



A Little Ingenuity With a Big Impact

CODMAN 3000 implantable drug delivery system provides continuous hepatic arterial infusion (HAI) of chemotherapy directly to the site of the tumor.

- Reliable, accurate drug administration
- Large, domed, single-septum access
 - Easy access pathway for bolus procedures
 - Secure needle retention for bolus infusions
 - Easy to refill
- Smooth contours for patient comfort
- Totally implantable
 - Improves patient's freedom of mobility



Targeted Drug Delivery: Improved Tumor Response¹

HAI therapy allows the administration of regional chemotherapy and demonstrates a trend toward increased survival.^{2,3}

- Regional chemotherapy increases time to progression⁴
- HAI therapy enhances quality of life³
- Recent clinical research reports that liver resection and regional chemotherapy in combination with systemic chemotherapy shows an improved trend toward survival²

HAI Patient Selection Criteria⁵

- Liver metastases from colorectal cancer
- Radiographically documented absence of extrahepatic tumor
- Appropriate arterial anatomy documented by angiography
- Portal vein patency
- Absence of infection



Model 3000 - 30 mL

HAI Therapy Provides the Potential for Improved 2-Year and 5-Year Survival

Improved Survival Rates With Addition of HAI Therapy²

Study Endpoints	Combined Therapy (n=74)*	Monotherapy (n=82) [†]
2-year Median Survival	86%	72%
5-years (Actuarial)	61%	49%
2-year Disease-Free Survival	90%	60%
Median Disease-Free Survival	Not yet reached	42.7 months
5-year Disease-Free Survival	74% (23 patients)	44% (21 patients)

*Combined Therapy = Hepatic resection + regional floxuridine (FUDR) (actual dose delivered 0.15 mg/kg/day) (HAI) + systemic 5-FU (325 mg/m²) + bolus leucovorin (200 mg/m²).
[†] Monotherapy = Hepatic resection + systemic 5-FU (370 mg/m²) + leucovorin (200 mg/m²).

"Regional hepatic chemotherapy significantly improves the control of local disease in patients who undergo resection of liver metastases from colorectal cancer. The use of HAI plus systemic chemotherapy not only decreased the rate of hepatic recurrence but also improved two-year overall survival, as compared with the use of systemic chemotherapy alone."²



Adjuvant Chemotherapy Provides Significant Control of Liver Tumor Recurrence Following Liver Resection^{5,6}

	Combined Therapy [†]	Resection Alone	P Value
4-year Recurrence Rate	46%	25%	0.04
4-year Recurrence-Free Rate	67%	43%	0.03
Median Survival	63.7 months	49 months	0.60

[†] Combined Therapy = Hepatic resection + regional FUDR (0.1-0.2 mg/kg/day) (HAI) + systemic 5-FU (200-300 mg/m²) for 14 days.
[‡] 75 of the 109 patients enrolled in the study were assessable.

"...adjuvant intra-arterial and intravenous chemotherapy [is] beneficial in prolonging time to recurrence...after hepatic resection of colorectal cancer."⁶

High Tumor Response Rates in Patients With Unresectable Liver Metastases

- 74% tumor response rate in patients treated with HAI therapy + systemic chemotherapy[†] who were not eligible for liver resection⁷

[†]Regional FUDR (0.16 mg/kg/day) for 14 days + systemic irinotecan (100 mg/m²) for 21 days (non-cryosurgery patients).

Randomized Trials of HAI[†] vs Systemic Chemotherapy for Colorectal Liver Metastases

Study	Regimen	Patients	Response (%)	Key Points
MSKCC ⁸ (1987)	HAI: FUDR (with Pump) IV: FUDR	48 51	50% 20%	Allowed crossover
NCOG ⁹ (1989)	HAI: FUDR (with Pump) IV: FUDR	50 65	42% 10%	Allowed crossover
MAYO ¹⁰ (1990)	HAI: FUDR (with Pump) IV: 5-FU	33 36	48% 21%	First study to use IV 5-FU control arm ¹
Lorenz et al. ¹¹ (2000)	HAI: FUDR (with Port)[†] HAI: 5-FU/LV (with Port)[‡] IV: 5-FU/LV [‡]	54 57 57	43% 45% 20%	31% did not receive planned HAI treatment

MSKCC = Memorial Sloan-Kettering Cancer Center. NCOG = Northern California Oncology Group. HAI = Hepatic arterial infusion. IV = Systemic infusion. FUDR = Floxuridine. 5-FU/LV = 5-fluorouracil + leucovorin.

[†]Studies used a 0.3 mg/kg/day dose of FUDR in pump.

¹Study used a 0.2 mg/kg/day dose of FUDR reduced after 3 cycles to 0.15 mg/kg/day for 14 days every 28 days.

[‡]5-FU (1000 mg/m²) continuous infusion for 5 days + leucovorin (200 mg/m²) bolus for 5 days every 28 days.

