Agence nationale de sécurité du médicament et des produits de santé

BRIEFING BOOK

INVESTIGATIONAL MEDICINAL PRODUCT

JANUARY 2020

Contents

I. GENERAL INFORMATION

I-1. General data concerning the therapeutic indication

a	Therapeutic indication claimed and general data concerning the disease	
b	Unmet medical need Description of current treatments and Standard of care	☐ Yes ☐ No

I-2. General data concerning the product under development

a	Product status (Chemical medicinal product, Biological medicinal product, ATMP, combined ATMP), Composition and pharmacotherapeutic class and biological activity/activities	
b	Mechanism of action envisaged in the claimed indication Degree of innovation (new mechanism of action, new entity) and justification of capacity to meet a potential unmet medical need	
d	Dose, frequency and route of administration envisaged (as monotherapy or in combination)	

I-3. Regulatory status

a	Regulatory status (*specify*):	☐ Orphan drug designation in the EU (date and procedure No.) ☐ PIP (submission or validation date, procedure No.) Select an item ☐ MA if yes, specify - date and - if in Europe, specify the procedure, the country for a national procedure and the RMS and countries concerned for a mutual recognition/decentralised procedure - if in another part of the world (specify) ☐ Scientific advice already provided; if yes, specify - the date(s) - if national with the list of countries (in Europe or outside Europe) - if European ☐ PRIME application envisaged ☐ Other, specify
b	Guidelines to which the applicant referred in its development	

II. QUALITY

II-1. Product composition

Molecule structure:	

II-2. Active substance

Is there a monograph for the active substance?	☐ Yes ☐ No	If yes, specify: ☐ Ph. Eur. ☐ Pharmacopoeia of an EU member country ☐ USP/JP
Does the active substance of a medicinal product authorised in the EU made by another manufacturer use the same process?	☐ Yes ☐ No	If yes, please indicate the authorised medicinal product:
Has the active substance described in an ASMF* already been submitted to the ANSM and accepted in support of a given pharmaceutical product?	☐ Yes ☐ No	If yes, indicate the ASMF number or the CEP number:
Control of starting materials: Are there any materials of animal or human origin used in the process	☐ Yes ☐ No	
Qualification of impurities Have the impurities been qualified in non-clinical studies	☐ Yes ☐ No	

II-3. Finished product

Excipients	Are any non-European Pharmacopoeia excipients used in the formulation?	☐ Yes ☐ No ☐NA
	Are any novel excipients used in the formulation?	☐ Yes ☐ No ☐NA
	Are there any excipients of animal or human origin?	☐ Yes ☐ No ☐NA
	Is the BSE/TSE risk documented?	☐ Yes ☐ No ☐NA
Dosing device	Presence of a dosing or administration device? If yes, describe the device: Is it CE marked? Have ongoing stability studies been conducted?	☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No

II-4. Product sterilisation

Is the product sterile	☐ Yes ☐ No
If yes, specify the type of sterilisation	Select an item
II-3 Pharmaceutical development status	
Formulations developed to date Other formulations envisaged Studies conducted Studies envisaged	

III. NON-CLINICAL DEVELOPMENT STATUS

Synoptic Tables of key studies and results and/or related to the request for scientific advice, details in the Investigator's Brochure.

III-1. Pharmacology

a	**Primary pharmacology:** In vivo / in vitro studies performed (Mechanism of action, proof of concept, justification of animal models, etc.):		
b	**Secondary pharmacology:** Screening of other restrictive targets ("off-target"):		
c	Safety	Cardiovascular:	☐ Yes ☐ No ☐NA
		Central nervous system:	☐ Yes ☐ No ☐NA
		Respiratory system:	☐ Yes ☐ No ☐NA
		Other (renal, etc.):	☐ Yes ☐ No ☐NA

III-2. Pharmacokinetics (in relevant species)

Species						
Dose						
Route of administration	Bioavailability	AUC (ng.h.ml)	Cmax (ng/ml)	Tmax (h)	T1/2	Vd
Describe elimination						

