

Bijlage Zoekverantwoording

Onderzoeksvraag 1: lokale medicamenteuze behandeling

Wat is het effect van local medicamenteuze behandeling op jeuk bij patiënten in de palliatieve fase?
What is the effect of local pharmacological treatment on pruritus in patients in the palliative phase?

Patients	patients in the palliative phase with pruritus (with the exception of pruritus due to primary dermatological conditions and pruritus due to kidney failure)
Intervention	local pharmacological treatment
Comparator	other pharmacological treatment, placebo, no treatment
Outcome	Critical: pruritus (NRS, VAS), quality of life, patient satisfaction Important: adverse events, depression

Onderzoeksvraag 2: systemische medicamenteuze behandeling

Wat is het effect van systemische medicamenteuze behandeling op jeuk bij patiënten in de palliatieve fase?
What is the effect of systemic pharmacological treatment on pruritus in patients in the palliative phase?

Patients	patients in the palliative phase with pruritus (with the exception of pruritus due to primary dermatological conditions and pruritus due to kidney failure)
Intervention	pharmacological treatment
Comparator	other pharmacological treatment, placebo, no treatment
Outcome	Critical: pruritus (NRS, VAS), quality of life, patient satisfaction Important: adverse events, depression

Search strategy

The search of research question 1 and 2 was combined.

On January 28 to February 1, 2021 the scientific literature is searched in databases OVID Medline, Embase and Cochrane Library. The search strings are shown in this appendix.

The literature has been selected systematically based on the following predefined criteria:

- design: meta-analyses, systematic reviews, randomized controlled trials, controlled clinical trials
- language: English, Dutch, French, German
- publication dates: from inception to search date
- the outcomes are reported

Literature was excluded when no quantitative data was presented, when the study population was not focused on pruritus or the palliative phase, when the study population was focused on patients with pruritus due to primary dermatological condition of kidney failure, or when the interventions did not include the listed pharmacological interventions.

Search results

The selection criteria were applied on the references yielded from the search. 3006 unique hits were screened on title and abstract (Table 1). Of these, 2930 were excluded. Of the remaining 76 papers, the full-text was retrieved. Based on the full-text, an additional 44 papers were excluded.

Table 1. Overall search results

Database	Number of hits
OVID Medline	1057
OVID PreMedline	15
EMBASE.com	1892
Cochrane Database of Systematic Reviews	16
CENTRAL	769
Total hits	3749
n excluded (language, duplicates)	743

Included studies

Research question 1

- Ibrahim, I.M., et al., Effectiveness of topical clove oil on symptomatic treatment of chronic pruritus. *Journal of Cosmetic Dermatology*. 2017;16(4):508-511.

Research question 2

- Ataei, S., et al., Comparison of Sertraline with Rifampin in the treatment of Cholestatic Pruritus: A Randomized Clinical Trial. *Reviews on Recent Clinical Trials*. 2019;14(3):217-223.
- Andrade A, et al., Interventions for chronic pruritus of unknown origin. *Cochrane Database Syst Rev*. 2020 Jan 25;1(1):CD013128.
- Bergasa, N.V., et al., A controlled trial of naloxone infusions for the pruritus of chronic cholestasis. *Gastroenterology*. 1992;102(2):544-9.
- Bergasa, N.V., et al., Effects of naloxone infusions in patients with the pruritus of cholestasis. A double-blind, randomized, controlled trial. *Annals of Internal Medicine*. 1995;123(3):161-7.
- Bergasa, N.V., et al., Oral nalmefene therapy reduces scratching activity due to the pruritus of cholestasis: a controlled study. *Journal of the American Academy of Dermatology*. 1999;41(3 Pt 1):431-4.
- Di Padova, C., et al., Double-blind placebo-controlled clinical trial of microporous cholestyramine in the treatment of intra- and extra-hepatic cholestasis: relationship between itching and serum bile acids. *Methods & Findings in Experimental & Clinical Pharmacology*. 1984;6(12):773-6.
- Floreani, A., et al. Diethylaminoethyl-dextran (DEAE-Dextran) for itching in primary biliary cirrhosis: a double blind trial. *Medical science research*, 1988. 16, 731-732.
- Juby, L.D., V.S. Wong, and M.S. Losowsky, Buprenorphine and hepatic pruritus. *British Journal of Clinical Practice*. 1994;48(6):331.
- Khurana, S. and P. Singh, Rifampin is safe for treatment of pruritus due to chronic cholestasis: a meta-analysis of prospective randomized-controlled trials. *Liver International*. 2006;26(8):943-8.
- Kumada, H., et al., Efficacy of nalfurafine hydrochloride in patients with chronic liver disease with refractory pruritus: A randomized, double-blind trial. *Hepatology Research*. 2017;47(10):972-82.
- McCormick, P.A., et al., Thalidomide as therapy for primary biliary cirrhosis: a double-blind placebo controlled pilot study. *Journal of Hepatology*. 1994;21(4):496-9.
- Pongcharoen, P. and A.B. Fleischer, An evidence-based review of systemic treatments for itch. *European Journal of Pain (United Kingdom)*. 2016;20(1):24-31.
- Schworer, H., H. Hartmann, and G. Ramadori, Relief of cholestatic pruritus by a novel class of drugs: 5-hydroxytryptamine type 3 (5-HT₃) receptor antagonists: effectiveness of ondansetron. *Pain*. 1995;61(1):33-7.
- Siemens, W., et al., Pharmacological interventions for pruritus in adult palliative care patients. *Cochrane Database of Systematic Reviews*. 2016;11:CD008320.
- Ständer, S., et al., Treatment of chronic pruritus with the selective serotonin re-uptake inhibitors paroxetine and fluvoxamine: Results of an open-labelled, two-arm proof-of-concept study. *Acta Dermato-Venereologica*. 2009;89(1):45-51.
- To, T.H.M., et al., The role of ondansetron in the management of cholestatic or uremic pruritus - A systematic review. *Journal of Pain and Symptom Management*. 2012;44(5):725-30.

