Date: March 18, 2025

Canadian Heart Rhythm Society
Ablation Committee

RE: VARIPULSE Ablation Field Safety Notice

(Health Canada Type 1 Recall*)

Nature of the Advisory:
The VARIPULSE catheter and ablation system are a pulse-field ablation (PFA) system from Biosense Webster approved by Health Canada for the ablation of paroxysmal atrial fibrillation. In a post- approval external evaluation in the United States (US) there was a higher-than-expected rate of peri- procedural stroke or transient ischemic attack (TIA). This resulted in the Company's decision to voluntarily pause the use of VARIPULSE in the United States. Biosense Webster has investigated these events and has released a Field Safety Notice in Canada (a Health Canada Type 1 recall*) to address the cause of the high stroke/TIA event rate and recommend measures to minimize the risk to patients. The product remains available for use in Canada. The purpose of this advisory from the Canadian Heart Rhythm Society is to provide guidance to Canadian Heart Rhythm professionals.

Scope of the problem:
In the post-approval external evaluation involving select US centres and a total of 132 patients, 4 (3%) developed a peri-procedural stroke. This rate was higher than that seen in prior evaluation studies of the VARIPULSE catheter. In the US (AdmIRE) and European/Canadian (InspIRE) evaluation studies, the rates of stroke/transient ischemic attack (TIA) within 7 days of the procedure were 1.1% (3/274) and 0% (0/206).(1, 2)
Biosense Webster has investigated the causes of the higher-than-expected rate of stroke/TIA in the post-approval external evaluation. Among the cases of stroke/TIA reported to Biosense Webster worldwide (including the external evaluation), 70% received ablation lesions beyond pulmonary vein isolation. No ablation outside of the pulmonary veins was investigated in the evaluation trials. The total number of energy applications was higher in those who experienced stroke/TIA. In 50% of stroke cases reported to Biosense Webster, there were more than 28 ablations, compared to a median of 16 and 23 ablations in the InspIRE and AdmIRE studies. Finally, there was a high proportion of patients with stroke/TIA who had "stacked" lesions where consecutive ablations were placed with ≤3mm movement of the catheter.

The updated recommendations in the Field Safety Notice are summarized as follows:

1. The safety of ablation with VARIPULSE outside the pulmonary veins has not been established
2. The safety of ablation with VARIPULSE outside of paroxysmal atrial fibrillation has not been established.
3. Reposition the catheter between each ablation (consisting of 3 applications)

4. For each pulmonary vein create a concentric ring of lesions using 4 ablations (12 applications) with 2 ostial ablations and 2 antral ablations
5. Deliver 8 ablations (24 applications) for common pulmonary veins

The Field Safety Notice does not provide guidance on a maximum recommended number of applications. They continue to recommend confirming an ACT ≥350 seconds prior ablation.

The dominant mechanism, and advantage, of PFA for the treatment of cardiac arrhythmias, including atrial fibrillation, is via non-thermal disruption of the cellular membrane leading to myocyte death. While PFA is generally considered a "non-thermal" ablation modality, the necessary delivery of high energy through ablation catheters can result in significant thermal energy/heat production at the electrode/polymer interfaces on catheters. This can lead to coagulum and char. Further, PFA delivery can result in other effects on the adjacent blood pool, including gaseous bubble formation and hemolysis, both of which can have potential adverse cerebrovascular effects.

Response of the CHRS Ablation Committee:
While PFA holds great promise with respect to efficiency of ablation, tissue selectivity and lesion durability, we must be cautious with the adoption of the first generation of PFA catheters. PFA is supposed to be minimally thermal and cardiac tissue preferential, but pulse, catheter or generator design can impact these theoretical benefits from being achieved. The presence of char demonstrates a significant thermal profile with this catheter and generator. That, coupled with the higher-than-expected risk of stroke/TIA in the post-approval study is of concern. Additional high quality data is required to definitively assess the risk of stroke/TIA with the VARIPULSE ablation catheter along with characterization of its thermal profile. It is not clear, based on the available data, that a modification of workflow will be sufficient to minimize patient risk.

The CHRS Ablation Committee recommends the following:
1. The recommended workflow modifications may not be sufficient to minimize patient risk.
2. Clinical use of the VARIPULSE catheter should be limited to pulmonary vein isolation alone, and preferably limited to patients with paroxysmal atrial fibrillation
3. Adherence to anticoagulation recommendations (heparin to achieve an ACT ≥350 seconds prior to ablation) should be adhered to.
4. The number of ablations should be limited, and additional ablations beyond 16 ablations (4 per pulmonary vein) should be performed with caution

As with the adoption of any new ablation modality, we encourage all physicians performing ablation procedures to report serious adverse events to Health Canada (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting/medical-device.html)

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References:

1. Duytschaever M, De Potter T, Grimaldi M, Anic A, Vijgen J, Neuzil P, et al. Paroxysmal Atrial Fibrillation Ablation Using a Novel Variable-Loop Biphasic Pulsed Field Ablation Catheter Integrated With a 3-Dimensional Mapping System: 1-Year Outcomes of the Multicenter inspIRE Study. Circulation: Arrhythmia and Electrophysiology. 2023;16(3):e011780.
2. Reddy VY, Calkins H, Mansour M, Wazni O, Di Biase L, Bahu M, et al. Pulsed Field Ablation to Treat Paroxysmal Atrial Fibrillation: Safety and Effectiveness in the AdmIRE Pivotal Trial. Circulation. 2024;150(15):1174-86.

* Health Canada definition of a recall includes "any action taken by the manufacturer, importer or distributor of a medical device, after the device has been sold, to recall or correct the device, or to notify its owners and users of its defectiveness or potential defectiveness, after becoming aware that the device i) may present a risk of injury to health ii) may fail to conform to any claim made by the manufacturer or importer relating to its effectiveness, benefits, performance characteristics or safety or iii) may not meet the requirements of the act or Medical Devices Regulations."
Guidance Document GUI-0054: Guide for recalling medical devices