]



Adapted from Farmer et al. 2019.
*The function of other GI sphincters can also be influenced by opioids such as the lower oesophageal sphincter and pylorus.

A highly schematic summary of basic neuronal mechanisms leading to OIBD including opioid induced constipation

1. Farmer AD, et al. *United European Gastroenterology Journal.* 2019;7(1):7-20

OIBD – Opioid-induced bowel dysfunction

Rome IV definition and diagnosis of OIC[1]

According to the Rome IV criteria, OIC is present if patients report new or worsening of symptoms of constipation when initiating, changing or increasing opioid therapy that must include.[1]

2 or more of the following:

- 1. Straining during at least 25% of defaecations ☐
- 2. Sensation of incomplete evacuation for at least 25% of defaecations ☐
- 3. Sensation of anorectal obstruction/blockage for at least 25% of defaecations ☐
- 4. Lumpy or hard stools in at least 25% of defaecations ☐
- 5. Manual manoeuvres to facilitate at least 25% of defaecations ☐
- 6. Fewer than three defaecations per week ☐

In addition, the following criteria must be met:

- Loose stools are rarely present without the use of laxatives ☐

The Rome process has sought to systematise the definition of OIC and has proposed Rome IV diagnostic criteria.[1]

1. Farmer AD, et al. *United European Gastroenterology Journal.* 2019;7(1):7-20

OIC – Opioid induced constipation

Patient assessment[1]

- Gather a comprehensive patient/drug history with a focus on baseline bowel habits and any changes post introduction of opioids
- Identify medications, other than opioids, that might be contributing to constipation - utilise Rome IV criteria to make a diagnosis of OIC
- Assess psychological aspects and additional symptoms such as bloating, abdominal pain, nausea and vomiting
- Given the prevalence of OIC, patients initiating and those maintained on opioids, should have a regular systematic review of their bowel function

1. Farmer AD, et al. *United European Gastroenterology Journal.* 2019;7(1):7-20

OIC – Opioid induced constipation

Barriers to the diagnosis of OIC[1]

- Lack of awareness among clinicians about OIC in patients on opioid therapy
- If clinicians are aware, they may not ask patients about constipation
- When considering constipation, most clinicians only ask questions about frequency of bowel movements,
  - Symptoms listed opposite can be prevalent and bothersome effects of OIBD
- Patients might feel ashamed to disclose their symptoms to clinicians
- Efforts to screen patients based on Rome IV criteria may not cover the whole spectrum of OIC
- Absence of a standard protocol for the treatment of OIC

Prevalent and bothersome features reflecting the pan-enteric effects of OIBD:

- Bloating
- Straining
- Hard stool consistence
- Incomplete bowel movements
- Abdominal discomfort

1. Farmer AD, et al. *United European Gastroenterology Journal.* 2019;7(1):7-20

OIBD – Opioid-induced bowel dysfunction
OIC – Opioid induced constipation

Patient reported outcomes in OIC[1]

- Numerous patient reported outcome measures are available to be used in daily practice or clinical studies (e.g.)
  - Patient assessment of constipation symptoms (PAC-SYM)
  - Patient assessment of constipation quality of life (PAC-QoL)
  - Knowles Eccersley Scott Symptom Score
  - Bristol Stool Form scale (BSFS)
  - Bowel Function Index (BFI)

The Bristol Stool Form scale (BSFS) and the Bowel Function Index (BFI) are simple, brief and validated questionnaires that can be a useful adjunct to standard clinical evaluation as well as providing an objective assessment of treatment response.[1]

