HAUTE AUTORITÉ DE SANTÉ

QUESTIONNAIRE

Questionnaire for patients' organisations' participation

Health technology assessment prior to reimbursement decision

Validated TC/CEESP1er septembre 2022

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Introduction

Two regulatory committees are in charge of providing health technologies assessments that produce advice for Ministry of Health's decision regarding drugs reimbursement in France. They are part of the French National Authority for Health.

Those two Commettees are :

- The Transparency Committee / Please click to read presentation
- The Economic and Public Health Committee / Please read presentation here

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THE TEAM OF THE HAS' PATIENTS INVOLVEMENT UNIT IS HERE TO ANSWER ANY QUESTION YOU MIGHT HAVE.
Contact : contact.contribution@has-sante.fr / +33 1 5593 7118.

For detailed information on the principles of evaluation of medicines by the Transparency Commission, you can consult the evaluation doctrines for reimbursement and for early access authorisation. This specialized reading is not necessary to complete this questionnaire.

NB: for ease of reading, the masculine is used in the sentences of this questionnaire – this is simply a convention in this document. The HAS promotes inclusion and equality at all levels, including gender and Sexual.

Important note

The questions as they are worded should not be constraining. Please feel free to skip any of them, and use the ‘ADDITIONAL ANSWERS’ fields to type any information you wish to relay.

The administrative part only is mandatory.

Administrative information (contact, financing) for HAS

Information on the financing of your structure

Would you like your answers to this section to be made public (posted on the HAS website)?

☒ Yes

☐ No

You must complete this section even if you have checked 'no' to the above question. Your decision will be respected.

Detail the sources of funding and the amounts for each organization (pharmaceutical laboratories, companies, institutions, foundations, etc.) at the origin of your funding (donations, grants, project funding, contracts, ...), over the last three years.

You can use the table below.

Total budget of the association for year N-3: Not being a legal representative of the foundation, I'm not able to answer this question

- Total budget of the association for year N-2: Not being a legal representative of the foundation, I'm not able to answer this question
- Total budget of the association for the past year (N-1): Not being a legal representative of the foundation, I'm not able to answer this question
- Total budget of the association for the current year (N): Not being a legal representative of the foundation, I'm not able to answer this question

Table 1: Sources of Funding

Year	Organization	Amount (euros)	Percentage of budget for the year concerned

Not being a legal representative of the foundation, I'm not able to answer this question

Medicinal product to which this contribution relates

Trade name:

ZOKINVY 50 - 75 mg*

International Nonproprietary Name (INN):

Lonafarnib

Indication for the evaluation of a drug for reimbursement or early access authorization:

Zokinvy is indicated for the treatment of patients 12 months of age and older with a genetically confirmed diagnosis of Hutchinson-Gilford syndrome (progeria) or progeroid laminopathy with either a heterozygous LMNA mutation with accumulation of progerin-like proteins or a homozygous or composite heterozygous ZMPSTE24 mutation.

This contribution relates to an evaluation (tick the corresponding box or both boxes if applicable):

As a reminder, this information appears next to the name of the drug on the page dedicated to contributions on the HAS website.

☒ With a view to reimbursement under ordinary law

☐ For an early access authorization request

1. Questionnaire – Part A

1.1. Impacts of the disease on quality of life

1.1.1. Impacts of the disease on patients

You can address the themes below if they seem relevant to you, and add as many aspects or parameters as you should consider.

You can prioritize themes, you can qualify their severity using a scale from 1 (less severe) to 5 (most severe)

You can detail the impacts by separating 'groups', e.g. male/female, child/adult, etc.:

- *Intellectual or physical fatigue*
- *Activities of daily living*
- *Mobility/travel*
- *In children: impact on growth and psychomotor development – schooling, sports and play activities, etc.*
- *Working life – Work capacity*
- *Emotional life*
- *Sexual life*
- *Social life*
- *Psychological impacts*
- *Pain*
- *Financial aspects*
- *Other aspects*

What are the impacts of the disease on patients?

