

Rectal Medication Literature Review

Drug Class	Medication	Rectal Bioavailability	References and Notes (ME= Micro-enema/Supp=Suppository)
Opioid Analgesics	Morphine	Similar to oral	Pain relief onset 10 min. (ME) vs. 60 min. (oral) [1] Tmax (ME) = 30min [2]
	Oxycodone	Similar to oral	Analgesia onset (supp) 30min - 1h [3,4]
	Methadone	80% - 90% of oral	Tmax (ME) 1.4hr vs (oral) 2.8hr [7] Analgesia onset (ME) 30min [5] Absorption (ME) 80% of oral vs (supp) 35% - 58% of oral [6]
	Hydromorphone	65% - 70% of oral	[8,9]

Drug Class	Medication	Rectal Bioavailability	References and Notes (ME= Micro-enema/Supp=Suppository)
NSAIDS / APAP	Aspirin	Similar to oral	[12]
	Indomethacin	80% of IV [43]	Tmax (ME) 20 min. vs (IM) 40 min. vs (supp) 60min [13]
	Ibuprofen	87% of oral	Tmax (ME) 1.1h vs (oral) 33min [14]
	Ketoprofen	73%- 93% of oral [15]	Same as IM [15]
	Naprosyn	Similar to oral	Studies done on both suppository and oral solution [16]
	Acetaminophen	Similar to oral	As aqueous suspension [17]

Drug Class	Medication	Rectal Bioavailability	References and Notes (ME= Micro-enema/Supp=Suppository)
Anesthetics	Lidocaine	200% of oral	Extensive first pass avoidance [10]
	Ketamine	150% of oral	Plasma concentrations similar for oral and rectal [11]

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Benzodiazepines	Lorazepam	80% of IV [28] Clinically effective [30,31]	Tmax (ME) 1.12 hr. vs (IM) 2.25 hr. vs (oral) 2.37hr vs (SL) 2.35hr [28,29] Seizure control (ME) in 37sec. average [30] Agitation control (ME) < 1 minute [31]
	Diazepam	Similar to oral	Tmax (ME) 17 min vs (IM) 95min vs (supp) 82 min vs (PO) 52 min [32]
	Midazolam	Similar to oral	Improved sedation (ME) vs (oral) [33] (ME) acceptable in children ages 2-7 [33] Tmax 16min in children [34] Tmax 31min in adult males [35]

Drug Class	Medication	Rectal Bioavailability	References and Notes (ME= Micro-enema/Supp=Suppository)
Anti-Psychotics / Neuroleptics	Chlorpromazine	Clinically effective	Supp as effective as IV in controlling restlessness and dyspnea in EOL patients [69]
	Haloperidol	Clinical effectiveness	Anecdotal reports support clinical effectiveness administered rectally [63]
	Olanzapine	Clinical effectiveness	Supp found clinically effective for delirium and N/V [64]
	Quetiapine	Supp 189% of oral	No topical absorption noted [65]

Drug Class	Medication	Rectal Bioavailability	References and Notes (ME= Micro-enema/Supp=Suppository)
Corticosteroids	Dexamethasone	Clinical effectiveness	Satisfactory results obtained in several studies [18] Case study on Benadryl, Reglan, Dexamethasone Supp (BRD) - effective for malignant bowel obstruction [19]

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Anti-Epileptics	Phenobarbital	Similar to oral [36]	(ME) showed faster absorption, improved overall absorption, decreased variability vs (supp) [37]
	Levetiracetam	Similar to oral	Tmax (Supp) 190 min. vs (oral) 90 min. [38]
	Lamotrigine	63% of oral	May need to titrate dose up from oral to rectal [39]
	Valproic Acid	Similar to oral	[40]
	Carbamazepine	Similar to oral [41]	Therapeutic blood levels [21]

Drug Class	Medication	Rectal Bioavailability	References and Notes
Anti-Emetics	Metoclopramide	100% absolute bioavailable [43]	Therapeutic blood levels. [43] (ME) Controlled gastroparesis symptoms [42]
	Prochlorperazine	Similar to oral	Absolute Absorption (supp) 23% vs (oral) 25% [44]
	Promethazine	70% - 97% of oral	[45]
	Ondansetron	ME similar to oral [46] Supp 50% of oral [47]	(ME) Cmax, Tmax, and bioavailability similar to oral [46] (Supp) bioavailability 50% vs oral [47]