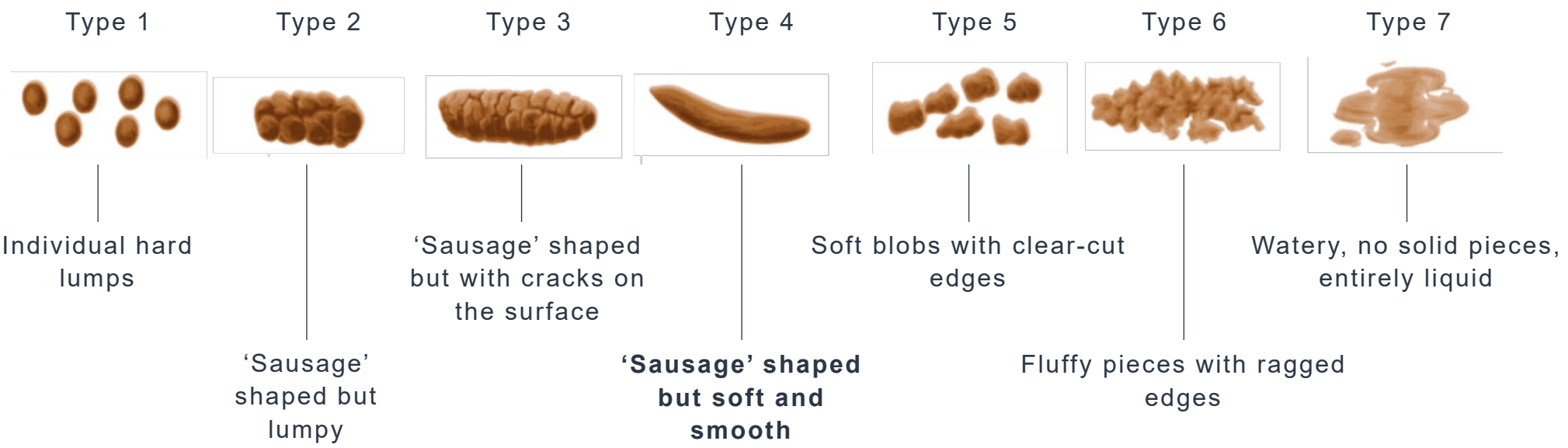
1. Farmer AD, et al. *United European Gastroenterology Journal.* 2019;7(1):7-20

OIC – Opioid induced constipation

The Bristol Stool Form scale (BSFS)

The Bristol Stool Form scale (BSFS) evaluates stool consistency and is a widely used tool which pictorially describes stool ranging from type 7 to type 1, with the latter representing separate hard lumps of stool.

BSFS type 1 and 2 would be consistent with, but not specific for, OIC.[1]



1. Farmer AD, et al. *United European Gastroenterology Journal.* 2019;7(1):7-20

OIC – Opioid induced constipation

The Bowel Function Index (BFI)

Ease of defaecation in the last 7 days:
During the last 7 days, how would you rate your ease of defaecation on a scale of 0 (no difficulty) to 100 (severe difficulty)?

The BFI is a validated tool developed specifically for OIC. It is a simple questionnaire that captures the patient's personal experience of their constipation.[1] Once the three questions have been discussed add the three scores together and divide by three to get an average score. Scores of >30 are consistent with OIC.[2]

Feeling of incomplete bowel evacuation during the last 7 days:
During the last 7 days, how would you rate your feeling of incomplete bowel evacuation on a scale of 0 to 100?

Personal judgement of patient regarding constipation during the last 7 days:
During the last 7 days, how would you rate your constipation on a scale of 0 to 100?

1. Ducrotté P, Caussé C. *Current Medical Research and Opinion.* 2012;28(3):457-466
2. Ueberall M, et al. *Journal of International Medical Research.* 2011;39(1):41-50