The following articles were also identified, but were already included in at least one of the included reviews:

- Bachs, L., et al., Comparison of rifampicin with phenobarbitone for treatment of pruritus in biliary cirrhosis. *Lancet*. 1989;1(8638):574-6.
- Bergasa, N., et al. Gabapentin therapy for pruritus in patients with chronic liver disease (CLD): a double blind, randomized, placebo controlled trial. *Hepatology (baltimore, md.)*, 2004. 40, 296a.
- Bergasa, N.V., et al., Gabapentin in patients with the pruritus of cholestasis: a double-blind, randomized, placebo-controlled trial. *Hepatology*. 2006;44(5):1317-23.
- Duncan, J.S., H.J. Kennedy, and D.R. Triger, Treatment of pruritus due to chronic obstructive liver disease. *British Medical Journal Clinical Research Ed*. 1984;289(6436):22.
- Ghent, C.N. and S.G. Carruthers, Treatment of pruritus in primary biliary cirrhosis with rifampin. Results of a double-blind, crossover, randomized trial. *Gastroenterology*. 1988;94(2):488-93.

- Kuiper, E.M., et al., The potent bile acid sequestrant colesevelam is not effective in cholestatic pruritus: results of a double-blind, randomized, placebo-controlled trial. *Hepatology*. 2010;52(4):1334-40.
- Mayo, M.J., et al., Sertraline as a first-line treatment for cholestatic pruritus. *Hepatology*. 2007;45(3):666-74.
- Muller, C., et al., Treatment of pruritus in chronic liver disease with the 5-hydroxytryptamine receptor type 3 antagonist ondansetron: a randomized, placebo-controlled, double-blind cross-over trial. *European Journal of Gastroenterology & Hepatology*. 1998;10(10):865-70.
- O'Donohue, J.W., et al., A controlled trial of ondansetron in the pruritus of cholestasis. *Alimentary Pharmacology & Therapeutics*. 2005;21(8):1041-5.
- Podesta, A., et al., Treatment of pruritus of primary biliary cirrhosis with rifampin. *Digestive Diseases & Sciences*. 1991;36(2):216-20.
- Smith, K.J., et al., Pruritus in HIV-1 disease: therapy with drugs which may modulate the pattern of immune dysregulation. *Dermatology*. 1997;195(4):353-8.
- Terg, R., et al., Efficacy and safety of oral naltrexone treatment for pruritus of cholestasis, a crossover, double blind, placebo-controlled study. *Journal of Hepatology*. 2002;37(6):717-22.
- Wolfhagen, F.H.J., et al., Oral naltrexone treatment for cholestatic pruritus: A double-blind, placebo-controlled study. *Gastroenterology*. 1997;113(4):1264-9.
- Woolf, G.M. and T.B. Reynolds, Failure of rifampin to relieve pruritus in chronic liver disease. *Journal of Clinical Gastroenterology*. 1990;12(2):174-7.
- Zylicz, Z., et al., Paroxetine in the treatment of severe non-dermatological pruritus: a randomized, controlled trial. *Journal of Pain & Symptom Management*. 2003;26(6):1105-12.

Excluded studies

Table 2 provides an overview of the excluded studies with reasons.

Table 2. Overview of excluded studies based on full-text evaluation

Reference	Reason for exclusion
Andrade Miranda, A., et al., Interventions for pruritus of unknown cause. <i>Cochrane Database of Systematic Reviews</i> , 2018. 2018(9).	SR protocol
Ataei, S., L. Kord, and M. Hasanzarrini Comparison of sertraline with rifampin in the treatment of cholestatic pruritus: a randomized clinical trial. <i>Iranian journal of pharmaceutical sciences</i> . Conference: 15th iranian pharmaceutical sciences congress, IPSC 2017. Iran, islamic republic of, 2017. 13, 52-53.	Conference abstract
Battezzati, P.M., et al., Ursodeoxycholic acid for symptomatic primary biliary cirrhosis. Preliminary analysis of a double-blind multicenter trial. Italian Multicenter Group for the Study of UDCA in PBC. <i>Journal of Hepatology</i> , 1993. 17(3): p. 332-8.	Wrong intervention (disease modifying)
Bergasa, N.V., et al., Open-label trial of oral nalmefene therapy for the pruritus of cholestasis. <i>Hepatology</i> , 1998. 27(3): p. 679-84.	No control group
Bhalerao, A. and G.S. Mannu, Management of Pruritus in chronic liver disease. <i>Dermatology Research and Practice</i> , 2015. 2015.	No critical appraisal
Brasileiro, L.E.E., D.P.C. Barreto, and E.A. Nunes, Psychotropics in different causes of itch: Systematic review with controlled studies. <i>Anais Brasileiros de Dermatologia</i> , 2016. 91(6): p. 791-798.	No critical appraisal
Browning, J., B. Combes, and M.J. Mayo, Long-term efficacy of sertraline as a treatment for cholestatic pruritus in patients with primary biliary cirrhosis. <i>American Journal of Gastroenterology</i> , 2003. 98(12): p. 2736-41.	Not a controlled trial
Brune, A., et al., [Antipruritic therapy with the oral opioid receptor antagonist naltrexone. Open, non-placebo controlled administration in 133 patients]. <i>Hautarzt</i> , 2004. 55(12): p. 1130-6.	No control group
Calmus, Y. and R. Poupon, Ursodeoxycholic acid (UDCA) in the treatment of chronic cholestatic diseases. <i>Biochimie</i> , 1991. 73(10): p. 1335-8.	Wrong intervention (disease modifying)

