

Appendix A
40.10.03a Instillation of Medication into Peritoneal Dialysis Solution

INTRA-PERITONEAL*	<u>Lidocaine without epinephrine</u>	<u>Metoclopramide</u>	<u>Sodium Bicarbonate</u>
Indication	Abdominal cramps or pain only after investigations support that the pain is related to the dialysate solution. Avoid risk of masking pain related to other causes (e.g infection). Not indicated if the source of pain is unknown.	Control of nausea or diabetic gastroparesis if the oral route is not tolerated or not beneficial.	Abdominal pain or cramps felt to be related to pH of dialysate.
Dose**	2.5 mL/L (50 mg per 2L exchange)	5 mg/L (10 mg per 2 L exchange)	2 – 5 mL/L (4 – 10 mmol per 2L exchange)
Availability	Injectable lidocaine 1% (10 mg/mL): 2 ml, 5 ml, 10 ml, 20 ml vials.	Injectable metoclopramide (5 mg/mL): 2 ml, 10 ml vials.	Injectable sodium bicarbonate 8.4% (1 mmol/mL): 50 ml vial. Discard vial 24 hours after initial puncture
Compatibility	Use only with standard solution (Dianeal). <i>Dose and compatibility based on practice. Use immediately after preparation.</i>	Use only with standard solution (Dianeal). <i>Dose and compatibility based on practice. Use immediately after preparation.</i>	Compatible with Dianeal 1.5%, 2.5%, 4.25% (based on compatibility studies) Stable for 24 hours at room temperature or 5 hours at body temperature (32-38 °C) Current site practice: compatible in 0.5% Dianeal (not verified by compatibility study)
Caution	Systemic absorption is unlikely but may occur. Monitor for <u>CNS</u> (disorientation, confusion, psychosis, tremors, convulsions, respiratory arrest) and <u>Cardiovascular</u> (myocardial depression, hypotension) adverse effects. Epinephrine can cause abdominal vasoconstriction, which may decrease the effectiveness of the dialysis so lidocaine mixed with epinephrine is not indicated.	Clinically significant systemic absorption has been reported with long term use (> 6 months). Monitor for extra-pyramidal symptoms (e.g. tremor, bradykinesia, dyskinesia).	Addition of sodium bicarbonate to the dialysate increases the sodium concentration and may increase risk of developing sodium overload with hypertension.

*Physician's order is required prior to administration of intra-peritoneal drugs

** Inject into dialysis solution before infusing

References attached.

Appendix A
40.10.03a Instillation of Medication into Peritoneal Dialysis Solution

<u>INTRA-PERITONEAL*</u>	<u>Heparin</u>	<u>Deferoxamine Mesylate</u> (Desferal, Desferrioxamine)	<u>Insulin</u>
Indication	Presence of fibrin in dialysate bags, for slow drainage and for hemoperitoneum Confirmation of catheter patency	Iron and Aluminum Chelating Agent Chronic iron overload due to transfusion-dependent anemias (e.g. thalassemia, sickle cell anemia, myelodysplastic syndrome) Chronic aluminum overload in patients with End-Stage Renal Failure (ESRF) undergoing maintenance dialysis	NOT RECOMMENDED Most Canadian PD units use subcutaneous insulin and not IP insulin. ² <u>Disadvantages:</u> <ul style="list-style-type: none"> ▪ More difficult to adjust when timing of meals or CAPD schedules altered ▪ Increased risk of peritonitis^{3,4} ▪ Higher total insulin dose^{3,5} ▪ High variability in peritoneal insulin absorption that is not related to membrane transport status.⁶ ▪ Lower HDL and higher triglyceride levels⁵
Dose**	500-1000 units/L - To each bag until effluent clears	500 – 1000 mg IP once daily [†] OR 2000 mg IP every 2-3 days [†] Given in night bag Allow to dwell for minimum of 6 hours <u>Alternate dose for Aluminium toxicity:</u> 5 mg/kg/dose given IP once per week in final daily exchange OR 2000 mg IP three times weekly in overnight exchange [†]	
Availability	1000 units/ml (10 ml vials)	Injectable 500 mg and 2 g vials. Reconstituted with Sterile Water For Injection to final concentration of 210 mg/mL.[refer to package insert or product monograph for reconstitution instructions.]	NOTE: Dextrose-containing dialysate can significantly raise the blood sugar. All patients who are starting PD should have their blood sugars monitored during the initiation phase with antihyperglycemic therapies adjusted appropriately. Note that when switching from PD to HD, a patient may require a significant decrease in antihyperglycemic therapy at time of switch.
Compatibility	Dextrose (Dianeal) – compatible (in vitro) Icodextrin (Extraneal) – compatible (in vitro) Nutrineal PD4 in Viaflex - compatible (in vitro)	Compatible with 1.5% and 4.25% dextrose PD fluids (Dianeal) <i>(Based on compatibility studies using dose of 700 mg/2 L bag (350 mg/L), compatibility of 1000 mg dose based on local practice)</i>	