HAI Can Enhance Quality of Life

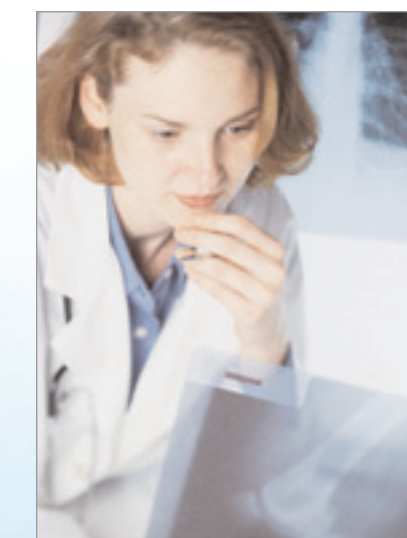
- A randomized trial by Allen-Mersh et al demonstrated that quality of life can be significantly improved for patients with colorectal liver metastases who receive HAI therapy⁸ vs no treatment or systemic therapy alone³



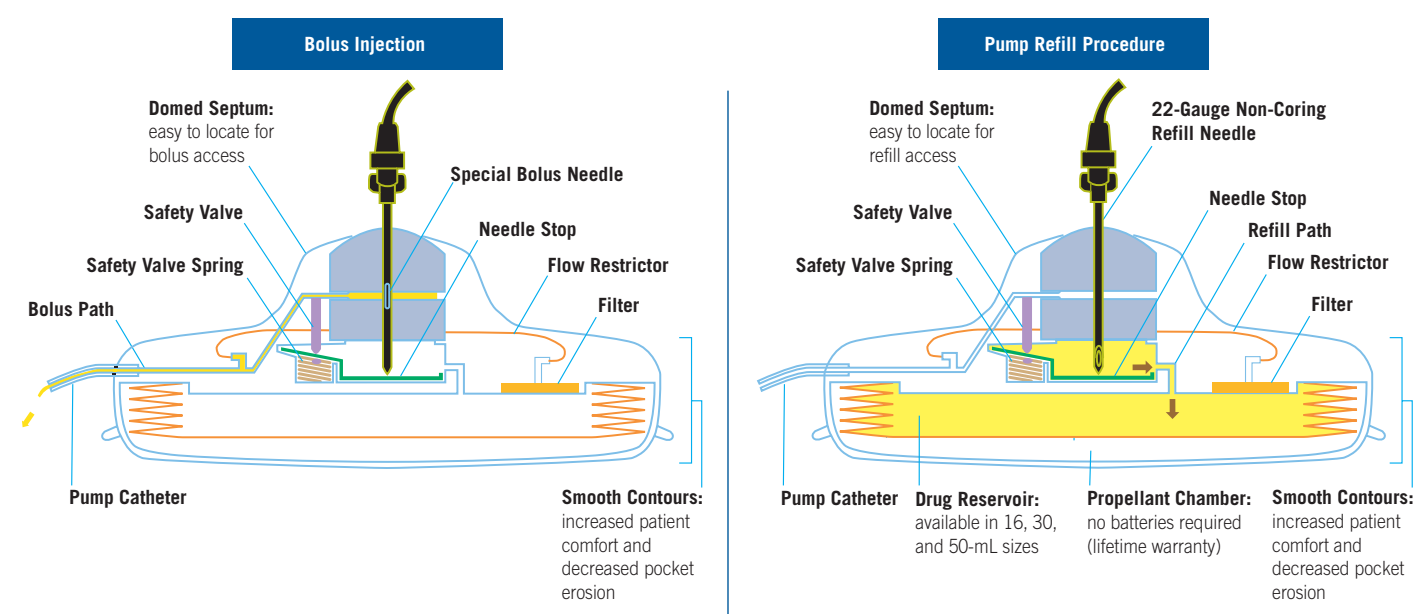
⁸Regional FUDR (0.2 mg/kg/day).

Factors Influencing Successful Use of HAI Therapy⁵

- Surgical ligation of collaterals to the stomach and duodenum
- Intraoperative perfusion of fluorescein dye to document liver perfusion, catheter placement, and missed collaterals
- Routine cholecystectomy to avoid drug-induced cholecystitis
- Postoperative HAPS study prior to initiation of HAI chemotherapy
- Careful monitoring of liver function tests (SGOT, alkaline phosphatase, bilirubin) with appropriate dose reduction or withholding of FUDR



CODMAN 3000 Delivers Reliable Single-Septum Access



Multiple Flow Rates Available

Pump Model	Labeled Intra-Arterial Flow Rate*†
16-mL Reservoir	1.00 mL/day
30-mL Reservoir	1.20 mL/day
50-mL Reservoir	2.50 mL/day

Glycerin Infusion‡ as Placebo During Interruption of HAI Chemotherapy in the CODMAN 3000 Pump

Pump Model	Labeled Intra-Arterial Flow Rate*	Approximate Refill Interval§
16-mL Reservoir	High	55 to 62 days
30-mL Reservoir	High	79 to 87 days
50-mL Reservoir	High	66 to 79 days

*Nominal flow rates are defined as the typical clinical flow rate in mL/day. The nominal or typical rate is defined at standard conditions: patient temperature 98.6°F; altitude sea level. Arterial manufactured flow rates are adjusted for arterial pressure (100 mm Hg with 1000 IU/mL heparin).

