Health Technology Review	
Technology Ref.:	HTA24041
Technology Name/Version/Model:	ReCor The Paradise™ Ultrasound Renal Denervation System
Approvals by International Bodies:	FDA PMA (USA), CE (EU). MoHa**P**
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Short Description of the Technology:	- Paradise Ultrasound Renal Denervation System is intended to reduce a person's blood pressure by using ultrasound energy to disrupt nervous system signals to the kidneys. The device is intended for use to reduce blood pressure. - The Paradise Ultrasound Renal Denervation System (Paradise System) includes the Paradise Catheter with ultrasound transducer, Paradise Generator, Paradise Cartridge, and the Paradise Connection Cable. The Paradise System is a catheter-based system that delivers ultrasound energy circumferentially to thermally ablate and disrupt the renal. - sympathetic nerves with the goal of achieving a reduction in systemic arterial blood pressure. - The Paradise Catheter is delivered percutaneously via femoral artery access, under fluoroscopic guidance using commercially available, compatible introducer sheaths and guiding catheters over a guidewire, into the renal artery. In addition, the Paradise System requires the use of commercially available sterile water as a coolant, to protect the arterial wall during thermal ablation. - The Paradise Generator is designed to be used exclusively in conjunction with the Paradise Cartridge and Paradise Connection Cable to circulate cooling fluid and deliver electrical energy to the Paradise Catheter to ensure proper ultrasound energy. - The Generator uses a series of sensors and control software for management of fluid flow and ultrasound energy delivery to the Paradise Catheter. Fluid flow through the system allows for the transmission of ultrasound from the Paradise Catheter and removes unwanted heat during treatment. The Paradise Generator contains a touch screen which allows users to operate the Paradise System through the appropriate sequence of steps. The Generator comes with a Paradise Remote that can be used during the procedure. - The applicant performed three clinical studies under IDE #G150144 to

establish a reasonable assurance of safety and effectiveness of the Paradise Ultrasound Renal Denervation (uRDN) System for the reduction of blood pressure in adult patients with mild to moderate or resistant hypertension.

- Data from these clinical studies, RADIANCE-HTN SOLO (SOLO), RADIANCE-HTN TRIO (TRIO) and RADIANCE II were the basis for the PMA approval decision. A summary of each of the clinical studies is presented in the table.

Study Design Parameters	RADIANCE- HTN SOLO (SOLO)	RADIANCE- HTN TRIO (TRIO)	RADIANCE II (R-II)
Patient Population	Uncontrolled (OBP ≥140/90 & <180/110 mmHg) on 0-2 anti-hypertensive medications or Controlled (OBP ≤140/90 mmHg) on 1-2 anti-hypertensive medications	Uncontrolled (OBP ≥140/90 mmHg) on 3 or more anti-hypertensive medications	Uncontrolled (OBP ≥140/90 & <180/110 mmHg) on 0-2 anti-hypertensive medications
Randomized patients	146 (1:1 uRDN:Sham)	136 (1:1 uRDN:Sham)	224 (2:1 uRDN:Sham)
Medications through primary endpoint at 2m	No anti-hypertensive medications	Single, fixed dose anti-hypertensive medication combination triple pill	No anti-hypertensive medications
Medications 2-6m	Standardized guideline driven medication escalation to target BP control		
Medications beyond 6m	Medications prescribed per physician discretion		
Primary Effectiveness Endpoint	The difference in the reduction in average daytime ambulatory systolic BP between uRDN and Sham control, from baseline to 2 months post procedure		
Follow up schedule	2, 6, and 12 months and annually thereafter through 3 years	2, 6, and 12 months and annually thereafter through 5 years	
Safety	All adverse events collected and reviewed		
Primary Safety Endpoint:	None	None	Patient level composite of the incidence of Major Adverse Events (MAE) at 30 days and the incidence of renal artery stenosis (>70% diameter stenosis)at 6-months
Imaging	• Renal duplex ultrasound performed for all randomized subjects at 2 and 6 months and for uRDN-treated subjects at 24 and 36 months; CTA/MRA was obtained if specific duplex ultrasound parameters (e.g., PSV) were elevated • CTA/MRA at 12 months for subjects treated with uRDN		CTA/MRA at 6 months for all randomized subjects and at 12 months for subjects treated with uRDN
Study Duration	3 years	3 or 5 years	5 years
Status	Complete follow up available through 36 months	Complete follow up available through 24 months	Complete follow up available through 6 months

- The primary effectiveness endpoint of average daytime ambulatory SBP reduction from baseline to 2 months post-procedure in patients favored uRDN treatment vs. Sham in the studies in which BP medications were withdrawn for two months: RADIANCE-HTN
- SOLO (-6.3 mmHg, p =0.0001) and RADIANCE II (-6.3 mmHg, p<0.0001). The primary effectiveness endpoint results in the on-standardized medication TRIO trial showed a trend but did not reach statistical significance: 4.5 mmHg mean difference reduction favoring uRDN (p=0.0809).
- The probable benefits and risks of the device are based on three randomized, blinded sham-controlled clinical studies and nonclinical studies conducted to support PMA approval. The probable benefits of the Paradise System include a reduction in blood pressure in adult patients with hypertension. The probable risks of the device based on data collected in clinical studies reflect the expected rates associated with invasive arterial catheter-based procedures without elevated