Reference	Reason for exclusion
Combes, B., et al., A randomized, double-blind, placebo-controlled trial of ursodeoxycholic acid in primary biliary cirrhosis. <i>Hepatology</i> , 1995. 22(3): p. 759-766.	Wrong intervention (disease modifying)
Connolly, C.S., G.R. Kantor, and H. Menduke, Hepatobiliary pruritus: what are effective treatments? <i>Journal of the American Academy of Dermatology</i> , 1995. 33(5 Pt 1): p. 801-5.	Narrative (medline) review
Diehn, F. and A. Tefferi, Pruritus in polycythaemia vera: prevalence, laboratory correlates and management. <i>British Journal of Haematology</i> , 2001. 115(3): p. 619-21.	Not a controlled trial
Eschler, D.C. and P.A. Klein, An evidence-based review of the efficacy of topical antihistamines in the relief of pruritus. <i>Journal of Drugs in Dermatology</i> , 2010. 9(8): p. 992-997.	Unclear what underlying disease is
Fawaz, B., B.H. Chamseddin, and J.R. Griffin, Defining the role of mirtazapine in the treatment of refractory pruritus. <i>Journal of Dermatological Treatment</i> , 2019.	Narrative (medline) review
Ghent, C. and S. Carruthers Treatment of pruritus of primary biliary cirrhosis with rifampicin Results of a double-blind crossover controlled trial. <i>Hepatology (baltimore, md.)</i> , 1986. 6, 1113.	Conference abstract
Ginsberg, D.L., Paroxetine effective for severe nondermatological pruritus. <i>Primary Psychiatry</i> , 2004. 11(7): p. 22-23.	Comment
Hague, W.M., et al., A multi-centre, open label, randomised, parallel-group, superiority Trial to compare the efficacy of URsodeoxycholic acid with RIFampicin in the management of women with severe early onset Intrahepatic Cholestasis of pregnancy: the TURRIFIC randomised trial. <i>BMC Pregnancy and Childbirth</i> , 2021. 21(1).	Wrong population
Hariharan, B. and M.R. Rajagopal, Re: Paroxetine in the treatment of severe non-dermatological pruritus. <i>Journal of Pain & Symptom Management</i> , 2005. 29(2): p. 115; author reply 115-6.	Letter
He, A., et al., Aprepitant for the Treatment of Chronic Refractory Pruritus. <i>BioMed Research International</i> , 2017. 2017: p. 4790810.	No critical appraisal
Jain, A., et al. The comparison of efficacy of ursodeoxycholic acid, ondansetron and naltrexone in the pruritus or acute cholestatic viral hepatitis. <i>Journal of clinical and experimental hepatology.</i> , 2013. 3, S47.	Abstract
Jain, A., et al. To compare the efficacy of urso-deoxycholic acid, ondansetron and naltrexone in the severe pruritus of acute cholestatic viral hepatitis ; a randomized trial. <i>Hepatology.</i> , 2013. 58, 1055a-1056a.	Abstract
Jain, A., et al. To compare the efficacy of urso-deoxycholic acid, ondansetron and naltrexone in the severe pruritus of acute cholestatic viral hepatitis; a randomized trial. <i>Journal of hepatology.</i> , 2014. 60, S438.	Abstract
Jones, E.A., H.A.J. Molenaar, and J. Oosting, Ondansetron and pruritus in chronic liver disease: A controlled study. <i>Hepato-Gastroenterology</i> , 2007. 54(76): p. 1196-1199.	No full-text
Kremer, A.E., et al., Advances in pathogenesis and management of pruritus in cholestasis. <i>Digestive Diseases</i> , 2014. 32(5): p. 637-45.	Narrative review
Martí-Carvajal, A.J. and C.E. Martí-Amarista, Interventions for treating intrahepatic cholestasis in people with sickle cell disease. <i>Cochrane Database of Systematic Reviews</i> , 2020. 2020(6).	Wrong population?
Metze, D., et al., Efficacy and safety of naltrexone, an oral opiate receptor antagonist, in the treatment of pruritus in internal and dermatological diseases. <i>Journal of the American Academy of Dermatology</i> , 1999. 41(4): p. 533-9.	No control group