Drug Class	Medication	Rectal Bioavailability	References and Notes
Anticholinergics	Atropine	32% of IM [25]	(ME) clinically as effective as (IM) [24] Tmax (ME) 15 - 33 minutes [25,26]
	Hyoscyamine	100% absolute bioavailability	[27]

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Drug Class	Medication	Rectal Bioavailability	References and Notes
Antidepressants	Imipramine	Similar to oral	[20]
	Clomipramine	Similar to oral	[20]
	Doxepin	Therapeutic blood levels	[21]
	Amitriptyline	Clinical effectiveness	Case study: clinical effectiveness [22]
	Trazodone	Clinical effectiveness	Clinically effective [23]

Drug Class	Medication	Rectal Bioavailability	References and Notes
Antibiotics	Amoxicillin	87 - 99% of oral	Study used hydrophilic suppository [48]
	Erythromycin	≅150% of oral [49,50]	Suppository 54% of IV [49] Oral 32% of IV [50]
	Ampicillin	Plasma concentrations well above MIC*	Rapidly absorbed, therapeutic plasma concentrations, same therapeutic effect rectal (89% cured) vs oral group (86% cured) N=683 [51]
	Sulfamethoxazole-Trimethoprim	Similar serum concentrations given rectal (TID) vs oral (BID)	Steady state blood levels achieved Serum concentrations comparable to oral with same dose given TID rectal vs BID oral [52]
	Metronidazole	80% of oral	PEG suppository compared to oral suspension [53]

*MIC = Minimum inhibitory concentrations

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Drug Class	Medication	Rectal Bioavailability	References and Notes
Cardio-Active Medications	Flecainide	98% of IV and 126% of oral	Rapid Tmax for ME (11min) vs oral tab (51min) [54]
	Lidocaine	200% of oral	Extensive first pass avoidance [55]
	Nifedipine	Similar to oral [56]	AUC comparable (oral) vs (supp) [56] Anti-hypertensive effects at 30min lasting 7hrs, heart rate increase associated with oral dosing did not occur with rectal dosing [57]
	Metoprolol	Similar to oral	AUC for (oral) vs (supp) not significantly different (0.05). (Supp) effective in lowering heart rate by (avg. 19 bpm) and BP by (syst. 14mmhg/dia. 15mmhg) [58]
	Propranolol	200% of oral	Significant first pass avoidance noted [59]
	Verapamil	PEG supp similar to oral	Faster Tmax 33min (PEG supp) vs 2.1h oral. (Fatty supp) AUC 50% oral [60]
	Digoxin	Clinical effectiveness	Therapeutic effects noted [61,62] NOTE: Early studies (1924 and 1932) with digitalis extracts.

Drug Class	Medication	Rectal Bioavailability	References and Notes
Diuretics	Furosemide	Clinical effectiveness	Therapeutic effect similar to oral at same dose [66]
	Bumetanide	52% - 62% compared to oral	Sufficient diuretic effects obtained after rectal dosing [67]

Drug Class	Medication	Rectal Bioavailability	References and Notes
Anticoagulants	Warfarin	Therapeutic PT ranges	Therapeutic PT ranges achieved within 24hrs (N=23) [68]

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Alphabetical Medication Listing