HGPS and similar progeroid diseases have such a great impact on the patients : usually these diseases reduce the lifespan to just two decades of age (for HGPS around 14,5 years), and the symtoms are heavy. To be enlightened are the delay and the reduction of the growth ; fragility of the bones and the articular capsules, difficulties on the movements, arthritis, osteoporosis and similar ; generalized lipodistrophy ; problems in the heart, the cardiac valves and the bloody vessels and many others.

All these reported symptoms affected a lot the quality of life of the patients : many can be the occasions to be in hospital, the occasions to be in pain or in which the life itself is in danger. The reduction of the mobility does not permitt to these patients a normal physical life and their autonomy is drastically reduced. Of course, all these problems, united to the peculiar physical aspect, affect greatly also the emotional life, that can berelated also to the social life.

Are you aware of quality-of-life data collection questionnaires or other patient-reported measures that you think are suitable for this disease? 1

☒ Non

☐ Yes, which ones?

Answer here (no lenght limit)

1.1.2. Impacts of the disease on relatives or caregivers

You can address the themes below if they seem relevant to you, and add as many aspects or parameters as you should consider.

You can prioritize themes, you can qualify their severity using a scale from 1 (less severe) to 5 (most severe)

You can detail the impacts by separating "groups", e.g. male/female, child/adult, etc.

- *Intellectual or physical fatigue*
- *Activities of daily living*
- *Mobility/travel*
- *Specific problems with genetic diseases impacting other family members*
- *Working life – Work capacity*
- *Emotional life*
- *Sexual life*
- *Social life*
- *Psychological impacts*
- *Financial aspects*
- *Other aspects*

What are the impacts of the disease on relatives or caregivers?

The impact of HGPS on the relatives and caregivers is great too : being such a complex disease, family are usually worried about the future of their sons and daughter. Additionally, being the autonomy of the patients very reduced, usually the parents have to choose if to work or not, knowing in any case to have a relative who averagely need help on conducing a normal life. As for the patients, the limitations that HGPS gives are not only physical but also emotional.

[1] Sometimes called PROMs. The '*Patient reported outcomes measures'* are questionnaires completed by patients themselves or their cares to measure care outcomes. PROMs can detect changes in the patient's state of health, regardless of their pathology. The questionnaires used can be generic, usable regardless of the pathology, or specific to a pathology.

1.2. Currently available treatments (apart from the drug being evaluated)

The information requested here is important for the Transparency Commission as it evaluates new products against treatment options already available. Opinions for reimbursement shall include in particular a gradation of the therapeutic progress brought about by a new medicinal product in relation to currently available treatments or usual coverage. This is called "Improvement of the Medical Service Rendered" (ASMR). ASMR has five levels ranging from "absent" (ASMR *V) to "major" (ASMR I).*

Please describe mainly treatments that have the same indication as the product being evaluated (same disease, same age, same goal, treatment given at the same stage of progression, e.g. first-line or after failure of another treatment, etc.).

Give a brief description of these treatments, their advantages and disadvantages, and their impact on the quality of life (beneficial or undesirable effects, ease or difficulty of use) and on the patient's care pathway (hospitalization, travel outside the home, frequency of assessments related to the follow-up of the treatment, etc.).

What are the current treatments used in the indication mentioned for this dossier? For example, medicines, medical devices, rehabilitation, supportive care, psychological support, etc.

By now, exept the product being evaluated, there are not other treatments able to reachh the same results. The only drugs the patients can take by now are the one prescribed by the family doctor of by specialists in order to contrast the symptoms. All these drugs are administered patient-specifically, following the clinical story of the patients themself. They are not treatments thought to contrast progeroid diseases, but just as a support. So, there are o real treatments to be compared with Zokinvy/Lonafarnib by now.

What are the benefits of currently available treatments?

See the answer before

What are the disadvantages of currently available treatments?

See the answer before

What are the arguments that would allow you to say that the treatments currently offered in this indication do not cover all your needs?