†Flow rates cited here are for CODMAN 3000 high-flow pumps.

‡50% glycerin solution.

§Refer to CODMAN 3000 glycerin instructions for refill period calculation.

The CODMAN 3000 is indicated for the continuous regional delivery of 2-deoxy-5-fluorouridine (FUDR) and glycerin as a placebo.

Reimbursement Assistance Program

To speak with a qualified reimbursement representative for information and assistance on reimbursement and precertification, call toll-free 1-800-609-1108, Monday through Friday, from 8:30 AM to 5:00 PM PST.

Accessories

To order any of the following accessories, please call 1-800-225-0460.

Hepatic Arterial Catheters:	AP-07003: Barbed Catheter Connector
	AP-01006: A•Port® Implantable Vascular Access System (0.6 mm ID x 2.3 mm OD) Pre-Attached Silicone Catheter With 3 Suture Beads
	AP-01007: A•Port Implantable Vascular Access System (0.6 mm ID x 2.3 mm OD) Detached Silicone Catheter With 3 Suture Beads
Pump Refill Supplies:	AP-07014: Model 3000 Series Refill Kit
	AP-04009: Non-Coring Refill Needle, 22 gauge x 1", Straight
	AP-04011: Non-Coring Refill Needle, 22 gauge x 1½", Straight
	AP-04030: Non-Coring Refill Needle, 22 gauge x 2", Straight
Special Bolus Needles:	AP-04013-5: Special Bolus Needles, 1⅜", Straight
	AP-04032-5: Special Bolus Needles, 2", Straight
	AP-04033-5: Special Bolus Winged Infusion Set, 1½", 90° Angle
	AP-04034-5: Special Bolus Winged Infusion Set, 1¾", 90° Angle

For additional information and assistance, call CODMAN Customer Service at 1-800-225-0460 or our 24-hour Technical Support Service at 1-800-660-2660.



References: 1. Skitzki JJ, Chang AE. Hepatic artery chemotherapy for colorectal liver metastases: technical considerations and review of clinical trials. *Surg Oncol.* 2002;11:123-135. 2. Kemeny M, Huang Y, Cohen AM, et al. Hepatic arterial infusion of chemotherapy after resection of hepatic metastases from colorectal cancer. *N Engl J Med.* 1999;341:2039-2048. 3. Allen-Mersh TG, Earlam S, Fordy C, Abrams K, Houghton J. Quality of life and survival with continuous hepatic-artery floxuridine infusion for colorectal liver metastases. *Lancet.* 1994;344:1255-1260. 4. Kemeny NE, Ron IG. Hepatic arterial chemotherapy in metastatic colorectal patients. *Semin Oncol.* 1999;26:524-535. 5. Venook AP. Update on hepatic intra-arterial chemotherapy. *Oncology.* 1997;11:947-954,957. 6. Kemeny MM, Adak S, Gray B, et al. Combined-modality treatment for resectable metastatic colorectal carcinoma to the liver: surgical resection of hepatic metastases in combination with continuous infusion of chemotherapy—an intergroup study. *J Clin Oncol.* 2002;20:1499-1505. 7. Kemeny N, Gonen M, Sullivan D, et al. Phase I study of hepatic arterial infusion of floxuridine and desamethasone with systemic irinotecan for unresectable hepatic metastases from colorectal cancer. *J Clin Oncol.* 2001;19:2687-2695. 8. Kemeny N, Daly J, Reichman B, Geller N, Bolef J, Oderman P. Intrahepatic or systemic infusion of fluorodeoxyuridine in patients with liver metastases from colorectal carcinoma: a randomized trial. *Ann Intern Med.* 1987;107:459-465. 9. Hohn DC, Stagg RJ, Friedman, et al. A randomized trial of continuous intravenous versus hepatic intraarterial floxuridine in patients with colorectal carcinoma metastatic to the liver: the Northern California Oncology Group Trial. *J Clin Oncol.* 1989;7(11):1646-1654. 10. Martin JK, O'Connell MJ, Wieand HS, et al. Intra-arterial floxuridine vs systemic fluorouracil for hepatic metastases from colorectal cancer: a randomized trial. *Arch Surg.* 1990;125:1022-1027. 11. Lorenz M, Müller H-H, for the German Cooperative Group on Liver Metastases. Randomized, multicenter trial of fluorouracil plus leucovorin administered via hepatic arterial or intravenous infusion versus fluorodeoxyuridine administered via hepatic arterial infusion in patients with nonresectable liver metastases from colorectal carcinoma. *J Clin Oncol.* 2000;18(2):243-254.

Codman
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For more information, contact your Codman Drug Delivery Sales Representative
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FOR PRODUCT INFORMATION, CALL: (800) 225-0460



There's Something Inside
Making a Big Difference...

CODMAN 3000
Implantable Constant-Flow Infusion Pump