Medication	Bioavailability	Notes
Acetaminophen	Similar to oral	As aqueous suspension [17]
Amitriptyline	Clinical effectiveness	Case study: clinical effectiveness [22]
Amoxicillin	87 - 99% of oral	Study used hydrophilic suppository [48]
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Chlorpromazine	Clinically effective	Supp as effective as IV in controlling restlessness and dyspnea in EOL patients [69]
Clomipramine	Similar to oral	[20]
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Doxepin	Therapeutic blood levels	[21]
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Haloperidol	Clinical effectiveness	Anecdotal reports support clinical effectiveness administered rectally [63]
Hydromorphone	65% - 70% of oral	[8,9]
Hyoscyamine	100% absolute bioavailability	[27]
Ibuprofen	87% of oral	Tmax (ME) 1.1h vs (oral) 33min [14]
Imipramine	Similar to oral	[20]
Indomethacin	80% of IV [43]	Tmax (ME) 20 min. vs (IM) 40 min. vs (supp) 60min [13]
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1. De Conno F, Ripamonti C, Saita L, MacEachern T, Hanson J, Bruera E. Role of rectal route in treating cancer pain: a randomized crossover clinical trial of oral versus rectal morphine administration in opioid-naive cancer patients with pain. *J Clin Oncol*. 1995;13(4):1004-8.
2. Moolenaar, F., Yska, J.P., Visser, J. et al. Drastic improvement in the rectal absorption profile of morphine in man. *Eur J Clin Pharmacol*. 1985;29, 119–121.
3. Leow KP, Smith MT, Watt JA, Williams BE, Cramond T. Comparative oxycodone pharmacokinetics in humans after intravenous, oral, and rectal administration. *Ther Drug Monit*. 1992;14(6):479-84.
4. Leow KP, Cramond T, Smith MT. Pharmacokinetics and pharmacodynamics of oxycodone when given intravenously and rectally to adult patients with cancer pain. *Anesth Analg*. 1995;80(2):296-302.
5. Ripamonti C, Zecca E, Brunelli C, Rizzio E, Saita L, Lodi F, De Conno F. Rectal methadone in cancer patients with pain. A preliminary clinical and pharmacokinetic study. *Ann Oncol*. 1995 Oct;6(8):841-3.
6. Moolenaar F, Fiets G, Visser J, Meijer DKF. Preliminary study on the absorption profile after rectal and oral administration of methadone in human volunteers. *Pharmaceutisch Weekblad*. 1984;6(6):237-240
7. Dale O, Sheffels P, Kharasch ED. Bioavailabilities of rectal and oral methadone in healthy subjects. *Br J Clin Pharmacol*. 2004;58(2):156–162.
8. Parab PV, Ritschel WA, Coyle DE, Gregg RV, Denson DD. Pharmacokinetics of hydromorphone after intravenous, peroral and rectal administration to human subjects. *Biopharm Drug Dispos*. 1988;9(2):187-99.
9. Ritschel WA, Parab PV, Denson DD, Coyle DE, Gregg RV. Absolute bioavailability of hydromorphone after peroral and rectal administration in humans: saliva/plasma ratio and clinical effects. *J Clin Pharmacol*. 1987;27(9):647-53.
10. deBoer AG et al. Rectal bioavailability of lidocaine in man: partial avoidance of "first pass" metabolism. *Clin Pharmacol Ther*. 1979;26(6):701-709
11. Yanagihara Y, Ohtani M, Kariya S, Uchino K, Hiraishi T, Ashizawa N, Aoyama T, Yamamura Y, Yamada Y, Iga T. Plasma concentration profiles of ketamine and norketamine after administration of various ketamine preparations to healthy Japanese volunteers. *Biopharm Drug Dispos*. 2003;24(1):37-43.
12. Parrott EL Salicylate absorption from rectal suppositories. *J Pharm Science*. 1971;60: 867–872
13. Jensen KM, Grenabo L. Bioavailability of indomethacin after intramuscular injection and rectal administration of solution and suppositories. *Acta Pharmacol Toxicol (Copenh)*. 1985;57(5):322-7
14. Eller MG, Wright C 3rd, Della-Coletta AA. Absorption kinetics of rectally and orally administered ibuprofen. *Biopharm Drug Dispos*. 1989;10(3):269-78.

