



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

16 May 2013
EMA/PRAC/290692/2013

PRAC List of questions

To be addressed by the marketing authorisation holders for renin-angiotensin system (RAS)-acting agents

Article 31 of Directive 2001/83/EC resulting from pharmacovigilance data

Procedure number: EMEA/HA/31/1370

Active substances: Angiotensin receptor blockers (ARBs)
 Angiotensin converting enzyme inhibitors (ACEis)
 Direct renin inhibitors (aliskiren)



The marketing authorisation holders (MAHs) for renin-angiotensin system (RAS)-acting agents are requested to:

1. Provide an overview for your product(s) of the approved indications, contraindications, warnings and precautions with regard to the dual blockade of the Renin Angiotensin System (RAS), as reflected in the current Summary of Product Characteristics (SmPC) and Package Leaflet (PL), in the tabular format attached to this document ¹. The table should also identify the main differences between the SmPCs/PLs in the different EU Member States.
2. Provide an analysis of the impact of the recent publication by Makani ² et al on the benefit-risk balance of your product(s). The analysis should also consider any other relevant available data on dual blockade of RAS, including post-authorisation safety studies and literature. The analysis should discuss any relevant specific patient sub-populations which may benefit from dual blockade therapy as well as any sub-populations which may be at risk of harm, such as patients with diabetes, with renal impairment (e.g. eGFR <60 mL/min x 1.73 m² versus ≥60 mL/min x 1.73 m²) or with chronic kidney disease.
3. Propose risk minimisations measures to address any identified changes to the benefit-risk balance of your product(s) in view of the above, including changes to the product information, the identification of special populations or further studies.

¹ If you are the MAH of a generic product, it is sufficient to identify any divergences between the PI of your product and that of the originator

² Makani H, Bangalore S, Desouza KA, Shah A, Messerli FH. Efficacy and safety of dual blockade of the renin-angiotensin system: meta-analysis of randomized trials. BMJ. 2013 Jan 28;346:f360. doi: 10.1136/bmj.f360

Attachment

Product Overview table – Information on the dual blockade of the Renin Angiotensin System (RAS)

INN	Product name	Indications	Contra-indications (SmPC)	Special warnings and precautions (SmPC)	Undesirable effects (SmPC)	Do not take (PL)	Take special care (PL)	Possible side effects (PL)	Main differences between the SmPC/PL in the different EU Member States