III-3. Toxicology

a	Non-clinical single-dose toxicity studies (species used, dose and route of administration of the investigational medicinal product, lethal dose, observed toxicities)			
b	Non-clinical repeated-dose toxicity studies (species used, dose, route and duration of administration of the investigational medicinal product, NOEL and NOAEL, exposure, observed toxicities)			
c	Is the product genotoxic?	☐ Yes	☐ No	☐NA/ Studies not performed (comment)
d	Reprotoxicity studies performed? If yes, synoptic table of studies/species/age/doses If yes, specify whether the product is reprotoxic	☐ Yes	☐ No	☐NA
e	Is the product phototoxic	☐ Yes	☐ No	☐NA/ Studies not performed (comment)
f	Have juvenile toxicity studies been performed? If yes, synoptic table of studies/species/age/doses	☐ Yes	☐ No	☐NA/ Studies not performed (comment)

III-4. Selection of doses (if First In Man)

a	Starting dose: non-clinical criteria used for selection of the 1st dose	Select an item
	What approach was used for the scale?	Select an item Specify
d	Safety margin	Describe the safety margins (AUC and Cmax) as well as the calculation methods

IV. CLINICAL DEVELOPMENT STATUS

IV-1. Completed and ongoing clinical trials

a	Number of clinical trials (completed or ongoing)	
b	Total number of patients included in these trials and in France	

IV-2. Synoptic tables of completed and ongoing clinical trials

a	Study title (and Eudract No.) and study phase	
b	Study objective(s)	- Primary - Secondary
c	Study design	In particular, specify whether randomised or non-randomised, open-label or single or double-blind, comparative or non-comparative, parallel groups or otherwise, number of arms, if add-on or not, etc.
d	Study population	Total number of subjects Healthy volunteers or patients (disease) Main inclusion and exclusion criteria (indication)
e	Product(s) tested	
f	Product dosage tested	Detail per arm: dose, frequency and route of administration, number of patients
g	Outcome measures	Primary outcome measure(s) Secondary outcome measure(s) Exploratory outcome measure(s)
h	Main efficacy results	On primary and main secondary outcome measure(s)
i	Main safety results	Number of events, SAEs, significant events

V. SCHEDULED CLINICAL DEVELOPMENT

V-1. Synoptic tables of scheduled clinical trials

a	Has the management of patients been provided for in the event of toxicity (management of toxicity, modification of doses, including reductions and interruptions)	☐ Yes ☐ No
b	Discontinuation criteria (by patient, by cohort, for the study)	☐ Yes ☐ No *Any divergence must be justified below:*
b	Presence of a DSMB	☐ Yes ☐ No *Any divergence must be justified below:*

V-2. Conditions of Study "XXX"

(Systematically if Application for clinical trial authorisation, only if relevant for Request for scientific advice); (In the event of several studies, complete another section V-3):

a	Study title (and Eudract No.) and study phase	
b	Study objective(s)	- Primary - Secondary
c	Study design	In particular, specify whether randomised or non-randomised, open-label or single or double-blind, comparative or non-comparative, parallel groups or otherwise, number of arms, if add-on or not, etc.
d	Study population	Total number of subjects Healthy volunteers or patients (disease) Main inclusion and exclusion criteria (indication)
e	Justification of the population and treatment line relative to the presumed clinical efficacy of the IMP	
f	Dosage	Detail per arm: dose per administration, frequency and route of administration, number of patients, maximum dose
g	Outcome measures	Primary outcome measure(s) Secondary outcome measure(s) Exploratory outcome measure(s)

VI. RATIONALE FOR REQUEST FOR SCIENTIFIC ADVICE (ONLY FOR A REQUEST FOR SCIENTIFIC ADVICE)

Existence of relevant guidelines	Yes ☐ ☐ No If yes, cite
Deviation planned from current Guidelines	Yes ☐ ☐ No List planned deviations (justification will be detailed in the questions asked)
Rationale for request for scientific advice	Input expected from the ANSM: nature, area of expertise, Justification of need

VII. QUESTIONS – RESPONSES

Question 1
Applicant's position

I hereby certify that the information provided in this document is accurate		
Signed on:	**Signatory's surname and first name**	
	Signature	

143/147, boulevard Anatole France
F-93285 Saint-Denis Cedex
Tél. : +33 (0) 1 55 87 30 00
@ansm

ansm.sante.fr