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15. Ishizaki T, Sasaki T, Suganuma T, Horai Y, Chiba K, Watanabe M, Asuke W, Hoshi H. Pharmacokinetics of ketoprofen following single oral, intramuscular and rectal doses and after repeated oral administration. *Eur J Clin Pharmacol.* 1980;18(5):407-14.
16. Desager JP, Vanderbist M, Harvengt C. Naproxen plasma levels in volunteers after single-dose administration by oral and rectal routes. *J Clin Pharmacol.* 1976;16(4):189-93.
17. Moolenaar, F., Olthof, L. & Huizinga, T. Biopharmaceutics of rectal administration of drugs in man. *Pharmaceutisch Weekblad.* 1979;1:201–206
18. DeBoer, AG, Moolenaar F, de Leede LG, Breimer DD., Rectal drug administration: clinical pharmacokinetic considerations. *Clin Pharmacokinet.* 1982 Jul-Aug;7(4):285-311.
19. Marijo Letizia, PhD, RN, C, APN, Ellen Norton, BSN, RN, CHPN. Successful Management of Malignant Bowel Obstruction. *Journal of Hospice and Palliative Nursing.* 2003;5(3); 152-158
20. Chaumeil JC, Khoury JM, Zuber M, Courteille F, Piraube C, Gard C. Formulation of suppositories containing imipramine and clomipramine chlorhydrates. *Drug Dev Ind Pharm.* 1988;14:2225–2239
21. Storey P, Trumble M. Rectal doxepin and carbamazepine therapy in patients with cancer. *N Engl J Med.* 1992;327:1318–1319
22. Adams S. Amitriptyline suppositories. *N Engl J Med.* 1982;306:996
23. Mirassou MM. Rectal antidepressant medication in the treatment of depression. *J Clin Psychiatry* 1998;59:29
24. De Jong PC, Verburg MP. Comparison of rectal to intramuscular administration of midazolam and atropine for premedication of children. *Acta Anaesthesiol Scand.* 1988 Aug;32(6):485-9.
25. Olsson GL, Bejersten A, Feychting H, Palmér L, Pettersson BM. Plasma concentrations of atropine after rectal administration. *Anaesthesia.* 1983 Dec;38(12):1179-82.
26. Bejersten A, Olsson GL, Palmér L. The influence of body weight on plasma concentration of atropine after rectal administration in children. *Acta Anaesthesiol Scand.* 1985 Nov;29(8):782-4.
27. Hyoscyamine Sublingual Tablet Information Dailymed:
<https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=e7953a64-3fa6-464c-bbce-8fc7efeebb91&type=display>.
Accessed 6/2/2022
28. Graves N, Kriel R, Jones-Saete C. Bioavailability of Rectally Administered Lorazepam. *Clinical Neuropharmacology.* 1987 Dec;10(6):555-559
29. Greenblatt D, Divoll M, Harmatz J, Shader R. Pharmacokinetic Comparison of Sublingual Lorazepam with Intravenous, Intramuscular, and Oral Lorazepam. *Journal of Pharmaceutical Sciences.* 1982;71(2):248-252
30. Appleton R, Sweeney A, Choonara I, Robson J, Molyneux E. Lorazepam versus diazepam in the acute treatment of epileptic seizures and status epilepticus. *Dev Med Child Neurol* 1995;37:682-8.

