

# Controlled Release Clindamycin Vaginal Hydrogel Insert for the Treatment of Bacterial Vaginosis - Evidence of Sustained Vaginal Drug Levels Above Reported MIC Values

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## 1. Summary

This study details the intravaginal concentrations observed in 12 healthy volunteers up to 96 hours after dosing for 24 hours with a controlled release clindamycin vaginal insert (CVI). The data reported demonstrate that clindamycin intravaginal concentrations remain above reported MIC values up to 72 hours after removal of a 24 hour CVI.

## 2. Introduction

Controlled Therapeutics Scotland is developing a clindamycin vaginal insert (CVI) for the delivery of clindamycin (C) to treat bacterial vaginosis. A phase I clinical trial on 12 healthy volunteers was carried out using a 50mg and a 100mg CVI. Each of the 12 subjects underwent a lavage procedure at one of four time points 25, 48, 72 or 96 hours after CVI insertion. In each case the CVI was removed at 24 hours after insertion. Panty liners were collected up to the time of lavage. No liners were collected after the lavage procedure. The lavage and liner samples were analysed by high performance liquid chromatography (HPLC) to determine the presence of any C. This paper details the results obtained from this analysis. These results have been assessed in relation to literature reported levels of vaginal fluid and documented Minimum Inhibitory Concentration (MIC) levels for C. Controlled Therapeutics are developing a product to take into phase II clinical trials.

## 3. Experimental Methods

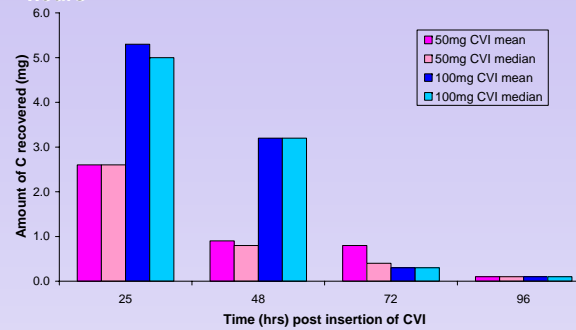
A stability indicating HPLC method for C phosphate was developed and adapted from the European Pharmacopoeia method. An aliquot of each lavage sample was diluted with acetonitrile to give a water/acetonitrile composition equivalent to the HPLC mobile phase aqueous/organic composition. Panty liners were extracted directly into mobile phase. Samples were filtered then injected onto the HPLC. The limit of quantitation of the assay is 0.1mg/liner and 0.1mg/lavage.

## 4. Results

Figure 1 details the mean and median amounts of C recovered from lavage samples (Table 1 in abstract). Mean C values ranging from 2.6mg to 0.1mg were recovered from lavage samples between 25 and 96 hours post insertion of a 50mg CVI. The corresponding values for a 100mg dose are 5.3mg to 0.1mg C.

**Acknowledgements:** LCG Bioscience

**Figure 1** Clindamycin recovered (mg) from lavage samples after dosing with 50mg or 100mg CVI for 24 hours

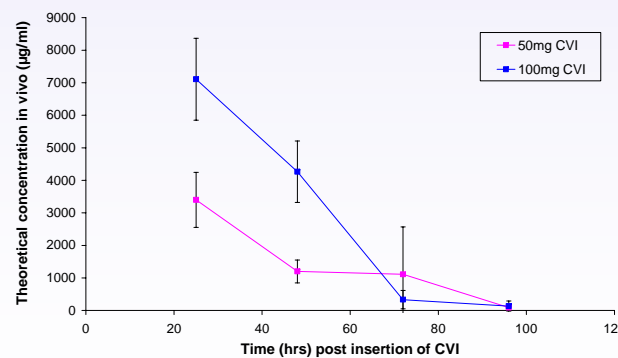


## 4. Results (cont'd)

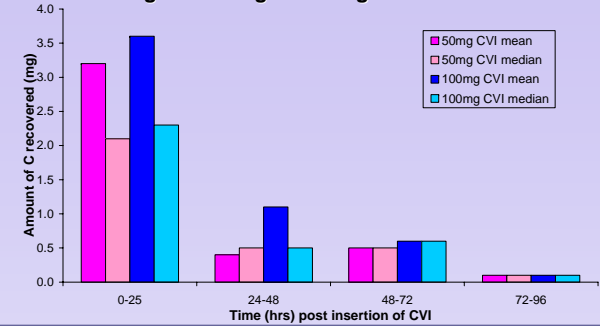
Figure 2 shows the calculated C concentrations based upon the mean values (Table 2 in abstract). These are based on reported vaginal fluid volumes of 0.75ml present in vivo at any given time<sup>(1)</sup>.

The amounts of C recovered from panty liners are detailed in figure 3 (Table 3 in abstract). A minimum of 0.1mg C was found in all but six of the total 57 measurements made. This corresponds to 17µg/ml C based on a reported literature value of 6ml of vaginal fluid generated per day<sup>(1)</sup>. This value is in excess of the MIC values for *Gardnerella* and *Bacteroides*<sup>(2,3)</sup>.

**Figure 2** Theoretical in vivo concentrations of clindamycin after dosing with a 50mg or 100mg CVI for 24 hours



**Figure 3** Clindamycin recovered (mg) from panty liners after dosing with 50mg or 100mg CVI for 24 hours



## 5. Conclusions

Based on a vaginal fluid volume of 0.75ml at any given time and a daily vaginal fluid volume of 6ml, the following conclusions can be drawn:

- ◆ Measurable amounts of clindamycin were determined in lavage samples from volunteers up to 48 and 72 hours post insertion for a 50mg and 100mg CVI.
- ◆ Concentrations of 133µg/ml clindamycin were measured for the samples described above. These are well above the 0.125µg/ml and 0.5µg/ml MIC levels for *Gardnerella* and *Bacteroides*, respectively.
- ◆ A concentration of ≥900µg/ml was found 48 hours after insertion. This approximates to 7000 and 2000 times the reported MIC for *Gardnerella* and *Bacteroides*, respectively.
- ◆ Data from the panty liners demonstrate favourable clindamycin concentrations in the vaginal fluid excreted. The concentrations were above 17µg/ml in the vast majority of samples.
- ◆ For all liner samples collected post removal of insert, irrespective of dose, (n=35) 89% had C concentrations >17µg/ml and 60% had concentrations >50µg/ml.
- ◆ These data are based on reported levels of vaginal fluid. Allowing for variations in this value by up to 200%, these results give confidence that MIC levels are being comfortably surpassed using this product.
- ◆ The CVI delivers drug into the vaginal fluid.

## References

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