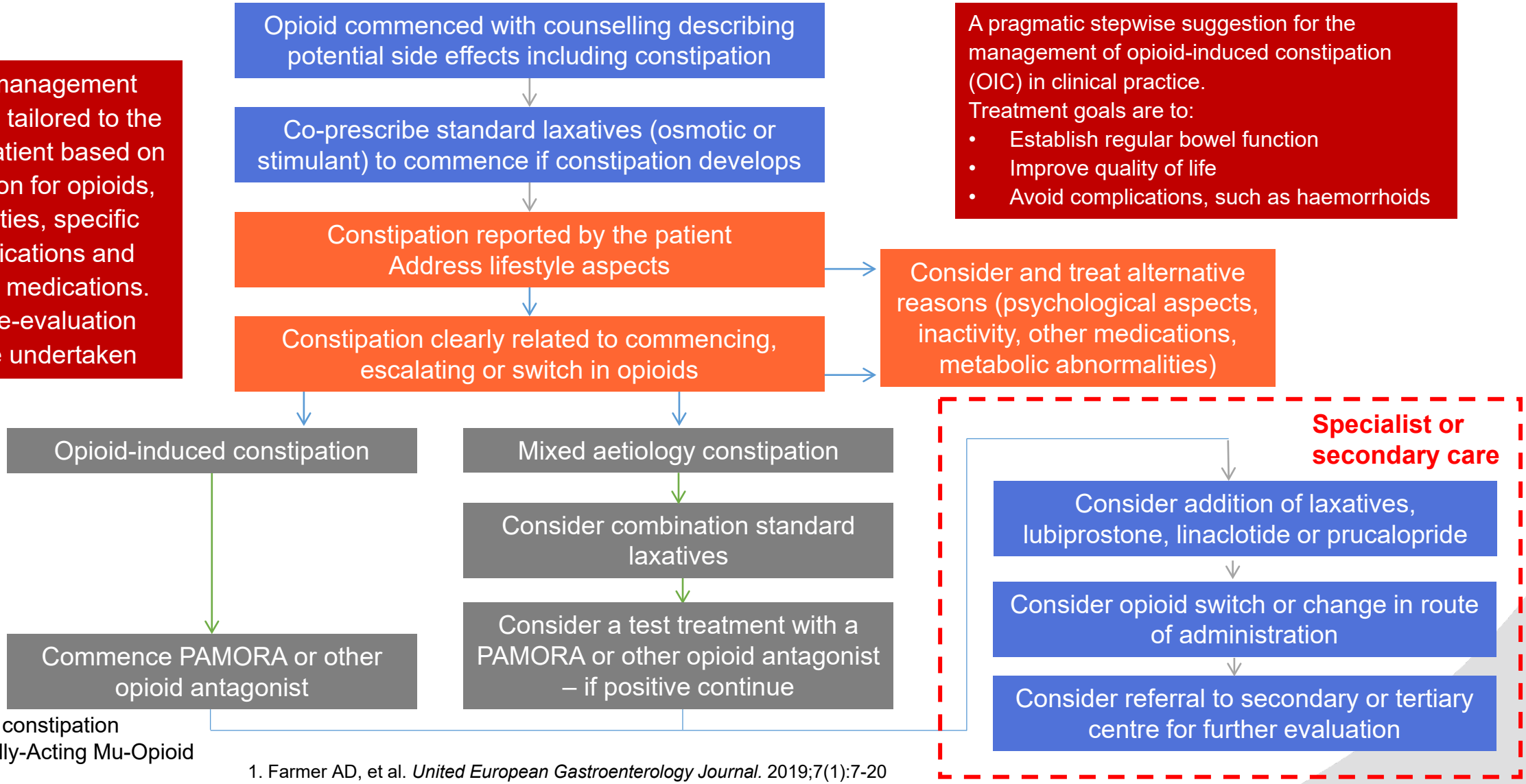
OIBD – Opioid-induced bowel dysfunction
OIC – Opioid induced constipation

Pragmatic clinical recommendations – algorithm for primary care[1]

Specific management needs to be tailored to the individual patient based on the indication for opioids, comorbidities, specific contraindications and concurrent medications. Regular re-evaluation should be undertaken

A pragmatic stepwise suggestion for the management of opioid-induced constipation (OIC) in clinical practice.
Treatment goals are to:

- Establish regular bowel function
- Improve quality of life
- Avoid complications, such as haemorrhoids



OIC – Opioid induced constipation
PAMORA – Peripherally-Acting Mu-Opioid Receptor Antagonist

1. Farmer AD, et al. *United European Gastroenterology Journal.* 2019;7(1):7-20

Summary

- The widespread use of opioids has been associated with a concomitant rise in OIBD and OIC[1]
- OIC is often under-recognised and sub-optimally managed[2-3]
- All patients initiating and those maintained on opioids, should have a regular systematic review of their bowel function[1]
- Management should be based on a step-wise approach to treatment aimed at improving outcomes[1]
- PAMORAs can be used to treat OIC if response to laxatives is inadequate[1]

1. Farmer AD, et al. *United European Gastroenterology Journal*. 2019;7(1):7-20
2. Ducrotté P, et al. *United European Gastroenterology Journal.* 2017;5(4):588-600
3. Gupta A, et al. *Pain Med.* 2018;19(12):2459-2468

OIBD – Opioid-induced bowel dysfunction
OIC – Opioid induced constipation
PAMORA – Peripherally-Acting Mu-Opioid Receptor Antagonist

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 were at 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:

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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
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KKI/INT/KKI/0803 June 2023