

Drug Dispensing through the EDC in a Flexible Titrating Double Blinded Drug Trial



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Study Background

- Childhood and Adolescent Migraine Prevention (CHAMP) Study is a double blinded drug trial with a flexible titrating schedule to test if amitriptyline and topiramate are superior to placebo
- Clinical Coordinating Center – Cincinnati Children's Hospital Medical Center
- Data Coordinating Center – Clinical Trials Statistical and Data Management Center Department of Biostatistics University of Iowa
- Research Pharmacy – Cincinnati Children's Hospital Medical Center

Drug Dispensing Factors

- Weight based dosing
- Flexible titration schedule
- Weaning
- Central distribution to sites that may or may not have a site pharmacy
- Quality assurance (ensuring correct bottle was dispensed)
- Inventory
- Ease of site pharmacist/site coordinator to organize the bottles

Weight based dosing

Amitriptyline Dosing Schedule

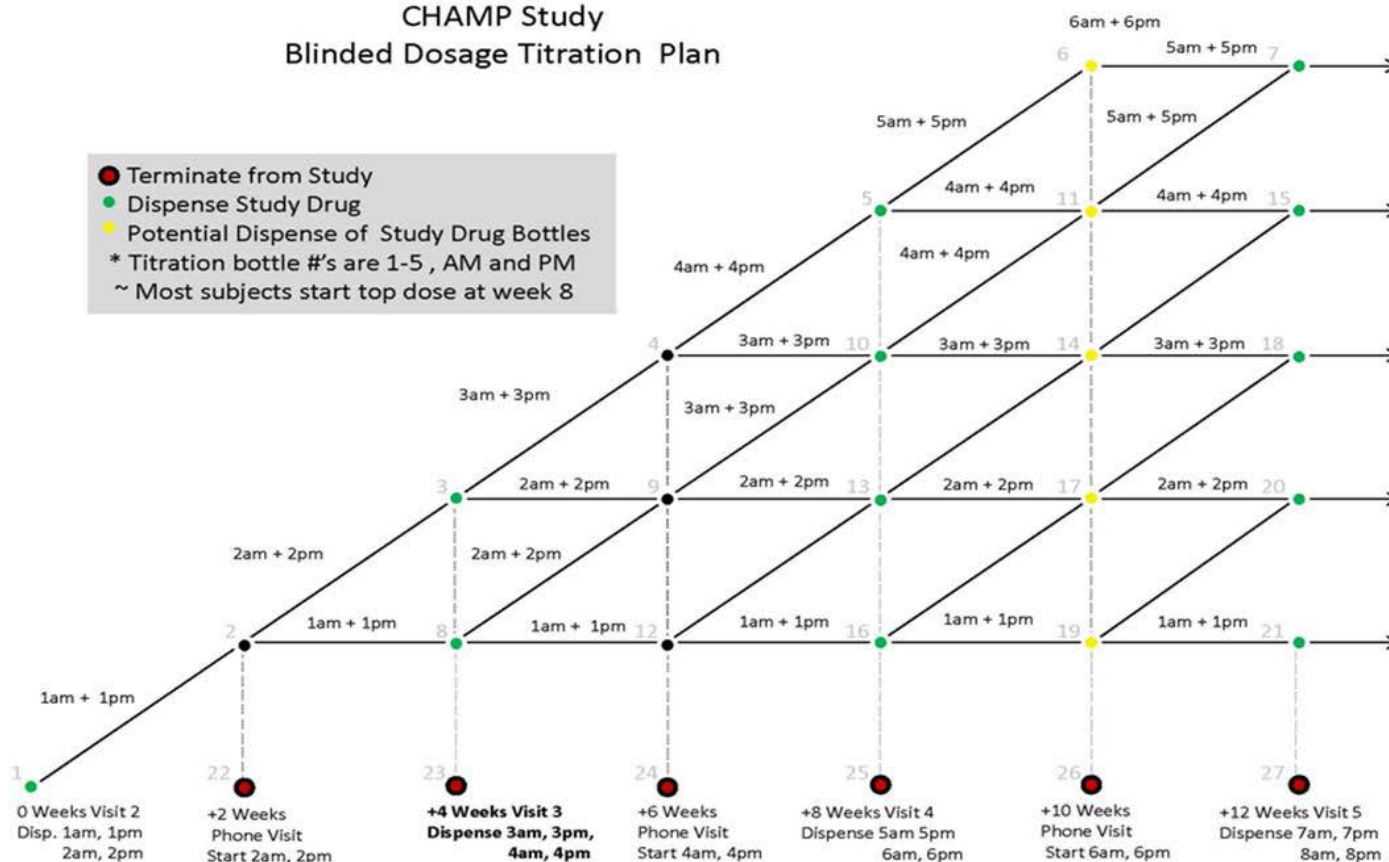
Weight Group (kg)	Weight Low (kg)	Range High (kg)	Start at Week 0		Start at Week 2		Start at Week 4		Start at Week 6		Start at Week 8	
			AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
40	30	44.9	0	10	0	20	0	20	0	30	0	40
50	45	54.9	0	10	0	20	0	30	0	40	0	50
60	55	64.9	0	10	0	20	0	30	0	50	0	75
70	65	74.9	0	20	0	30	0	40	0	50	0	75
80	75	84.9	0	20	0	30	0	50	0	75	0	75
90	85	94.9	0	20	0	40	0	50	0	75	0	75
100	95	120	0	20	0	40	0	50	0	75	0	100

