# Codeine

NOT RECOMMENDED AS AN ESSENTIAL MEDICINE



ATC codes: Pending

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| **Indication** | Diarrhoea ICD11 code: MG31 |
| **Medicine type** | Chemical agent |
| **List type** | Core |
| **Formulations** | Oral > Solid: 30 mg tablet (codeine phosphate) |
| **EML status history** | First added in 1977 (TRS 615)<br>Removed in 2011 (TRS 965) |
| **Sex** | All |
| **Age** | Adolescents and adults |
| **Therapeutic alternatives** | The recommendation is for this specific medicine |
| **Patent information** | Patents have expired in most jurisdictions<br>Read more about patents. |
| **Wikipedia** | Codeine |
| **DrugBank** | Codeine |

## Summary of evidence and Expert Committee recommendations

In 2005 an application for the deletion of codeine was considered by the Expert Committee. A review prepared by the International Society of Drug Bulletins (ISDB) showed that there was no high-quality evidence to support efficacy of codeine in the treatment of diarrhoea. It was retained on the Model List at that time based on the need for a treatment for symptomatic diarrhoea in adults with certain conditions, such as HIV/AIDS The Expert committee considered an application that provided safety and efficacy data for both codeine phosphate and/or loperamide compared with other treatments or placebo. There were 17 RCTs for the treatment of acute, chronic or chemotherapy-induced diarrhoea but only 1 of these included codeine (1-17). All the studies reported at least one clinically relevant outcome but the majority of the studies had serious methodological flaws and a high risk of bias. When compared to placebo, loperamide improved control of diarrhoea, in both acute and chronic diarrhoea, although the results were not considered clinically significant (2-5). None of the studies reported any serious adverse events associated with the use of loperamide; the most commonly reported adverse effects were nausea, abdominal pain, and constipation. No studies were identified comparing loperamide with codeine phosphate for the treatment of acute diarrhoea. Loperamide was not found to be as effective as octreotide in the treatment of chemotherapy-induced diarrhoea (322-323). The Committee also noted that no studies were found that evaluated the effectiveness of loperamide or codeine phosphate for the treatment of diarrhoea in people with HIV/AIDS. The Committee did not recommend the inclusion of loperamide on the WHO Model List, due to the lack of high-quality evidence of efficacy for the use of loperamide in the treatment of acute or chornic diarrhoea in adults and the lack of evidence that loperamide is effective and safe in the treatment of diarrnoea in people with HIV/AIDS or for the treatment of chemotherapy-induced diarrhoea. Based on the findings of the previous ISDB review of codeine phosphate and the lack of new evidence presented in the current application to support the use of codeine phosphate in the treatment of symptomatic diarrhoea in adults, the Committee recommended that it should be deleted from the Model List. References: 1. Palmer KR et al. Double-blind cross-over study comparing loperamide, codeine and diphenoxylate in the treatment of chronic diarrhoea. Gastroenterology, 1980, 79:1272–1275. 2. Van Loon FP et al. Double blind trial of loperamide for treating acute watery diarrhoea in expatriates in Bangladesh. GUT, 1989, 30:492–495. 3. BarbezatGOetal.Adouble-blindtrialofloperamideinthetreatmentofchronicdiarrhoea. South African Medical

Journal, 1979, 55(13):502–503. 4. Allison MC et al. A double-blind crossover comparison of limidine, loperamide and placebo for the control of chronic diarrhoea. Alimentary Pharmacology and Therapeutics, 1988, 2:347–351. 5. Bergström T et al. Symptomatic treatment of acute infectious diarrhoea: loperamide versus placebo in a double-blind trial. Journal of Infection, 1985, 12:35–38. 6. CascinuSetal.Octreotideversusloperamideinthetreatmentof uorouracil-induceddiarrhea: a randomized trial. Journal of Clinical Oncology, 1993, 11(1):148–151. 7. Gebbia V et al. Subcutaneous octreotide versus oral loperamide in the treatment of diarrhea following chemotherapy. Anti-Cancer Drugs, 1993, 4:443–445. 8. Dupont HL et al. Comparative e cacy of loperamide hydrochloride and bismuth subsalicylate in the management of acute diarrhea. American Journal of Medicine, 1990, 88(6A):15S–19S. 9. Johnson PC et al. Comparison of loperamide with bismuth subsalicylate for the treatment of acute travellers' diarrhea. Journal of the American Medical Association, 1986, 255(6):757–760. 10. Dupont HL et al. A randomized, open-label comparison of nonprescription loperamide and attapulgite in the symptomatic treatment of acute diarrhea. American Journal of Medicine, 1990, 88(6A):20S–23S. 11. Wang HH et al. A blind, randomized comparison of racecadotril and loperamide for stopping acute diarrhoea in adults. World Journal of Gastroenterology, 2005, 11(10):1540–1543. 12. Gallelli L et al. Prospective randomized double-blind trial of racecadotril compared with loperamide in elderly people with gastroenteritis living in nursing homes. The Journal of Clinical Pharmacology, 2009, 66:137–144. 13. Vetel JM et al. Comparison of racecadotril and loperamide in adults with acute diarrhoea. Alimentary Pharmacology and Therapeutics, 1999, 13(Suppl. 6):S21–S26. 14. Prado D (for the Global Adult Racecadotril Study Group). A multinational comparison of racecadotril and loperamide in the treatment of acute watery diarrhoea in adults. Scandinavian Journal of Gastroenterology, 2002, 6:656–661. 15. Kaplan MA et al. Loperamide-simethicone vs loperamide alone, simethicone alone and placebo in the treatment of acute diarrhea with gas-related abdominal discomfort. Archives of Family Medicine, 1999, 8:243–248. 16. HanauerSBetal.Randomized,doubleblind,placebo-controlledclinicaltrialofloperamide plus simethicone versus loperamide alone and simethicone alone in the treatment of acute diarrhea with gas-related abdominal discomfort. Current Medical Research and Opinion, 2007, 23(5):1033–1043. 17. Mainguet P, Fiasse R. Double-blind placebo-controlled study of loperamide (Imodium) in chronic diarrhoea caused by iliocolic disease or resection. GUT, 1977, 18:575–579.