Reference	Reason for exclusion
Nowak, D. and J. Yeung, Diagnosis and treatment of pruritus. Canadian Family Physician, 2017. 63(12): p. 918-924 and 925-931.	Narrative (medline) review
Olansky, S., Clinical Trial of an Antihistamine for Relief of Pruritus. Clinical Medicine, 1963. 70: p. 1657-60.	Not a controlled trial
Pojawa-Gołąb, M., K. Jaworecka, and A. Reich, NK-1 Receptor Antagonists and Pruritus: Review of Current Literature. Dermatology and Therapy, 2019. 9(3): p. 391-405.	No critical appraisal
Rowe, B. and G. Yosipovitch, Paraneoplastic Itch Management. Current Problems in Dermatology, 2016. 50: p. 149-54.	Narrative review
Schaffert-Witvliet, B., [Pruritus without skin manifestation--what kind of state of the art nursing intervention?]. Pflege, 2003. 16(5): p. 257-64.	Narrative presentation of results
Scheinfeld, N., The role of gabapentin in treating diseases with cutaneous manifestations and pain. International Journal of Dermatology, 2003. 42(6): p. 491-5.	No critical appraisal
Sharma, D. and S.G. Kwatra, Thalidomide for the treatment of chronic refractory pruritus. Journal of the American Academy of Dermatology, 2016. 74(2): p. 363-9.	Narrative (medline) review
Siemens, W., et al., Drug treatments for pruritus in adult palliative care. Deutsches Arzteblatt International, 2014. 111(50): p. 863-70.	Update of Cochrane review, which was updated by Siemens 2016
Stander, S., et al., Targeting the neurokinin receptor 1 with aprepitant: a novel antipruritic strategy. PLoS ONE [Electronic Resource], 2010. 5(6): p. e10968.	No control group
Tajiri, K. and Y. Shimizu, Recent advances in the management of pruritus in chronic liver diseases. World Journal of Gastroenterology, 2017. 23(19): p. 3418-3426.	Narrative review
Talwalkar, J.A., et al., Natural history of pruritus in primary biliary cirrhosis. Clinical Gastroenterology & Hepatology, 2003. 1(4): p. 297-302.	Natural history of pruritus
Tefferi, A. and R. Fonseca, Selective serotonin reuptake inhibitors are effective in the treatment of polycythemia vera-associated pruritus. Blood, 2002. 99(7): p. 2627.	Letter
Thebaut, A., et al. Sertraline as an additional treatment for cholestatic pruritus in children. Journal of pediatric gastroenterology and nutrition, 2017. 64, 431-435.	Wrong population?
Van Hoogstraten, H.J.F., et al., Budesonide or prednisone in combination with ursodeoxycholic acid in primary sclerosing cholangitis: A randomized double-blind pilot study. American Journal of Gastroenterology, 2000. 95(8): p. 2015-2022.	Wrong intervention (disease modifying)
Wiesner, R.H., et al., A controlled trial of cyclosporine in the treatment of primary biliary cirrhosis. New England Journal of Medicine, 1990. 322(20): p. 1419-24.	Wrong intervention (disease modifying)
Wolfhagen, F.H.J., et al., Triple therapy with ursodeoxycholic acid, prednisone and azathioprine in primary biliary cirrhosis: A 1-year randomized, placebo-controlled study. Journal of Hepatology, 1998. 29(5): p. 736-742.	Wrong intervention (disease modifying)
Xander, C., et al., Pharmacological interventions for pruritus in adult palliative care patients. Cochrane Database of Systematic Reviews, 2013(6): p. CD008320.	Updated by Siemens 2016
Yosipovitch, G., et al., Serlopitant for the treatment of chronic pruritus: Results of a randomized, multicenter, placebo-controlled phase 2 clinical trial. Journal of the American Academy of Dermatology, 2018. 78(5): p. 882-891.e10.	Patients in good health Included in Andrade 2020

Search strings

MEDLINE (OVID)

- 1 Palliative Care/ (55446)
- 2 exp Terminal Care/ (52230)
- 3 Terminally Ill/ (6592)
- 4 palliat*.mp. (88495)
- 5 (terminal* adj6 (care or ill* or diseas*)).mp. (41446)
- 6 (terminal-stage* or terminal stage* or dying or (close adj6 death)).mp. (35852)
- 7 (end adj3 life).mp. (22336)
- 8 hospice*.mp. (16027)
- 9 ((end-stage* or end stage*) adj6 (disease* or illness* or care)).mp. (47102)
- 10 (incurable adj6 (disease* or illness*)).mp. (3896)
- 11 (advanced adj6 disease*).mp. (45577)
- 12 or/1-11 (257259)
- 13 exp Liver Diseases/ (562176)
- 14 (liver or hepat* or cirrhosis or fibrosis).mp. (1458321)
- 15 exp hiv infections/ (287750)
- 16 ("acquired immunodeficiency syndrome" or "acquired immunodeficiency syndrome" or "acquired immuno-deficiency syndrome" or "acquired immune-deficiency syndrome").mp. (88899)
- 17 HIV.mp. (333657)
- 18 exp neoplasms/ (3409483)
- 19 (neoplasm* or cancer* or carcinoma* or tumour* or adenocarcinoma* or leukemi* or leukaemi* or lymphoma* or tumor* or malignan* or myeloma*).mp. (4008569)
- 20 (radiochemotherap* or chemoradi* or chemotherap*).mp. (457444)
- 21 hypersensitivity/ or exp drug hypersensitivity/ (94438)
- 22 allerg*.mp. (205454)
- 23 or/13-22 (5885750)
- 24 12 or 23 (6021990)
- 25 pruritus/ (12062)
- 26 antipruritics/ (1026)
- 27 prurit*.mp. (23410)
- 28 itch*.mp. (12856)
- 29 antiprurit*.mp. (1434)
- 30 anti prurit*.mp. (147)
- 31 scratch*.mp. (13200)
- 32 or/25-31 (43925)
- 33 exp Histamine H1 Antagonists/ (36109)
- 34 Loratadine/ (1186)
- 35 desloratadin*.mp. (572)
- 36 cetirizin*.mp. (1773)
- 37 levocetirizin*.mp. (375)
- 38 mizolastin*.mp. (118)
- 39 fexofenadin*.mp. (884)
- 40 Hydroxyzine/ (1418)
- 41 hydroxyzin*.mp. (1772)
- 42 Promethazine/ (3017)
- 43 promethazin*.mp. (3848)
- 44 Betahistine/ or betahistin*.mp. (532)
- 45 Histamine H2 Antagonists/ or Cimetidine/ or Ranitidine/ or Nizatidine/ or Famotidine/ or (cimetidin* or raniditin* or nizatidin* or famotidin*).mp. (18833)
- 46 exp serotonin uptake inhibitors/ or fluvoxamine/ or paroxetine/ or sertraline/ (42773)
- 47 SSRI*.mp. (9014)
- 48 paroxetin*.mp. (5897)
- 49 doxepin*.mp. (1434)
- 50 Doxepin/ (830)
- 51 fluvoxamin*.mp. (2788)

