

**ICCTG – Elmiron and Hydroxyzine / SAS Datasets  
Documentation**

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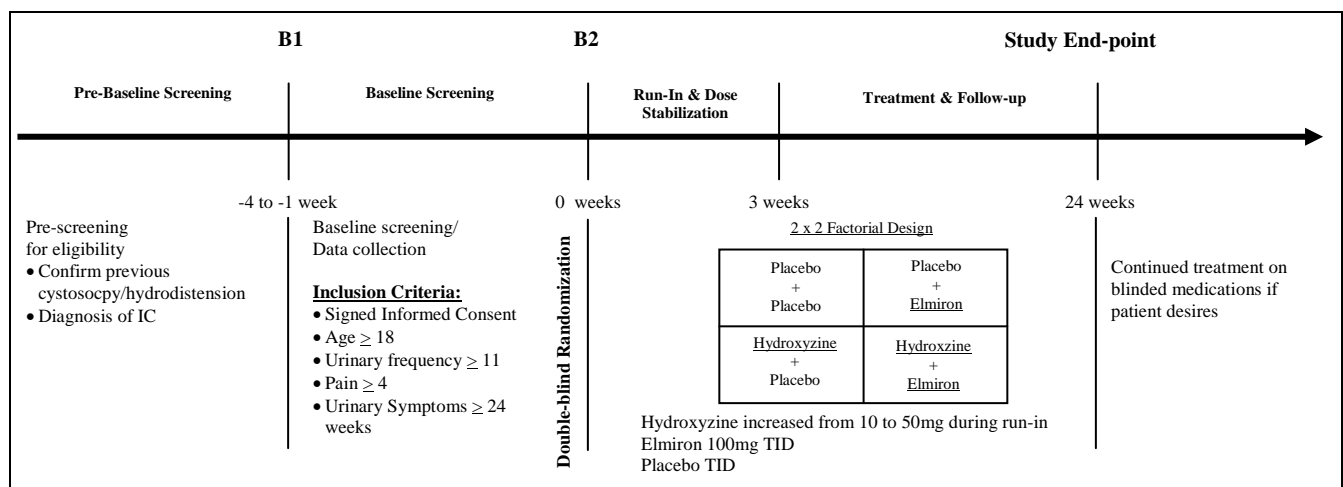
## **I. Overview of Elmiron and Hydroxyzine Study**

## Elmiron and Hydroxyzine Study Design

This study will utilize a 2 x 2 factorial design to evaluate the effectiveness of 1) placebo plus placebo, 2) placebo plus Elmiron® 3) hydroxyzine plus placebo 4) hydroxyzine plus Elmiron® in the improvement of moderate to severe symptoms of pain/discomfort and frequency in IC participants. Approximately 136 participants with clinically diagnosed moderate to severe IC will be recruited from eight clinical sites throughout the United States.

This study is comprised of two distinct phases for each participant: i) the screening phase and ii) the treatment and follow-up phase (figure 1). The screening phase, which assesses a participant's eligibility via inclusion, exclusion and deferral criteria, will consist of two "baseline" visits no more than 4 weeks and no less than 7 days apart. Any candidate failing any of the inclusion or exclusion criteria will be considered ineligible for the protocol and treated according to usual clinical care. Some participants who initially fail study entry criteria may later be reconsidered for inclusion if the exclusionary conditions resolve. Any participant meeting all of the criterion will then be eligible for randomization to one of the four treatment arms. After randomization, participants are asked to return to the clinic for follow-up visits at weeks 3, 10, 17 and 24. Study medications will be dispensed at each clinic visit and participants will be asked to complete several quality of life and symptom scale questionnaires. At week 24, any participant requesting to continue on study medication will be provided masked medication until the study is closed. These participants will be followed every 12 weeks.

**Figure 1**



## **Eligibility Criteria**

### **Inclusion criteria**

1. Participant must be at least 18 years of age.
2. Participant must sign and date the informed consent.
3. Participant (male or female) must agree to use an effective method of birth control.
4. Participant must report a urinary frequency of at least 11 times per 24-hour day, on average over the previous four weeks. This frequency criterion must be met at each of the two baseline-screening visits as reported by the participant.
5. Participant must report a pain/discomfort score of 4 or greater on a 0 - 9 Likert scale. This pain/discomfort criterion must be met at each of the two baseline-screening visits.
6. These reported urinary symptoms of frequency and pain/discomfort must have been present for at least the previous 24 weeks prior to the first baseline screening visit (B1).