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31. Lyons N, Nejak D, Lomotan N, Mokszycki R, Jamieson S, McDowell M, Kulstad E. An alternative for rapid administration of medication and fluids in the emergency setting using a novel device. *Am J Emerg Med.* 2015 Aug;33(8):1113. e5-6.doi: 10.1016/j.ajem.2015.01.028.Epub 2015 Jan 21.
32. F. Moolenaar, S. Bakker, J. Visser, T. Huizinga, Biopharmaceutics of rectal administration of drugs in man IX. Comparative biopharmaceutics of diazepam after single rectal, oral, intramuscular and intravenous administration in man. *International Journal of Pharmaceutics.* 1980;5(2):127–137
33. Jensen B1, Matsson L.Oral versus rectal midazolam as a pre-anaesthetic sedative in children receiving dental treatment under general anaesthesia. *Acta Paediatr.* 2002;91(8):920-925.
34. Saint-Maurice C, Meistelman C, Rey E., Esteve C, De Lauture D, Olive G. The Pharmacokinetics of Rectal Midazolam for Premedication in Children. *Anesthesiology.* 1986;65:536–538
35. Clausen TG, Wolff J, Hansen PB, et al. Pharmacokinetics of midazolam and alpha-hydroxy-midazolam following rectal and intravenous administration. *British Journal of Clinical Pharmacology.* 1988 Apr;25(4):457-463.
36. Moolenaar F, Koning B, Huizinga T. Biopharmaceutics of rectal administration of drugs in man. Absorption rate and bioavailability of phenobarbital and its sodium salt from rectal dosage forms. *International Journal of Pharmaceutics.* 1979;4:99-109
37. Lam Y, Lam A, Macy B. Pharmacokinetics of phenobarbital in micro- enema via Macy Catheter versus suppository. *J Pain Symptom Manage.* 2016;51(6):994-1001.
38. Slikkerveer, M & Van Rossum, L & Krings, A.W.H. Pharmacokinetics of levetiracetam after rectal administration in healthy volunteers. *Pharmaceutisch Weekblad.* 2010;145:151-153.
39. Birnbaum AK1, Kriel RL, Burkhardt RT, Rimmel RP. Rectal absorption of lamotrigine compressed tablets. *Epilepsia.* 2000;41(7): 850-3.
40. Yoshiyama Y, Nakano S, Ogawa N. Chronopharmacokinetic study of valproic acid in man: comparison of oral and rectal administration. *J Clin Pharmacol.* 1989;29:1048-1052
41. Graves NM, Kriel RL, Jones-Saete C, Cloyd JC. Relative bioavailability of rectally administered carbamazepine suspension in humans. *Epilepsia.* 1985;26(5):429-33
42. Trapnell BC, Mavko LE, Birkovich LM, Falko JM. Metoclopramide suppositories in the treatment of diabetic gastroparesis. *Arch Intern Med.* 1986;146(11):2278-9.
43. Hardy F, Warrington PS, MacPherson JS, Hudson SA, Jefferson GC, Smyth JF. A pharmacokinetic study of high-dose metoclopramide suppositories. *J Clin Pharm Ther.* 1990 Feb;15(1):21-4.
44. Cantisani C, Ricci S, Grieco T, Paolino G, Faina V, Silvestri E, Calvieri S. Topical promethazine side effects: our experience and review of the literature. *Biomed Res Int.* 2013;2013:151509.

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45. Strenkoski-Nix LC, Ermer J, DeCleene S, Cevallos W, Mayer PR. Pharmacokinetics of promethazine hydrochloride after administration of rectal suppositories and oral syrup to healthy subjects. *Am J Health Syst Pharm.* 2000 Aug 15;57(16):1499-505.
46. Hsyu PH, Pritchard JF, Bozigian HP et al. Comparison of the pharmacokinetics of an ondansetron solution (8 mg) when administered intravenously, orally, to the colon and to the rectum. *Pharm Res.* 1994;11:156-159.
47. VanDenBerg CM, Kazmi Y, Stewart J, Weidler DJ, Tenjarla SN, Ward ES, Jann MW. Pharmacokinetics of three formulations of ondansetron hydrochloride in healthy volunteers: 24-mg oral tablet, rectal suppository, and i.v. infusion. *Am J Health Syst Pharm.* 2000;57(11):1046-50.
48. Webster JA, Dowse R, Walker RB. In vitro release of amoxicillin from lipophilic suppositories. *Drug Dev Ind Pharm.* 1998;24:395-399
49. Stratchunsky LS, Nazarov AD, Firsov AA, Petrachenkova NA. Age dependence of erythromycin rectal bioavailability in children. *Eur J Drug Metab Pharmacokinet.* 1991;3:321-3.
50. Somogyi AA, Bochner F, Hetzel D, Williams DB. Evaluation of the intestinal absorption of erythromycin in man: absolute bioavailability and comparison with enteric coated erythromycin. *Pharm Res.* 1995 Jan;12(1):149-54.
51. Bergström BK, Bertilson SO, Movin G. Clinical evaluation of rectally administered ampicillin in acute otitis media. *J Int Med Res.* 1988 Sep-Oct;16(5):376-85.
52. Liedtke, R. and Haase, W. Steady-state pharmacokinetics of sulfamethoxazole and trimethoprim in man after rectal application. *Arzneimittel-Forschung.* 1979;29:345-349.
53. Vromans H, Moolenaar F, Visser J, Meijer DK (1984) Rectal absorption of metronidazole from polyethylene glycol suppositories. *Pharm Weekbl* 6:18-20
54. Lie-A-Huen, L., Proost, J.H., Kingma, J.H. et al. Absorption kinetics of oral and rectal flecainide in healthy subjects. *Eur J Clin Pharmacol.* 1990;38:595-598.
55. de Boer AG, Breimer DD, Mattie H, Pronk J, Gubbens-Stibbe JM. Rectal bioavailability of lidocaine in man: partial avoidance of "first-pass" metabolism. *Clin Pharmacol Ther.* 1979 Dec;26(6):701-9
56. Kurosawa, N., Owada, E., Ito, K., Ueda, K., Takahashi, A., & Kikuri, T. Bioavailability of nifedipine suppository in healthy subjects. *International Journal of Pharmaceutics.* 1985;27:81-88.
57. Kurosawa, S., Kurosawa, N., Owada, E., Matsuhashi, N., & Ito, K. Rectal Administration of Nifedipine: Haemodynamic Effects and Pharmacokinetics in Hypertensives. *Journal of International Medical Research.* 1987;15:121-127.
58. de Stoppelaar FM, Stolk LM, Beysens AJ, Stappers JL, Gorgels AP. The relative bioavailability of metoprolol following oral and rectal administration to volunteers and patients. *Pharm World Sci.* 1999 Oct;21(5):233-8.