Appendix A
40.10.03a Instillation of Medication into Peritoneal Dialysis Solution

Stability		Protect from light <i>Use immediately after preparation</i>	
Caution/ Safety Notes	<p>Limited animal and ex vivo studies suggest that heparin may have dose-dependent adverse effect on peritoneal mesothelial cells. The use of the smallest effective dose is therefore recommended. Doses of 500 to 1000 units per liter of peritoneal dialysate do not appear to cause peritoneal toxicity.</p> <p>Although intraperitoneal instillation of heparin does not affect systemic coagulation parameters or increase bleeding risk, heparin may still reach the systemic circulation. This is believed to occur by lymphatic absorption or with peritonitis due to increased peritoneal membrane permeability. IP heparin is therefore contraindicated in patients with heparin-induced thrombocytopenia (HIT).</p>	<p>Visual and auditory toxicity have been reported with chronic administration. Auditory and ophthalmic testing, including slit-lamp examination and dilated-fundus exam, should be performed at baseline and repeated yearly.</p> <p>-May increase risk of infection and peritonitis due to rise in dialysate iron concentrations.</p> <p>-May increase risk of infection with mucormycosis (zygomycosis), Yersinia, and Vibrio vulnificus.</p> <p>-Long term effect of deferoxamine on peritoneal membrane function unknown.</p> <p>-Deferoxamine may also be administered I.M., by slow I.V., or S.C. infusion. The mode of administration should be individually determined and the dosage adapted during the course of therapy.</p>	

*Physician's order is required prior to administration of intra-peritoneal drugs

** Inject into dialysis solution before infusing

† Dosing information obtained from Case Reports

References attached

Appendix A

40.10.03a Instillation of Medication into Peritoneal Dialysis Solution

References:

Intra-peritoneal lidocaine

1. Kathuria P et al. Peritoneal Dialysis Access and Exit-Site Care Including Surgical Aspects. In: Nolph and Gokal's Textbook of Peritoneal Dialysis, 3rd edition, 2009, pg 371-446.
2. Holley JL, Schmidt RJ. Noninfectious complications of continuous peritoneal dialysis. UpToDate Online 17.3.
3. Bunchman TE, Ballal SH. Treatment of inflow pain by pH adjustment of dialysate in peritoneal dialysis. Perit Dial Int 1991;11:179-80.
4. University Health Network Division of Nephrology Housestaff/ACNP Guidebook, June 2007, Toronto, Canada.
5. Davis V, Lavandero R. Caring for the catheter carefully ...before, during, and after peritoneal dialysis. Nursing 2010 1980:10; 67-71.
6. Lidocaine Adult Parenteral Drug Monograph, WRHA.

Intra-peritoneal metoclopramide

1. Seibert DO. Intraperitoneal metoclopramide improves symptoms of gastroparesis in a CAPD patient. Perit Dial Int 1989;9:223-4.
2. Perez MG. Intraperitoneal metoclopramide causing a movement disorder. Nephrol Dial Transplan 2002;17:945.
3. University Health Network Division of Nephrology Housestaff/ACNP Guidebook, June 2007, Toronto, Canada.

Intra-peritoneal Sodium Bicarbonate

1. Dorval et al. Practical aspects of the addition of sodium bicarbonate to peritoneal dialysate. Perit Dial Int 2000; 20:791-3.
2. Bunchman TE, Ballal SH. Treatment of inflow pain by pH adjustment of dialysate in peritoneal dialysis. Perit Dial Int. 1991;11:179-80.
3. Kathuria P et al. Peritoneal Dialysis Access and Exit-Site Care Including Surgical Aspects. In: Nolph and Gokal's Textbook of Peritoneal Dialysis, 3rd edition, 2009, pg 371-446.
4. Holley JL, Schmidt RJ. Noninfectious complications of continuous peritoneal dialysis. UpToDate Online 17.3.
5. Bailie GR et al. Peritoneal Dialysis 2006, A guide to medication use. Nephrology Pharmacy Associates.
6. University Health Network Division of Nephrology Housestaff/ACNP Guidebook, June 2007, Toronto, Canada.

