Review Form 1.6

Journal Name:	**Journal of Pharmaceutical Research International**
Manuscript Number:	**Ms_JPRI_77677**
Title of the Manuscript:	**Sacubitril/valsartan in advanced heart failure: is it just a matter of contractility or are there effects on the pulmonary circulation? A real life monocentric experience.**
Type of the Article	**Original Research Article**

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty'**, provided the manuscript is scientifically robust and technically sound.
To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Compulsory REVISION comments	**See comments bellow.**	
Minor REVISION comments	**See comments bellow.**	
Optional/General comments	Congestive left heart failure patients do have passive pulmonary hyperemia and secondary pulmonary hypertension (PH) and proper drug therapy intends to correct both abnormalities, hyperemia and PH. Blocking the renin-angiotensin system with enalapril o valsartan improve left ventricular ejection fraction and reduces hyperemia, PH and, at the same time, reduces de extracellular volume and improve symptoms, PH and patient survival. The title suggests that the experience to be communicated has a design that will intend to differentiate two interventions on the pulmonary vasculature; the first trying to isolate an effect on left ventricular contractility and another focused on pulmonary vasculature itself. Regrettably, the experience just focuses on the pulmonary pressure before and after the prescription of sacubitril/valsartan (S/V) neither describing in detail the protocol used nor the period to be awaited to do the control visits. Moreover, the three month period stated seem to be an average to reach the maximal tolerated dose of S/V more that the period to repeat the echocardiographic evaluation of the pulmonary pressure. In the Paradigm-HF trail the S/V dose was 375±71 mg, almost the maximal theoretical dose of 400 mg/d in total. In the authors´ experience the S/V doses was less than 200 mg/d because symptomatic hypotensive episodes: Concomitant high diuretic doses? Table2 shows main findings: less PH and better left ventricular ejection fraction, but the experience did not isolate S/V effect on contractility or on pulmonary circulation as it was written in the title. The discussion section did not consider pitfalls in, at least, the communication of the trial design, but is it is well written and honest, especially when it is recognized that hemodynamic monitoring would be desirable to answer the investigative question.	

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PART 2:

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	

Reviewer Details:

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