




ATC codes: Pending

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

### 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 chronic diarrhoea in adults and the lack of evidence that loperamide is effective and safe in the treatment of diarrhoea 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. Barbezat GO et al. A double-blind trial of loperamide in the treatment of chronic diarrhoea. *South African Medical*

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