Intra-peritoneal heparin

1. Goel S et al. The rationale for, and role of, heparin in peritoneal dialysis. Adv Perit Dial 1998;14:111-5.
2. Takahashi S et al. Effect of intraperitoneal administration of heparin to patients on continuous ambulatory peritoneal dialysis (CAPD). Perit Dial Int. 1991;11:81-3.
3. Kam-Tao Li et al. Peritoneal Dialysis-Related Infections Recommendations: 2010 Update. Perit Dial Int 2010;30:397.
4. Bailie GR et al. Peritoneal Dialysis, A guide to medication use, 2006. Nephrology Pharmacy Associates, Inc. www.nephrologypharmacy.com
5. University Health Network Division of Nephrology Housestaff/ACNP Guidebook, June 2007, Toronto, Canada. http://ukidney.com/images/stories/uhnmanual_2007.pdf



Appendix A

40.10.03a Instillation of Medication into Peritoneal Dialysis Solution

6. St Micheal's Hospital Resident Orientation to Nephrology & Renal Transplant, 3rd edition, Jan 2010, Toronto, Canada.
<http://ukidney.com/images/stories/smhmanual.pdf>
7. De Vin F. et al. Intraperitoneal Administration of Drugs in Peritoneal Dialysis Patients: A Review of Compatibility and Guidance for Clinical Use. *Perit Dial Int* 2009;29(1):5-15.
8. Voges M et al. Stability of Drug Additives in Peritoneal Dialysis Solutions in a New Container. *Perit Dial Int* 2004;24:590-595.
9. Crabtree JH et al. Care of the Adult Patient on Peritoneal Dialysis: Access Care and Complications Management Update 2012. Baxter Healthcare Corp.
10. Kaplan GG, Manns B, McLaughlin K. Heparin induced thrombocytopenia –to intraperitoneal heparin exposure. *Nephrol Dial Transplant*. 2005; 20:2561-2562.

Intra-peritoneal deferoxamine mesylate

1. Product Information: Desferal®. Deferoxamine Mesylate for Injection. Novartis Pharmaceuticals Canada Inc., Dorval, QC, 2011.
2. Taber TE et al. Treatment of Iron Overload in Continuous Ambulatory Peritoneal Dialysis Patients. *Trans Am Soc Artif Inter Organs* 1987;36:654-656.
3. Falk RI et al. Iron removal during continuous ambulatory peritoneal dialysis using deferoxamine. *Kidney Int* 1982;24:110-112.
4. Swartz RD et al. Long-term Intraperitoneal Deferoxamine For Hemochromatosis. *Am J Med* 1996;100:308-312.
5. Hercz G et al. Aluminum removal by peritoneal dialysis: intravenous vs intraperitoneal deferoxamine. *Kidney Int* 1986;30:944-48.
6. Molitoris et al. Efficacy of intramuscular and intraperitoneal deferoxamine for aluminum chelation. *Kidney Int* 1987;31:986-991.
7. Mactier RA. Aluminum and Deferoxamine Kinetics in CAPD. *Adv Perit Dial* 1991;7:26-9.
8. Deferoxamine. Micromedex Healthcare Series. DRUGDEX System. Greenwood Village, CO: Truven Health Analytics, 2013. <http://www.thomsonhc.com/>. Accessed May 12, 2014
9. Kane MP et al. Stability of Deferoxamine Peritoneal Dialysis Solutions. *Perit Dial Int* 1994; 14(4):396-8.
10. Brittenham GM et al. Iron-Chelating Therapy for Transfusional Iron Overload. *NEJM* 2011;364:146-56.

Intra-peritoneal insulin

1. St Micheal's Hospital Resident Orientation to Nephrology & Renal Transplant, 3rd edition, Jan 2010, Toronto, Canada.
<http://ukidney.com/images/stories/smhmanual.pdf>
2. Blake PG et al. Clinical Practice Guidelines and Recommendationson Peritoneal Dialysis Adequacy 2011. *Perit Dial Int* 2011;31:218-39
3. Selgas R et al. Comparative study of two different routes for insulin administration in CAPD diabetic patients. A multicenter study. *Adv Perit Dial* 1989;5:181-4.
4. Huang CC. Treatment targets for diabetic patients on peritoneal dialysis: any evidence? *Perit Dial Int* 2007;27(S2):S176-9.
5. Almalki MH, et al. Subcutaneous versus intraperitoneal insulin for patients with diabetes mellitus on continuous ambulatory peritoneal dialysis: meta-analysis of non-randomized clinical trials. *Clin Invest Med* 2012;35:E132-E143
6. Fine A, Parry D, Ariano R, Dent W. Marked variation in peritoneal insulin absorption in peritoneal dialysis. *Perit Dial Int* 2000; 20:652–5.