Topiramate Dosing Schedule

Weight Group (kg)	Weight Low (kg)	Range High (kg)	Start at Week 0		Start at Week 2		Start at Week 4		Start at Week 6		Start at Week 8	
			AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
40	30	44.9	0	12.5	12.5	25	25	25	25	37.5	37.5	37.5
50	45	54.9	12.5	12.5	12.5	25	25	37.5	37.5	37.5	50	50
60	55	64.9	12.5	12.5	25	25	37.5	37.5	50	50	50	75
70	65	74.9	12.5	12.5	25	25	37.5	50	50	50	75	75
80	75	84.9	12.5	25	25	37.5	50	50	50	75	75	75
90	85	94.9	12.5	25	37.5	37.5	50	50	75	75	75	100
100	95	120	25	25	37.5	50	50	50	75	75	100	100

Flexible titration schedule

CHAMP Study Blinded Dosage Titration Plan



Weaning

Maximum dosage achieved	Week	Week	Week	Week	Week	Week	Week	Week
	24 – 26 Day 1-5	24 – 26 Day 1-5	24 – 26 Day 6-10	24 –26 Day 6-10	24-26 Day 11-14	24-26 Day 11-14	26-30	26 - 30
Amitriptyline	AM	PM	AM	PM	AM	PM	AM	PM
10	0	0	0	0	0	0	No drug	No drug
20	0	10	0	0	0	0	No drug	No drug
30	0	20	0	10	0	5	No drug	No drug
40	0	30	0	20	0	10	No drug	No drug
50	0	40	0	20	0	10	No drug	No drug
75	0	50	0	40	0	20	No drug	No drug
100	0	75	0	50	0	20	No drug	No drug
Topiramate	AM	PM	AM	PM	AM	PM	AM	PM
12.5	0	0	0	0	0	0	No drug	No drug
25	0	12.5	0	0	0	0	No drug	No drug
37.5	0	25	12.5	12.5	0	12.5	No drug	No drug
50	12.5	25	12.5	12.5	0	12.5	No drug	No drug
62.5	25	25	12.5	25	12.5	12.5	No drug	No drug
75	25	25	12.5	25	12.5	12.5	No drug	No drug
87.5	37.5	37.5	25	25	12.5	12.5	No drug	No drug
100	25	50	25	25	12.5	12.5	No drug	No drug
125	50	50	37.5	37.5	12.5	25	No drug	No drug
150	50	50	25	50	12.5	25	No drug	No drug
175	50	75	25	37.5	12.5	25	No drug	No drug
200	75	75	37.5	37.5	25	25	No drug	No drug

Designing the EDC Drug Dispensing System

Dose schedule

ScheduleID	RandTypeID	WeightGrp	wghtLow	wghtHigh	ScheduleTxt	DoseAM	DosePM	DoseTotal
1	1	40	30	44.9	Titration 1	0	10	10
2	1	40	30	44.9	Titration 2	0	20	20
3	1	40	30	44.9	Titration 3	0	20	20
4	1	40	30	44.9	Titration 4	0	30	30
5	1	40	30	44.9	Maintenance	0	40	40
9	1	50	45	54.9	Titration 1	0	10	10
10	1	50	45	54.9	Titration 2	0	20	20
11	1	50	45	54.9	Titration 3	0	30	30
12	1	50	45	54.9	Titration 4	0	40	40
13	1	50	45	54.9	Maintenance	0	50	50
57	2	40	30	44.9	Titration 1	0	12.5	12.5
58	2	40	30	44.9	Titration 2	12.5	25	37.5
59	2	40	30	44.9	Titration 3	25	25	50
60	2	40	30	44.9	Titration 4	25	37.5	62.5
61	2	40	30	44.9	Maintenance	37.5	37.5	75
65	2	50	45	54.9	Titration 1	12.5	12.5	25
66	2	50	45	54.9	Titration 2	12.5	25	37.5
67	2	50	45	54.9	Titration 3	25	37.5	62.5
68	2	50	45	54.9	Titration 4	37.5	37.5	75
69	2	50	45	54.9	Maintenance	50	50	100