52 sertralin*.mp. (4717)
53 Mirtazapine/ (1330)
54 mirtazapin*.mp. (2078)
55 Naloxone/ (18928)
56 naloxon*.mp. (26459)
57 Naltrexone/ (8012)
58 (naltrexon* or methylnaltrexon*).mp. (9773)
59 Buprenorphine/ (5423)
60 buprenorfin*.mp. (125)
61 buprenorphin*.mp. (6989)
62 exp Narcotic Antagonists/ (38005)
63 Ondansetron/ or Palonosetron/ (3460)
64 (ondansetron* or palonosetron* or ropisetron*).mp. (4898)
65 Cholestyramine Resin/ (2635)
66 cholestyramin*.mp. (3419)
67 Rifampin/ (18145)
68 rifampi*.mp. (28195)
69 Aspirin/ (45530)
70 acetylsalicylic.mp. (9305)
71 prednison*.mp. (51693)
72 cyclosporin*.mp. (55963)
73 dexamethason*.mp. (68127)
74 cimetidin*.mp. (12453)
75 gabapentin*.mp. (6369)
76 pregabalin*.mp. (3134)
77 thalidomide.mp. (10963)
78 Janus Kinase Inhibitors/ or (baricitinib or filgotinib or tofacitinib or upadacitinib).mp. (1652)
79 Neurokinin-1 Receptor Antagonists/ (2046)
80 (aprepitant or fosaprepitant or netupitant).mp. (1010)
81 serlopitant.mp. (10)
82 anti-interleukin 31.mp. (8)
83 ("anti-interleukin 4/13" or dupilumab).mp. (503)
84 Antidepressive Agents, Tricyclic/ (10374)
85 amitriptylin*.mp. (8951)
86 nortriptylin*.mp. (3020)
87 Clomipramine/ or clomipramin*.mp. (3859)
88 Granisetron/ (1105)
89 granisetron*.mp. (1564)
90 exp Serotonin Antagonists/ (54271)
91 or/33-90 (466055)
92 clobetasol.mp. or Clobetasol/ (1706)
93 Betamethasone Valerate/ (541)
94 exp Betamethasone/ (7452)
95 betamethason*.mp. (7446)
96 fluticason*.mp. (4275)
97 Triamcinolone Acetonide/ (5803)
98 desoximetason*.mp. (111)
99 desoximethason*.mp. (6)
100 Hydrocortisone/ (72623)
101 (local adj corticosteroid*).mp. (558)
102 Tacrolimus/ (16194)
103 pimecrolimus.mp. (856)
104 Emollients/ (1883)
105 or/92-104 (108243)
106 91 or 105 (556240)
107 24 and 32 and 106 (2311)
108 randomized controlled trial.pt. (521477)
109 controlled clinical trial.pt. (94022)

110 randomized.ab. (434321)
 111 placebo.ab. (193385)
 112 clinical trials as topic.sh. (194465)
 113 randomly.ab. (294684)
 114 trial.ti. (198517)
 115 108 or 109 or 110 or 111 or 112 or 113 or 114 (1200123)
 116 exp animals/ not humans.sh. (4781704)
 117 115 not 116 (1093717)
 118 meta-analysis.mp,pt. or review.pt. or search:.tw. (2800649)
 119 117 or 118 (3709932)
 120 107 and 119 (1057)

PREMEDLINE (OVID)

1 Palliative Care/ (47)
 2 exp Terminal Care/ (39)
 3 Terminally Ill/ (5)
 4 palliat*.mp. (1998)
 5 (terminal* adj6 (care or ill* or diseas*)).mp. (316)
 6 (terminal-stage* or terminal stage* or dying or (close adj6 death)).mp. (760)
 7 (end adj3 life).mp. (1038)
 8 hospice*.mp. (445)
 9 ((end-stage* or end stage*) adj6 (disease* or illness* or care)).mp. (1140)
 10 (incurable adj6 (disease* or illness*)).mp. (110)
 11 (advanced adj6 disease*).mp. (990)
 12 or/1-11 (5268)
 13 exp Liver Diseases/ (341)
 14 (liver or hepat* or cirrhosis or fibrosis).mp. (17828)
 15 exp hiv infections/ (186)
 16 ("acquired immunodeficiency syndrome" or "acquired immunodeficiency syndrome" or
 "acquired immuno-deficiency syndrome" or "acquired immune-deficiency syndrome").mp.
 (116)
 17 HIV.mp. (4414)
 18 exp neoplasms/ (2445)
 19 (neoplasm* or cancer* or carcinoma* or tumour* or adenocarcinoma* or leukemi* or leukaemi*
 or lymphoma* or tumor* or malignan* or myeloma*).mp. (55155)
 20 (radiochemotherap* or chemoradi* or chemotherap*).mp. (6775)
 21 hypersensitivity/ or exp drug hypersensitivity/ (42)
 22 allerg*.mp. (2336)
 23 or/13-22 (74119)
 24 12 or 23 (77065)
 25 pruritus/ (5)
 26 antipruritics/ (1)
 27 prurit*.mp. (419)
 28 itch*.mp. (373)
 29 antiprurit*.mp. (12)
 30 anti prurit*.mp. (7)
 31 scratch*.mp. (313)
 32 or/25-31 (992)
 33 exp Histamine H1 Antagonists/ (2)
 34 Loratadine/ (0)
 35 desloratadin*.mp. (6)
 36 cetirizin*.mp. (20)
 37 levocetirizin*.mp. (5)
 38 mizolastin*.mp. (2)
 39 fexofenadin*.mp. (17)
 40 Hydroxyzine/ (0)
 41 hydroxyzin*.mp. (14)
 42 Promethazine/ (0)

