

Annex 29

to the Procedure of registration materials examination of medicinal products,
submitted for state registration (re-registration),
as well as expert review of material for changes to registration materials
during the validity of the registration certificate
(art. 4, section IV)

Preclinical research report

1. Name of medicinal product (if available – number of registration certificate):	VALKUBIT 24 mg/26 mg, 49 mg/51 mg, 97 mg/103 mg film-coated tablet				
1) the type of medicinal product for which the registration was made or planned	Generic medicinal product				
2) the undertaken study:	o	yes	X	no	Pharmacodynamic, pharmacokinetic and toxicological properties of both active substances are well known. Therefore, additional studies are not required.
2. Pharmacology:					
1) primary pharmacodynamics	/				
2) secondary pharmacodynamics	/				
3) safety pharmacology	/				
4) pharmacodynamic interactions	/				
3. Pharmacokinetics:					
1) analytical methods and reports concerning their validation	/				
2) absorption	/				
3) distribution	/				

4) metabolism	/
5) excretion	/
6) pharmacokinetic interactions (preclinical)	/
7) other pharmacokinetic studies	/
4. Toxicology:	
1) single-dose toxicity	/
2) toxicity in case of repeated injections	/
3) genotoxicity: <i>in vitro</i>	/
<i>in vivo</i> (including additional toxicokinetic assessment)	/
4) carcinogenicity:	/
long-term studies	/
short-term or medium-term studies	/
additional research	/
5) reproductive toxicity and toxic effects on offspring development:	/
impact on fertility and early embryonic development	/
embryotoxicity	/
prenatal and postnatal toxicity	/

studies in which the medicine is administered to offspring (non-mature animals) and/or evaluated for long-term effects	
6) local tolerability	/
7) additional toxicity studies:	/
antigenicity (antibody formation)	/
immunotoxicity	/
study of mechanisms of action	/
drug dependance	/
metabolite toxicity	/
toxicity of impurities	/
other	/
5. Conclusions on preclinical study	Based on the available data of the individual compounds, preclinical data and data from comparable product there are no causes for significant toxicological concern for sacubitril/valsartan.
Applicant (holder of registration certificate)	 Janja Recelj