### **Exclusion criteria**

1. Currently participating in another intervention study.
2. Any imminent change in residence outside the driving distance of the ICCTG network within the next 24 weeks.
3. Participant unlikely to be compliant due to medical or psychological problem.
4. A history of having been previously treated with Cytosan<sup>®</sup>/cyclophosphamide.
5. A history of pelvic radiation treatment.
6. Having been previously treated with at least 100 mg TID of Elmiron<sup>®</sup> or greater than 10 mg of hydroxyzine per day for greater than 12 consecutive weeks.
7. Having had augmentation cystoplasty.
8. Having had a cystectomy or cystolysis.
9. Having had a neurectomy (i.e. hypogastric nerve plexus ablation) or implanted peripheral nerve stimulator which has affected bladder function.
10. A history of a bladder calculus.
11. A history of tuberculous cystitis.
12. A history of neurologic disease or diabetic cystopathy.

13. A history of malignant bladder tumors.
14. A history of urethral cancer.
15. Reports a urinary void with a maximum volume > 350 cc, as measured by a 24 hour-voiding diary.
16. Currently has an active urethral calculus.
17. Currently has a ureteral calculus.
18. Symptomatic urethral diverticulum.
19. Has an LFT > 1.5 times the respective institution's upper limits of normal at the Baseline 1 screening visit.
20. Has abnormal blood coagulation tests results: INR or PTT (aPTT).
21. Has platelet test results outside the respective institution's normal range.
22. Reports any allergies to Elmiron<sup>®</sup> or hydroxyzine.
23. Currently taking cimetidine or currently on intravesical heparin.
24. Chronic use (more than 3 out of 7 days each week) of greater than one gram of acetylsalicylic acid (e.g. aspirin, Bayer<sup>®</sup>, Anacin<sup>®</sup>, Excedrin<sup>®</sup>, etc.).
25. Chronic use (more than 3 out of 7 days each week) of aspirin replacement products (acetaminophen, NSAIDs, etc.) of more than the amount of milligrams in the maximum single dose allowed by the Physicians' Desk Reference for prescription use, spread out over 24 hours.
26. Chronic use (more than 3 out of 7 days each week) of sedating histamine-1 receptor antagonists (only those containing diphenhydramine, brompheniramine, or chlorpheniramine).

Exclusion criteria for men only:

27. Having a residual urine volume >150 cc by ultrasound or catheter.
28. Having had a TURP, TUIP, TUIBN, TUMT, TUNA, balloon dilation of the prostate, open prostatectomy or any other prostate surgery or treatment such as cryotherapy or thermal therapy.
29. Currently being treated for chronic bacterial prostatitis as documented by a positive urine culture.

Exclusion criteria for women only:

30. Having had uterine, cervical or vaginal cancer during the past 3 years.
31. Having active vaginitis.
32. Currently pregnant.
33. Currently breastfeeding.