43 promethazin*.mp. (27)
 44 Betahistine/ or betahistin*.mp. (5)
 45 Histamine H2 Antagonists/ or Cimetidine/ or Ranitidine/ or Nizatidine/ or Famotidine/ or
 (cimetidin* or ranitidin* or nizatidin* or famotidin*).mp. (46)
 46 exp serotonin uptake inhibitors/ or fluvoxamine/ or paroxetine/ or sertraline/ (27)
 47 SSRI*.mp. (199)
 48 paroxetin*.mp. (73)
 49 doxepin*.mp. (17)
 50 Doxepin/ (0)
 51 fluvoxamin*.mp. (29)
 52 sertralin*.mp. (86)
 53 Mirtazapine/ (1)
 54 mirtazapin*.mp. (44)
 55 Naloxone/ (5)
 56 naloxon*.mp. (250)
 57 Naltrexone/ (3)
 58 (naltrexon* or methylnaltrexon*).mp. (135)
 59 Buprenorphine/ (6)
 60 buprenorfin*.mp. (1)
 61 buprenorphin*.mp. (239)
 62 exp Narcotic Antagonists/ (17)
 63 Ondansetron/ or Palonosetron/ (1)
 64 (ondansetron* or palonosetron* or ropisetron*).mp. (73)
 65 Cholestyramine Resin/ (0)
 66 cholestyramin*.mp. (23)
 67 Rifampin/ (5)
 68 rifampi*.mp. (255)
 69 Aspirin/ (32)
 70 acetylsalicylic.mp. (85)
 71 prednison*.mp. (316)
 72 cyclosporin*.mp. (340)
 73 dexamethason*.mp. (685)
 74 cimetidin*.mp. (13)
 75 gabapentin*.mp. (177)
 76 pregabalin*.mp. (113)
 77 thalidomide.mp. (68)
 78 Janus Kinase Inhibitors/ or (baricitinib or filgotinib or tofacitinib or upadacitinib).mp. (200)
 79 Neurokinin-1 Receptor Antagonists/ (0)
 80 (aprepitant or fosaprepitant or netupitant).mp. (30)
 81 serlopitant.mp. (1)
 82 anti-interleukin 31.mp. (0)
 83 ("anti-interleukin 4/13" or dupilumab).mp. (119)
 84 Antidepressive Agents, Tricyclic/ (0)
 85 amitriptylin*.mp. (67)
 86 nortriptylin*.mp. (24)
 87 Clomipramine/ or clomipramin*.mp. (26)
 88 Granisetron/ (1)
 89 granisetron*.mp. (5)
 90 exp Serotonin Antagonists/ (16)
 91 or/33-90 (3419)
 92 clobetasol.mp. or Clobetasol/ (19)
 93 Betamethasone Valerate/ (0)
 94 exp Betamethasone/ (3)
 95 betamethason*.mp. (70)
 96 fluticason*.mp. (66)
 97 Triamcinolone Acetonide/ (1)
 98 desoximetason*.mp. (2)
 99 desoximethason*.mp. (1)

100 Hydrocortisone/ (27)
 101 (local adj corticosteroid*).mp. (10)
 102 Tacrolimus/ (5)
 103 pimecrolimus.mp. (14)
 104 Emollients/ (1)
 105 or/92-104 (211)
 106 91 or 105 (3608)
 107 24 and 32 and 106 (22)
 108 randomized controlled trial.pt. (459)
 109 controlled clinical trial.pt. (9)
 110 randomized.ab. (12042)
 111 placebo.ab. (3290)
 112 clinical trials as topic.sh. (70)
 113 randomly.ab. (5772)
 114 trial.ti. (5779)
 115 108 or 109 or 110 or 111 or 112 or 113 or 114 (19994)
 116 exp animals/ not humans.sh. (2073)
 117 115 not 116 (19891)
 118 meta-analysis.mp.pt. or review.pt. or search:.tw. (58302)
 119 117 or 118 (74196)
 120 107 and 119 (15)

EMBASE (VIA EMBASE.COM)

