



TRANSPARENCY COMMITTEE

SUMMARY

2 JUNE 2021

The legally binding text is the original French opinion version

raw opium (tincture of *Papaver somniferum* L., succus siccus)
DROPIZAL 10 mg/mL oral solution in drops

First assessment

► Key points

Unfavourable opinion for reimbursement in the symptomatic treatment of severe diarrhoea in adults when the use of other anti-diarrhoeal treatments has not had a sufficient effect.

► Role in the care pathway?

The clinical situations responsible for diarrhoea are very numerous and varied. To relieve recurrent functional bowel disorders in which diarrhoea is the predominant symptom, loperamide (IMODIUM) is prescribed to slow intestinal transit; it has no effect on abdominal pain.

In the event of severe acute diarrhoea, anti-diarrhoeal agents are symptomatic treatments which reduce stool frequency. They do not dispense with the need for dietary measures and rehydration if required. No anti-diarrhoeal agents have a demonstrated effect on preventing dehydration. Acute diarrhoea with dehydration (case of patients in care homes for the elderly) should not be treated with an anti-diarrhoeal but by rehydration. In rare circumstances, such as profuse diarrhoea on returning from a country with a high risk of "traveller's diarrhoea", and pending the results of bacteriological (*Salmonella*) and parasitological (amoebiasis) analyses, anti-diarrhoeal treatment may be useful,

relieving diarrhoea and abdominal pain, but restriction of prescription to gastroenterologists will make prescription difficult in this context (expert opinion).

In the event of chronic diarrhoea, it is essential to determine the cause in order to be able to initiate specific aetiological treatment. The mechanisms for chronic diarrhoea may be multiple, or be unknown or imprecise, as is the case in drug-induced diarrhoea (more than 700 medicines implicated and a total of 7% of medicinal product adverse effects).

Loperamide, which is the most assessed anti-diarrhoeal agent, is an opiate derivative with the main effect of slowing transit. In patients not responding to loperamide, in whom quality of life is severely impaired due to numerous and abundant stools, the need is not covered.

Role of the medicinal product in the care pathway

Considering:

- the absence of clinical data supporting the efficacy and safety of DROPIZAL (opium tincture) particularly compared to well-managed anti-diarrhoeal treatment,
- the potential risk of misuse, particularly in the event of long-term prescription renewal, and
- the risk of interactions with other medicinal products (addition of adverse effects, in particular respiratory depression) in patients already treated with morphine-based analgesia (morphine, codeine, etc.),

the Transparency Committee deems that DROPIZAL (opium tincture) has no role in the treatment of adults with severe diarrhoea not responding to other anti-diarrhoeals (in particular loperamide).

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

- ▶ Severe diarrhoea impairs quality of life and can be life-threatening in the immediate term or following complications.
- ▶ DROPIZAL 10 mg/mL oral solution in drops (tincture of *Papaver somniferum L., succus siccus* (raw opium brut)) is a symptomatic treatment.
- ▶ The efficacy/adverse effects ratio of DROPIZAL (opium tincture) in the treatment of severe diarrhoea in adults not controlled by other anti-diarrhoeal agents has not been established. The efficacy and safety of opium tincture have not been assessed in this clinical situation; a risk of misuse is possible in the event of prescription renewal (long-term treatment), as well as a risk of interactions with other medicinal products (addition of adverse effects, in particular respiratory depression) in patients already treated with morphine-based analgesia (morphine, codeine, etc.).
- ▶ There is no medicinal alternative if severe diarrhoea is not controlled by loperamide (see paragraph 05).
- ▶ The role of DROPIZAL (opium tincture) has not been established in the care pathway (see paragraph 08).

Public health impact

Considering:

- the seriousness of severe diarrhoea due to complications and impairment of quality of life, as well as its prevalence,
- the medical need that is unmet or inadequately met in the event of failure of loperamide treatment, in particular,
- the non-established response to the inadequately met or unmet identified need, in the absence of clinical data in patients not responding to other anti-diarrhoeals,
- the lack of any expected impact on the care and/or life pathway in the absence of data,
- the risk of dependence leading to addiction, liable to have a negative public health impact in the event of misuse, remembering that, in accordance with the SPC, treatment with this medicinal product must be initiated by an oncologist or a gastroenterologist and that the medicinal product is dispensed in accordance with the mechanism for narcotics, with secure prescriptions, limited to a maximum of 28 days for each prescription,

DROPIZAL 10 mg/mL oral solution in drops (opium tincture) is unlikely to have an additional impact on public health. A negative impact on public health cannot be excluded in the event of prolonged use (risk of dependence).

Considering all these elements, the Committee deems that the clinical benefit of DROPIZAL 10 mg/mL oral solution in drops (tincture of *Papaver somniferum L., succus siccus* (raw opium)) is insufficient to justify its public funding cover in the MA indication.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and/or the retail formulary list of reimbursed proprietary medicinal products approved for use in the marketing authorisation indication and dosages.