**Mock Document #2: Investigator Brochure (IB)**

**Title:** *Investigator’s Brochure for Dapagliflozin – Cardiovascular Program*  
**Version:** 6.0  
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**1. Introduction**

Dapagliflozin is a selective sodium-glucose co-transporter 2 (SGLT2) inhibitor approved for the treatment of type 2 diabetes mellitus. This brochure summarizes the nonclinical and clinical data supporting its use in patients with heart failure with reduced ejection fraction (HFrEF), including rationale, pharmacology, safety, and prior trial findings.

**2. Physical, Chemical, and Pharmaceutical Properties**

* **Chemical Name:** Dapagliflozin propanediol monohydrate
* **Molecular Formula:** C21H25ClO6
* **Appearance:** White to off-white oral tablet
* **Strength:** 10 mg
* **Dosage Form:** Immediate-release film-coated tablets

**3. Mechanism of Action**

Dapagliflozin inhibits SGLT2 in the proximal renal tubules, reducing glucose reabsorption and increasing urinary glucose excretion. In heart failure, its benefit is attributed to hemodynamic modulation, natriuresis, and potential effects on cardiac remodeling and oxidative stress.

**4. Nonclinical Studies**

* **Pharmacology:** Demonstrated dose-dependent reduction in blood glucose and preserved renal function in rodent models
* **Toxicology:** No carcinogenicity or mutagenicity noted in long-term rodent studies
* **Reproductive Toxicity:** Not teratogenic at therapeutic exposures

**5. Summary of Clinical Experience**

* **Diabetes Program:** Over 10,000 patients studied in global T2DM trials (DEPICT, DECLARE-TIMI 58)
* **Cardiorenal Trials:** Benefits observed in CKD and HFrEF subgroups, including reduced HF hospitalization rates
* **Safety Database:** Over 18,000 patients exposed in clinical trials to date

**6. Safety and Tolerability**

**Known Risks:**

* Genital infections, urinary tract infections
* Volume depletion (especially in elderly)
* Rare: ketoacidosis (primarily in diabetics), acute kidney injury  
  **Monitoring Guidance:**
* Renal function (eGFR), blood pressure, signs of volume depletion
* Discontinue in cases of suspected DKA or pregnancy

**7. Summary of Ongoing and Planned Trials**

* **Study HF-203 (NCT03036124):** Evaluating dapagliflozin in HFrEF population (Phase 3)
* **Study CKD-101:** Examining renal outcomes in non-diabetic chronic kidney disease
* **Label Expansion:** Seeking HF indication irrespective of glycemic status

**8. Benefit-Risk Assessment**

Dapagliflozin’s emerging cardioprotective profile makes it an attractive candidate for addressing residual risk in HFrEF. While urinary tract infections and hypotension remain risks, these are considered manageable within a clinical study environment.

**9. References**

* DECLARE-TIMI 58 Primary Results (NEJM, 2019)
* DAPA-HF Study Publication (NEJM, 2020)
* FDA Summary Review for NDA 202293

This mock IB can now serve as the **primary source document** for prompts like:

* #HC\_AI\_Study\_Drug\_Overview#
* #HC\_AI\_Benefit\_Risk\_Assessment#
* #HC\_AI\_Laboratory\_And\_Safety\_Assessments#
* #HC\_AI\_Adverse\_Event\_Monitoring#