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59. Cid E, Mella F, Lucchini L, Cárcamo M, Monasterio J. Plasma concentrations and bioavailability of propranolol by oral, rectal, and intravenous administration in man. *Biopharm Drug Dispos.* 1986 Nov-Dec;7(6):559-66.
60. Hammouda, Y, Nada, A, & Kasim, N.A. Formulation and in-vivo evaluation of verapamil HCl suppositories. *European Journal of Pharmaceutics and Biopharmaceutics.* 1996;42:340-344.
61. Levy, R. Rectal Digitalis Therapy. *Archives of Internal Medicine.* 1924;33(6):742-757.
62. Porter, E. Therapeutic Use of Drugs of the Digitalis Group. *Quarterly Journal of Medicine.* 1932;5(New Series):33 - 47
63. Haloperidol Summary Report. UMB digital Archive.
https://archive.hshsl.umaryland.edu/bitstream/handle/10713/14906/Haloperidol_Final_2020_12.pdf?sequence=1
Accessed 6/7/2022
64. Matsumoto K, Kimura S, Takahashi K, Yokoyama Y, Miyazawa M, Kushibiki S, Katamachi M, Kizu J. Pharmaceutical studies on and clinical application of olanzapine suppositories prepared as a hospital preparation. *J Pharm Health Care Sci.* 2016 Sep 21;2:20
65. Leung JG et al. A Single-Dose Crossover Pharmacokinetic Comparison Study of Oral, Rectal and Topical Quetiapine in Healthy Adults. *Clin Pharmacokinetics.* 2016 Aug;55(8):971-6.
66. Regdon G, Fazekas T, Regdon G Jr, Selmeczi B. Formulation and in vitro examination of furosemide-containing suppositories and preliminary experiences of their clinical use. *Die Pharmazie* 1996; 51(2):116-119.
67. Yagi N, Kenmotsu H, Shimode Y, Oda K, Sekikawa H, Takada M. Bioavailability and diuretic effect of bumetanide following rectal administration of suppositories containing weak acids in human subjects. *Biol Pharm Bull.* 1993 Nov;16(11):1124-9
68. Freeman DJ, Meyer OO. Rectal Administration of Warfarin (Coumadin) Sodium. Sodium [3(2-acetonyl-benzyl)-4-hydroxycoumarin]. *Proceedings of the Society for Experimental Biology and Medicine.* 1956;92(1):52-55
69. McIver B, Walsh D, Nelson K. The use of chlorpromazine for symptom control in dying cancer patients. *J Pain Symptom Manage.* 1994 Jul;9(5):341-5.