

Table 2. Characteristics of included studies

Study	Participants	Comparison	Follow-up	Outcome measures	Comments	Risk of bias (per outcome measure)*
<i>Opioids</i>						
<i>Included in ERS guideline (Morice, 2020)</i>						
Morice, 2007	N at baseline Intervention: 27 Control: 27 Age (mean, SD) Not reported in ERS guideline Sex Not reported in ERS guideline	Intervention: 5-10mg morphine twice daily Control: Placebo	Not reported in ERS guideline	cough-specific quality of life, cough severity	Patients with chronic refractory cough	ERS guideline reports: not serious for all outcome measures
<i>Gabapentin</i>						
<i>Included in ERS guideline (Morice, 2020)</i>						
Ryan, 2012	N at baseline Intervention: 32 Control: 30 Age (mean, SD) Not reported in ERS guideline Sex Not reported in ERS guideline	Intervention: maximum tolerable daily dose of 1800mg gabapentin Control: Placebo	8 weeks for cough frequency and cough severity, not reported in ERS guideline for other outcomes	cough-specific quality of life, cough severity, cough frequency	Patients with chronic refractory cough	ERS guideline reports: not serious for all outcome measures
<i>Pregabalin</i>						
<i>Included in ERS guideline (Morice, 2020)</i>						
Vertigan, 2016	N at baseline Intervention: 20 Control: 20 Age (mean, SD)	Intervention: Speech pathology therapy + pregabalin	14 weeks for cough frequency and cough severity, not reported in	cough-specific quality of life, cough severity, cough frequency	Patients with chronic refractory cough	ERS guideline reports: not serious for all outcome measures

	Not reported in ERS guideline Sex Not reported in ERS guideline	Control: Speech pathologie therapy + placebo	ERS guideline for other outcomes			
<i>Individual studies</i>						
Adeli, 2023	N at baseline Intervention: 16 Control: 14 Age (mean, SD) Only reported for total study group: 56.7 (18.2) years Sex (n, % female) Intervention: 11, 68.8% Control: 8, 57.1% Having an underlying disease (n, % yes) Intervention: 13, 81.2% Control: 13, 92.9%	Intervention: Dextromethorphan (15mg, every 8 hours) + pregabalin (50mg, per day) for at least two weeks Control: Dextromethorphan (15mg, every 8 hours) + placebo for at least two weeks	4 weeks after start of treatment	cough-specific quality of life	Single center study Patients with chronic refractory cough > 8 weeks After 4 weeks, doses pregabalin were increased if insufficient improvement was noted	Low risk of bias for all outcome measures
<i>Gefapixant</i>						
McGarvey, 2022	N at baseline Intervention: 1a: 244 1b: 440 2a: 243 2b: 239 Control: a: 243 b: 435 Age (mean, SD) Intervention: 1a: 59.6 (11.7) year 1b: 58.6 (11.4) years	Intervention 1a: gefapixant 15mg twice daily for 12 weeks Intervention 1b: gefapixant 15mg twice daily for 24 weeks Intervention 2a: gefapixant 45mg twice daily for 12 weeks Intervention 2b: gefapixant 45mg BID for 24 weeks Control a:	12/24 weeks	cough-specific quality of life, cough severity, cough frequency	Multi-center study: a: 146 sites b: 175 sites Chronic cough >12 months a: Refractory: 58.6% Unexplained: 41.4% b: Refractory: 63.1% Unexplained: 36.924 h%	Some concerns due to sponsoring Merck & Co

Table 2. Characteristics of included studies bij module Hoestdempende middelen Richtlijn Chronische hoest bij volwassenen 2026

	<p>2a: 59.4 (13.1) years 2b: 57.8 (12.4) years Control: a: 579 (13.1) years b: 58 (12.6) years</p> <p>Sex (n, %female) Intervention: 1a: 181, 74.5% 1b: 329, 74.8% 2a: 180, 74.1% 2b: 329, 74.9% Control: a: 181, 74.5% b: 326, 73.9%</p>	<p>placebo for 12 weeks</p> <p>Control b: placebo for 24 weeks</p>				
McGarvey, 2023	<p>N at baseline Intervention: 206 Control: 209</p> <p>Age (mean, SD) Intervention: 52.5 (13.8 years) Control: 52.5 (13.8 years)</p> <p>Sex (n,%female) Intervention: 134, 65% Control: 134, 64.1%</p> <p>Comorbid cough-associated conditions (n,%): Intervention: Asthma: 88,42.7% Gastroesophageal reflux disease: 63, 30.6% Alergic rhinitus: 35, 17% Chornic gastritis: 35, 17%</p>	<p>Intervention: gefapixant 45mg twice daily for 12 weeks Control: placebo</p>	12 weeks after start treatment	cough-specific quality of life, cough severity	<p>Multicenter study</p> <p>Chronic cough <12 months: Refractory: 71% Unexplained: 29%</p>	Some concerns due to sponsoring Merck & Co

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	Control: Asthma: 82, 39.2% Gastroesophageal reflux disease: 61, 29.2% Allergic rhinitis: 34, 16.3% Chronic gastritis: 23, 11%					
Smith, 2020	N at baseline Intervention: 1: 64 2: 63 3: 63 Control: 63 Age (mean, SD) Intervention: 1: 59.9 (10.5) years 2: 61.8 (9.1) years 3: 59.3 (9.2) years Control: 60.0 (10.9) years Sex (n, %female) Intervention: 1: 48 (75%) 2: 48 (76%) 3: 50 (79%) Control: 47 (75%)	Intervention 1: gefapixant 7.5mg twice daily for 84 days Intervention 2: gefapixant 20mg twice daily for 84 days Intervention 3: gefapixant 50mg twice daily for 84 days Control: placebo	12 weeks after start treatment	cough-specific quality of life, cough severity, cough frequency	Multicenter study: 44 centers Chronic cough >12 months	Some concerns due to sponsoring Merck & Co

**For further details, see risk of bias table under Evidence tabellen*

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