	rates of renal or renal arterial injury. - Patient follow-up was satisfactory and was completed through 36 months for SOLO, 24 months for TRIO, and 6 months for RADIANCE II. Follow-up will continue through 5 years to evaluate the longer-term device performance and adverse event rates. - In conclusion, the data demonstrate a reasonable assurance of device safety and effectiveness and that the probable benefits outweigh the probable risks for using the device to reduce blood pressure as an adjunctive treatment in hypertension patients in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure. - The pooled SOLO, TRIO, and RADIANCE-II safety event rate of composite MAEs through 30 days and RAS through 6 months was 1.1% (95% confidence interval 0.3%- 2.75%). The majority of events were non-serious and typical of catheter-based - procedures such as vascular access site complications, back pain, and transient vasospasm. There was no evidence of renal injury, clinically significant renal artery stenosis, or renal arterial events requiring intervention (based on 238 uRDN subjects) - The Paradise Ultrasound Renal Denervation System has been marketed in France, Germany, Spain, Switzerland, Italy, UK, Belgium and the Netherlands. The device has not been withdrawn from marketing for any reason related to its safety or effectiveness. - In the SOLO Study, there were few serious adverse events (SAEs) during the post procedure period – 1.4% rate of SAE and 3.4% rate of SADE. ADEs within the first 30 days were reported in 42% of the randomized uRDN and Sham patients with the majority associated with vascular access site complications (hematoma, swelling, pain). ADEs were primarily procedure-related, and no events were classified as only device-related based on assessment by the treating physician. - In the TRIO Study, there were few serious events during the post-procedure period – 3% rate of SAE and 3% rate of SADE. ADEs were reported in 41% of the randomized population (in both the uRDN and Sham groups) with the majority associated with vascular access site complications (hematoma, pain) and self-limited vasospasm. ADEs were primarily procedure-related (e.g., access site complications) - In the RADIANCE II Study, there were few serious events during the post-procedure period – 9% rate of SAE and 5% rate of SADE. ADEs were reported in 56% of the According to U.S Food & Drug Administration summary there is a long a list of potential adverse effects (e.g., complications) associated with device use. And along a

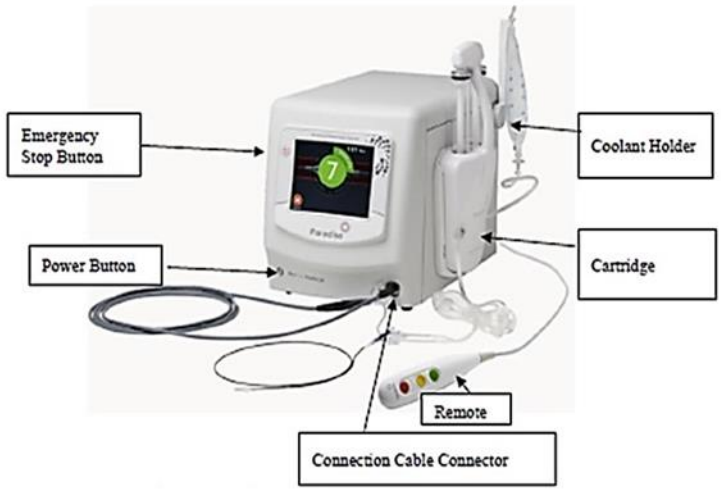
	list of possible risks associated with the denervation procedure or response to treatment. - The primary safety endpoint event rate, defined as a composite of 30-day MAEs and 6-month RAS in the RADIANCE II study was 0%, which met the 9.8% performance goal. The pooled SOLO, TRIO, and RADIANCE-II safety event rate of composite MAEs through 30 days and RAS through 6 months was 1.1% (95% confidence interval 0.3%- - 2.75%). The majority of events were non-serious and typical of catheter-based procedures such as vascular access site complications, back pain, and transient vasospasm. There was no evidence of renal injury, clinically significant renal artery stenosis, or renal arterial events requiring intervention - Renal denervation may be of use in adults with uncontrolled or resistant hypertension (triple drug therapy, one of which is a diuretic) and may be an option for patients unable to tolerate long-term medications at the necessary doses or who cannot tolerate medications at all. - There may be a role for renal denervation in patients who simply do not wish to be on medication. Patients must be fully informed about the risks and potential benefits of renal denervation when compared to drug therapy. - Renal denervation should be offered mainly to patients with high global cardiovascular risk, for whom intensive BP treatment may have a particularly pronounced benefit. - Hospital offering renal denervation should include a multidisciplinary team of hypertension specialists and expert interventionalists who are trained specifically for renal denervation and whose outcomes are closely monitored.

Health Technology Assessment Team Recommendation:	**Approve**
Summary of Review:	
Paradise Ultrasound Renal Denervation System is intended to reduce a person's blood pressure by using ultrasound energy to disrupt nervous system signals to the kidneys. The device is intended for use to reduce blood pressure. We recommend approval of using this technology for Market entry with the following conditions: • According to the U.S Food & Drug Administration summary there is a long list of potential adverse effects (e.g., complications) associated with device use. And along a list of possible	

risks associated with the denervation procedure or response to treatment.

- The procedure is performed in the Cath Lab under fluoroscopy guidance via the right femoral artery under deep sedation and may be performed as a day case procedure in experienced Hospital /centre.
- Studies have demonstrated sustained reduction in blood pressure maintained up to 24 months following this procedure

Technology Image



Population, setting and intended user for Technology "ReCor The Paradise™ Ultrasound Renal Denervation System"

- **Population/ Intended User;**
  - Age 18 above
- **To be performed by:**
  - The procedure is performed in the Cath Lab under fluoroscopy guidance via the right femoral artery under deep sedation and may be performed as a day case procedure in experienced hospital.
- **Clinical Setting:**
  - Specialist Hospitals/Centers.
- **Condition of use:**
  - The Paradise Ultrasound Renal Denervation System is used together with lifestyle modifications and anti-hypertensive medications to reduce blood pressure in people with high blood pressure (hypertension).

- **Exclusion criteria:**
  - Renal arteries diameter<3mm and >8mm.

- Renal artery fibromuscular disease (FMD).
- Stented renal artery.
- Renal artery aneurysm**.**