#1 'palliative therapy'/exp (116470)
 #2 'terminal care'/exp (72363)
 #3 'terminally ill patient'/exp (8781)
 #4 palliat*:ti,ab (122736)
 #5 (terminal* NEAR/6 (care OR caring OR ill*)):ti,ab (13227)
 #6 (end NEAR/3 life):ti,ab (36650)
 #7 hospice*:ti,ab (20776)
 #8 'terminal stage*':ti,ab (4442)
 #9 dying:ti,ab (46173)
 #10 (close NEAR/6 death):ti,ab (1374)
 #11 ((incurable OR advanced) NEAR/6 (ill* OR disease*)):ti,ab (94963)
 #12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 (357800)
 #13 'liver disease'/exp (1091078)
 #14 liver:ti,ab OR hepat*:ti,ab OR cirrhosis:ti,ab OR fibrosis:ti,ab (1892304)
 #15 'human immunodeficiency virus infection'/exp (388076)
 #16 'acquired immunodeficiency syndrome':ti,ab OR 'acquired immunodeficiency syndrome':ti,ab
 OR 'acquired immuno-deficiency syndrome':ti,ab OR 'acquired immune-deficiency
 syndrome':ti,ab (16730)
 #17 hiv:ti,ab (405757)
 #18 'neoplasm'/exp (5132984)
 #19 neoplasm*:ti,ab OR cancer*:ti,ab OR carcinoma*:ti,ab OR tumour*:ti,ab OR
 adenocarcinoma*:ti,ab OR leukemi*:ti,ab OR leukaemi*:ti,ab OR lymphoma*:ti,ab OR
 tumor*:ti,ab OR malignan*:ti,ab OR myeloma*:ti,ab (4976082)
 #20 radiochemotherap*:ti,ab OR chemoradi*:ti,ab OR chemotherap*:ti,ab (697310)
 #21 'hypersensitivity'/exp (677332)
 #22 'drug hypersensitivity'/exp (63128)
 #23 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
 (8801805)
 #24 'pruritus'/exp (98644)
 #25 'antipruritic agent'/exp (54907)
 #26 prurit*:ti,ab OR itch*:ti,ab OR antiprurit*:ti,ab OR scratch*:ti,ab (77735)
 #27 #24 OR #25 OR #26 (189270)
 #28 'histamine h1 receptor antagonist'/exp (171544)
 #29 desloratadin*:ti,ab OR cetirizin*:ti,ab OR levocetirizin*:ti,ab OR mizolastin*:ti,ab OR
 fexofenadin*:ti,ab OR hydroxyzin*:ti,ab OR promethazin*:ti,ab (9383)

- #30 'serotonin uptake inhibitor'/exp (285900)
- #31 ssri*:ti,ab OR paroxetin*:ti,ab OR fluvoxamin*:ti,ab OR sertralin*:ti,ab (28848)
- #32 'serotonin noradrenalin reuptake inhibitor'/exp (192853)
- #33 'mirtazapine'/exp (12961)
- #34 doxepin*:ti,ab (1800)
- #35 mirtazapin*:ti,ab (3438)
- #36 'morphine derivative'/exp (210850)
- #37 naltrexon*:ti,ab OR buprenorfin*:ti,ab OR naloxon*:ti,ab OR buprenorphin*:ti,ab OR methylnaltrexon*:ti,ab (45249)
- #38 'serotonin antagonist'/exp (272992)
- #39 ondansetron*:ti,ab OR granisetron*:ti,ab OR palonosetron*:ti,ab OR ropisetron*:ti,ab (9221)
- #40 'colestyramine'/exp (10850)
- #41 colestyramin*:ti,ab OR cholestyramin*:ti,ab (3252)
- #42 'rifampicin'/exp (91236)
- #43 rifampi*:ti,ab (32636)
- #44 'acetylsalicylic acid'/exp (219259)
- #45 acetylsalicylic:ti,ab OR aspirin*:ti,ab (88627)
- #46 'prednisone'/exp (181437)
- #47 prednison*:ti,ab (51085)
- #48 'cyclosporine'/exp (153663)
- #49 cyclosporin*:ti,ab (68207)
- #50 'dexamethasone'/exp (157388)
- #51 dexamethason*:ti,ab (80493)
- #52 cimetidin*:ti,ab (13094)
- #53 gabapentin*:ti,ab (10947)
- #54 pregabalin*:ti,ab (6292)
- #55 thalidomide:ti,ab (13429)
- #56 'janus kinase inhibitor'/exp OR baricitinib:ti,ab OR filgotinib:ti,ab OR tofacitinib:ti,ab OR upadacitinib:ti,ab (16618)
- #57 'neurokinin 1 receptor antagonist'/exp (2442)
- #58 'aprepitant'/exp (3355)
- #59 'serlopitant'/exp (66)
- #60 aprepitant*:ti,ab OR serlopitant*:ti,ab OR fosaprepitant*:ti,ab OR netupitant*:ti,ab (2088)
- #61 'anti-interleukin 31':ti,ab OR 'anti-interleukin 4/13':ti,ab OR dupilumab:ti,ab (1439)
- #62 'tricyclic antidepressant agent'/exp (115151)
- #63 amitriptylin*:ti,ab OR nortriptylin*:ti,ab OR clomipramin*:ti,ab (14735)
- #64 #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 (1503084)
- #65 'clobetasol'/exp (2931)
- #66 'betamethasone'/exp (18254)
- #67 'betamethasone valerate'/exp (3323)
- #68 'triamcinolone acetonide'/exp (15574)
- #69 'fluticasone'/exp (8362)
- #70 'desoximetasone'/exp (811)
- #71 'hydrocortisone'/exp (139306)
- #72 'tacrolimus'/exp (83122)
- #73 'pimecrolimus'/exp (3314)
- #74 'emollient agent'/exp (6108)
- #75 clobetasol:ti,ab OR betamethason*:ti,ab OR fluticason*:ti,ab OR desoximetason*:ti,ab OR desoximethason*:ti,ab OR ((local NEAR/1 corticosteroid*):ti,ab) (17110)
- #76 #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 (272688)
- #77 #64 OR #76 (1681866)
- #78 #23 AND #27 AND #77 (22936)