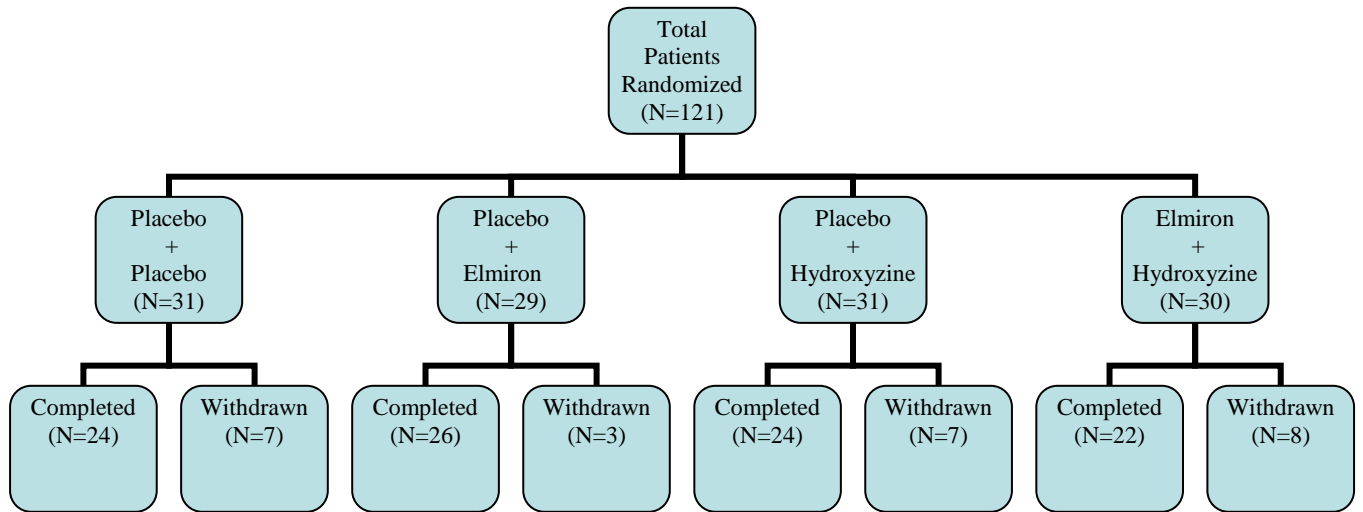
## **Deferral criteria**

1. If a participant has initiated any new medications for IC during the past 4 weeks, he/she will be deferred until he/she has been on the same dose for at least 4 weeks.
2. If a participant has undergone any of the following during the past 6 weeks: urethral dilation, cystometrogram, urodynamics, bladder cystoscopy /hydrodistention under general or regional anesthesia, or bladder biopsy under general or regional anesthesia, he/she will be deferred until at least 6 weeks from the date of the procedure.
3. If a participant has had a positive urine culture and/or clinical evidence of bacterial UTI during the past 6 weeks, he/she will be deferred until the participant has been without the condition for at least 6 weeks.
4. If a participant has had gross hematuria during the past 12 weeks, he/she will be deferred until the participant has been without the condition for at least 12 weeks.
5. If a participant has active genital herpes or has had active genital herpes during the past 12 weeks, he/she will be deferred until the participant has been without the condition for at least 12 weeks.
6. If a participant has received treatment with Elmiron<sup>®</sup> or hydroxyzine, he/she will be deferred until the participant has been off drug for a minimum of 12 weeks prior to study entry.
7. If a participant has had any intravesical treatment, other than BCG during the past 12 weeks, he/she will be deferred until at least 12 weeks after the last treatment received.
8. If a participant has received intravesical BCG during the past 24 weeks, he/she will be deferred until at least 24 weeks have passed since the last dose of BCG.
9. If a participant has had a cystocele, rectocele, or urinary incontinence surgery, he/she will be deferred until at least 24 weeks from the date of the procedure.

### Deferral criteria for women only:

10. If a participant has had any form of hysterectomy, prolapse, vaginal delivery or C-section, she will be deferred until at least 24 weeks from the date of the procedure.

## Flow of Subjects Through Study



## **Type of Data Collected**

**Final Data Entry Case Report Forms**  
(See separate documents)



## **II. SAS Datasets**

| <b>SAS data set name</b>           | <b>II.1.1 Description/Form Title</b>  |
|------------------------------------|---|
| <b>1. Primary Analysis Dataset</b> |   |
| icctgrct1.sas7bdat                 | Include variables for the primary manuscript: demographics, primary endpoint and secondary endpoint variables |
| <b>2. Individual Dataset</b>       |   |
| aelog.sas7bdat                     | Adverse events and serious adverse events / AE  |
| basesymp.sas7bdat                  | Baseline Symptoms / BSYM1 and BSYM2   |
| demopk.sas7bdat                    | Demographics / DEMO   |
| diarylog.sas7bdat                  | Medication Diary Record / DIARYREC  |
| drugdic2.sas7bdat                  | Medication Code List  |
| fusympk.sas7bdat                   | Follow-up Symptoms / FUSYMP   |
| phonepk.sas7bdat                   | Telephone Contact / PHONE   |
| Ptclssg.sas7bdat                   | Patient Close-out / PTCLOSE   |
| sf36pk.sas7bdat                    | Health Status Questionnaire (SF-36TM) / SF36  |
| stopsg.sas7bdat                    | Study Stop Point / STOP   |
| stvispk.sas7bdat                   | Standard Visit Inventory / STVISIT  |
| symprop.sas7bdat                   | Interstitial Cystitis Symptom Index and Problem Index / SYMPROB   |
| univwpk.sas7bdat                   | University of Wisconsin Symptom Survey / univwis  |
| unmasksg.sas7bdat                  | Unmasking Record / UNMASK   |
| urinepk.sas7bdat                   | Urine Screening / URINE   |
| voidlog.sas7bdat                   | Voiding Log data / VOID   |