Designing the EDC Drug Dispensing System

Drug Dispensing eCRF

1. Date of visit: ___ / ___ / 20 ___ (mm/dd/yyyy)

2. Study phase

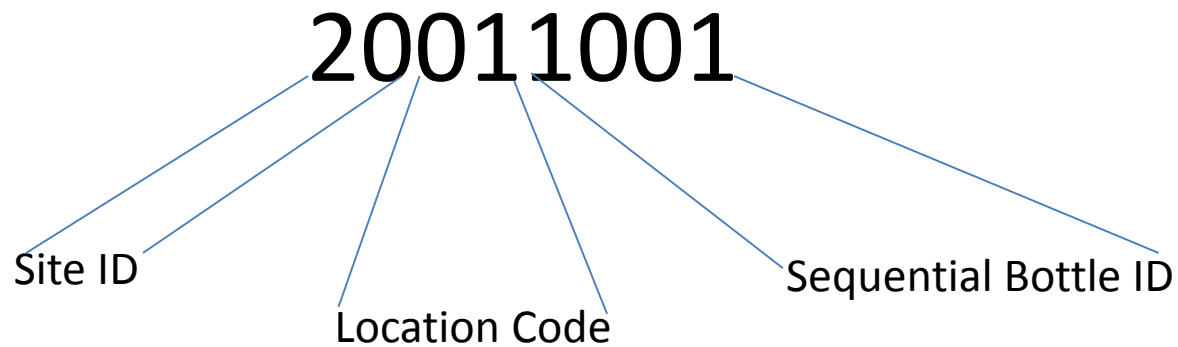
- Titration (Complete item 2.a)
- Maintenance
- Weaning

a. Titration decision

- Advance to next scheduled dose
- Maintain current dose
- Decrease dose

Designing the EDC Drug Dispensing System

Bottle number



Inventory

Order/Create bottles module

[Drug Activity](#) [Pharmacists Lookup](#)

Order bottles for center: ▼

Indicate the type of bottle and the quantity of bottle numbers of that type to generate:

Supply	Time Period	Drug	Dose	Expiration Date (mm/dd/yyyy)	Number of Bottles of Type
<input type="radio"/> Titration/Maintenance <input type="radio"/> Weaning	<input type="radio"/> AM <input type="radio"/> PM	- Not Selected - ▼	- Not Selected - ▼	<input type="text"/>	<input type="text"/>

[View Report](#)

Inventory

Bottle Lookup module

[Pharmacists Bottles](#)

Center:

Lookup Criteria				
Supply	Time Period	Drug	Dose	Status
<input type="radio"/> Titration/Maintenance <input type="radio"/> Weaning <input checked="" type="radio"/> Both	<input type="radio"/> AM <input type="radio"/> PM <input checked="" type="radio"/> Both	<input type="text" value="- All Drugs -"/>	<input type="text" value="- All Doses -"/>	<input type="radio"/> Not Shipped <input type="radio"/> Shipped <input type="radio"/> Available <input type="radio"/> Dispensed <input type="radio"/> Confirmed <input type="radio"/> Returned <input type="radio"/> Unavailable <input type="radio"/> Expired <input checked="" type="radio"/> All But Expired

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Inventory

Ship Bottles

[Pharmacists Lookup](#)

Enter Bottle Number:

Add to List of Shipped Items

Receive Bottles

Enter Bottle Number:

Add to List of Available Items

Inventory

Inventory Control

[Pharmacists Bottles](#)

Drug Activity Criteria		
Center	Start Date	End Date
10 Akron Children's Hospital <input type="checkbox"/>	4/30/2014	5/1/2014

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Subject ID	Drug Assignment	Dose Decision	AM Dose Set 1	PM Dose Set 1	AM Dose Set 2	PM Dose Set 2	Visit Name	Date Dispensed
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Inventory

Early Termination Weaning

Weaning Lookup

Enter PID:

Weaning doses for subject 20-1001:

Drug	AM Dose	PM Dose
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Offline Dispensing

- Used only when the system was used improperly
- Central Pharmacist directly dispenses to subject
- Drug dispensing eCRF marked as unobtainable
- Bottles assigned to subject directly in the database

Summary

- 32 active sites
- 223 users
- 275 randomized subjects
- 4552 bottles dispensed
- 2 subjects dispensed offline

Designing the EDC Drug Dispensing System

Questions?