#79 #23 AND #27 AND #77 AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [randomized controlled trial]/lim) AND ([article]/lim OR [article in press]/lim OR [review]/lim) AND ([dutch]/lim OR [english]/lim OR [french]/lim OR [german]/lim) (1892)

COCHRANE LIBRARY (VIA WILEY)

#1 pallia*:ti,ab
#2 MeSH descriptor: [Palliative Care] explode all trees
#3 (terminal* NEAR/6 (care or caring or ill*)):ti,ab
#4 (terminal-stage* or terminal stage* or dying or (close NEAR/6 death)):ti,ab
#5 (end NEAR/3 life):ti,ab
#6 hospice*:ti,ab
#7 ((end-stage* or end stage*) NEAR/6 (disease* or ill* or care or caring)):ti,ab
#8 ((incurable or advanced) NEAR/6 (ill* or disease*))
#9 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8
#10 (liver or hepat* or cirrhosis or fibrosis):ti,ab
#11 MeSH descriptor: [HIV] explode all trees
#12 ("acquired immunodeficiency syndrome" or "acquired immunodeficiency syndrome" or "acquired immuno-deficiency syndrome" or "acquired immune-deficiency syndrome"):ti,ab
#13 HIV:ti,ab
#14 (neoplasm* or cancer* or carcinoma* or tumour* or adenocarcinoma* or leukemi* or leukaemi* or lymphoma* or tumor* or malignan* or myeloma*):ti,ab
#15 (radiochemotherap* or chemoradi* or chemotherap*):ti,ab
#16 MeSH descriptor: [Hypersensitivity] explode all trees
#17 MeSH descriptor: [Drug Hypersensitivity] explode all trees
#18 allerg*:ti,ab
#19 #9 or #10 or #11 or #12 or #13 #14 or #15 or #16 or #17 or #18
#20 MeSH descriptor: [Pruritus] explode all trees
#21 MeSH descriptor: [Antipruritics] explode all trees
#22 (prurit* or itch* or antiprurit* or anti prurit* or scratch*):ti,ab
#23 #20 or #21 or #22
#24 #19 and #23
#25 MeSH descriptor: [Histamine H1 Antagonists] explode all trees
#26 MeSH descriptor: [Loratadine] explode all trees
#27 MeSH descriptor: [Hydroxyzine] explode all trees
#28 MeSH descriptor: [Promethazine] explode all trees
#29 MeSH descriptor: [Serotonin Uptake Inhibitors] explode all trees
#30 MeSH descriptor: [Fluvoxamine] explode all trees
#31 MeSH descriptor: [Paroxetine] explode all trees
#32 MeSH descriptor: [Sertraline] explode all trees
#33 MeSH descriptor: [Doxepin] explode all trees
#34 MeSH descriptor: [Mirtazapine] explode all trees
#35 MeSH descriptor: [Naloxone] explode all trees
#36 MeSH descriptor: [Naltrexone] explode all trees
#37 MeSH descriptor: [Buprenorphine] explode all trees
#38 MeSH descriptor: [Narcotic Antagonists] explode all trees
#39 MeSH descriptor: [Ondansetron] explode all trees
#40 MeSH descriptor: [Cholestyramine Resin] explode all trees
#41 MeSH descriptor: [Rifampin] explode all trees
#42 MeSH descriptor: [Aspirin] explode all trees
#43 MeSH descriptor: [Janus Kinase Inhibitors] explode all trees
#44 MeSH descriptor: [Neurokinin-1 Receptor Antagonists] explode all trees
#45 MeSH descriptor: [Antidepressive Agents, Tricyclic] explode all trees
#46 MeSH descriptor: [Serotonin Antagonists] explode all trees
#47 (desloratadin* or cetirizin* or levocetirizin* or mizolastin* or fexofenadin* or hydroxyzin* or promethazin* or betahistin* or cimetidin* or raniditin* or nizatidin* or famotidin* or SSRI* or paroxetin* or doxepin* or fluvoxamin* or sertralin* or mirtazapin* or naloxon* or naltrexon* or methylnaltrexon* or buprenorfin* or buprenorphin* or ondansetron* or palonosetron* or ropisetron* or cholestyramin* or rifampi* or acetylsalicylic or prednison* or cyclosporin* or

- dexamethason* or cimetidin* or gabapentin* or pregabalin* or thalidomide or aprepitant or serlopitant or fosaprepitant or netupitant or "anti-interleukin 31" or amitriptylin* or nortriptylin* or granisetron* or baricitinib or filgotinib or tofacitinib or upadacitinib or "anti-interleukin 4/13" or dupilumab or clomipramin*):ti,ab
- #48 MeSH descriptor: [Clobetasol] explode all trees
 - #49 MeSH descriptor: [Betamethasone Valerate] explode all trees
 - #50 MeSH descriptor: [Betamethasone] explode all trees
 - #51 MeSH descriptor: [Triamcinolone Acetonide] explode all trees
 - #52 MeSH descriptor: [Hydrocortisone] explode all trees
 - #53 MeSH descriptor: [Tacrolimus] explode all trees
 - #54 MeSH descriptor: [Emollients] explode all trees
 - #55 (clobetasol or betamethason* or fluticason* or desoximetason* or desoximethason* or pimecrolimus or (local NEAR/1 corticosteroid*)):ti,ab
 - #56 #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55
 - #57 #24 and #56