

CORCAP CSD PMA CLINICAL SUMMARY

The safety and efficacy results presented in this PMA application indicate that the CorCap CSD is safe and effective for its Intended Use. This conclusion is based on a benefit-risk assessment characterized by the following factors defined in 21 CFR 860.7:

Well-Controlled Clinical Investigation

The CorCap CSD clinical trial, “*Clinical Evaluation of Acorn Cardiac Support Device Therapy in Patients with Dilated Cardiomyopathy*”, clearly meets FDA’s definition of a well-controlled clinical investigation. The objectives of the study, the methods for patient selection, the data procurement methods, the study design (including the use of an active treatment control), and the analysis methods all meet or exceed FDA criteria. Additionally, the CorCap CSD was standardized in its design and performance throughout the trial.

Valid Scientific Evidence

The safety and efficacy results presented in this PMA application are derived from a well-controlled clinical investigation and, therefore, meet FDA’s definition of Valid Scientific Evidence. As such, qualified experts will be able to fairly and responsibly evaluate whether the CorCap CSD is safe and effective for its Intended Use.

Reliability of the CorCap CSD

There were no reliability issues associated with the CorCap CSD during its IDE clinical investigation or per its commercial use in the EU. The CorCap CSD has proven to be consistent in its design, method of delivery, and performance. There have been no deaths or AE’s related to the CorCap CSD. Further, Acorn has not received any user complaints regarding the CorCap CSD. Finally, there were no Serious Unexpected Adverse Events in the CorCap CSD IDE trial, and there have been no Vigilance reports associated with its usage in the EU.

Efficacy

The Valid Scientific Evidence presented in this PMA application provides reasonable assurance that the CorCap CSD (per its intended use and instructions for use) is efficacious in a significant portion of its target population as evidenced by the clinically significant results. The basis for this assertion is as follows:

- The CorCap CSD IDE study met study objectives.
- The primary objective of the study showed that the CorCap CSD improved patient functional status as measured by a clinical composite consisting of mortality, major cardiac procedures, and change in NYHA functional class (p=0.024).
- When analyzed by stratum, the odds-ratios achieved for the clinical composite were directionally similar to the all-patient cohort, demonstrating similar treatment effect.
- The secondary objective of the study showed that the CorCap CSD improved a combination of patient functional status and LV structural parameters as measured by meeting a Hochberg success criterion for LVEDV, LVEF, MLHF, and NYHA (p=0.032).
- The CorCap CSD significantly improved structural and functional endpoints as experienced by: reduction in LVEDV (p=0.008), reduction in LVESV (p=0.02), change to a more elliptical shape (p=0.031), reduction in LVEDD (p=0.02), improvement in MLHF (p=0.04), improvement in SF-36 (SF-36GH: p<0.0001 and SF-36PF: p= 0.015) and improvement in core lab NYHA (p=0.049).
- The statistical significance demonstrated by the primary and secondary objectives of the study, the CorCap CSD demonstrated clinically significant results as demonstrated by the treatment difference in both the primary and secondary endpoints.
- Furthermore, clinical significance of the secondary study objectives is bolstered by the statistically significant correlations between cardiac structural and patient functional endpoints.
- The pre-clinical studies and human safety studies conducted by Acorn demonstrate treatment results consistent with the efficacy results in the CorCap CSD IDE study.
- There is an unmet need in heart failure for a therapy to treat LV dilation.

Safety

Since the probable benefits from the CorCap CSD (when used per its Indications for Use and Instructions for Use) outweigh any probable risks as demonstrated by Valid Scientific Evidence, there is reasonable assurance that the CorCap CSD is safe. The basis for this assertion is as follows:

- The CorCap CSD showed a non-significant mortality difference as measured against control ($p=0.85$). (*Note: updated results on 15 April 2005 showed 29 deaths in treatment and 33 deaths in control which yielded a p-value of 0.59*).
- The CorCap CSD demonstrated a non-significant difference in serious adverse events as measured against control ($p=0.43$) (*note: updated results on 15 April 2005 yielded a p-value of $p=0.33$*).
- The CorCap CSD demonstrated a non-significant difference in the combination of death or serious adverse events as measured against control ($p=0.18$).
- The CorCap CSD significantly reduced Major Cardiac Procedures indicated for worsening heart failure as measured against control ($p=0.01$).
- Risk associated with the design, delivery, and performance of the CorCap CSD was successfully analyzed through a Risk Management process and mitigated through Acorn's physician training program and labeling for the CorCap CSD.