See the answer before

1.3. The drug being evaluated

The categories below are indicative and *can be used in some questions. It is not necessary to complete them all. The important thing is to tell us the 3 main improvements or disadvantages that can relate to one or the other of these categories, for example:*

- *the state of health of the person concerned, his recovery, his lifespan if serious illness;*
- *quality of life (including impact on intellectual or physical fatigue, activities of daily living, mobility and travel, work life or work capacity, emotional life, Sexual life, social life or other aspects to be specified. In the context of paediatrics, this could include growth, schooling, recreational and sports activities;*
- *the quality of life of their relatives;*
- *the use of this processing;*
- *the patient's health and life course;*
- *Other: Feel free to add any other item you want.*

1.3.1. Your comments on the indication requested by laboratory

Does the wording of the indication requested (which refers to the patients concerned) by the laboratory seem adequate to you? Is the entire patient population included in this wording? Should other patient groups be included? Please justify your answer.

I think this wording is adeguate : I think that all the categories of patients and relatives is included in the previous list. I will answer as a patient, so this will be a personal perspective, but I will include in my next answers the experience of several patients and families I had the opportunity to meet and to be in conact.

If your opinion is based on the experience of people who have used this treatment, fill in the section "If you have experience..." " below (§ 1.3.2).

If you do not know of any patients who have used this treatment, fill out only the section "If you do not have experience..." (§ 1.3.3).

You can leave either of these topics blank.

1.3.2. If you have experience with the drug under study (otherwise proceed to the next section 1.3.3)

1.3.2.1. Advantages observed when using the study drug compared to other treatments currently used:

What are the main improvements compared to current treatments?

Examples of improvement (this list gives only a few possible examples): fewer side effects, more effectiveness on one aspect of the disease, more comfortable frequency or mode of administration, etc.

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The advantages are not easy to see as patient, because HGPS is a progressive degenerative disease that the treatment under exam is not able to block or to reverse, but surely, this treatment is able to decrease the progression ratio of the disease itself. As showed by the scientific reports regarding this treatment, as patient I can affirm that always higher is the number of patients able to live more than 14,5 years (the lifespan of HGPS patients) and able to survive over the second decades. So, more than in the past, the number of patients able to become adult is growing, almost all these patients are under Zokinvy/Lonafarnib treatment. This treatment seems to be the only changed variable than in the past. More than this, despite this treatment is not able to arrest the disease progression, and so, patients usually have to face mortal cardiac problems, the quite good health of patients under this treatment, is able to make them survive pivotal cardiac surgery. After these surgery, solving one of the main death causes of this disease, I can expect the Zokinvy/Lonafarnib treatment will continue to act benefical in these patients.

So, if the Zokinvy/Lonafarnib is far to be a cure, and despite the advantages can be reported only looking at the past lack of this treatment, I strongly believe that this treatment is the best one we have so far, able to prolong the life of patients, and so, to increase the possibility for them to have access also to future treatments that will be studied.

1.3.2.2. Observed disadvantages of the study drug compared to other drugs currently in use

What are the main disadvantages found with the drug studied, especially compared to those of current treatments?

Zokinvy/Lonafarnib is not without side effects, sometime also quite strong. Many of the patients under treatment faced vomit, diarrea, stomach pain, nausea and related problems. My personal experience was quite hard in the first years, but I was in the first group of patients on which the treatment was experimented. Right now, the experience on managing the side effects is greater than then, and so it is easier to start the treatment without too strong side effects. In any case, whenever the side effects start to increase too much, the temporal sospension of the treatment was enough to make the side effects to stop. The dosage seems to be important and very variable from patient to patient in order to avoid any side effects or at least too strong side effects. In any case, I think it is important to report that for me and for the other patients these side effects were not so strong to limit us in the daily life activities.

1.3.3. If you do not have experience with the drug being evaluated: what are your expectations and fears?

1.3.3.1. Your expectations for the drug studied in this evaluation

Examples of expectations (this list gives only a few possible examples): fewer side effects, more effectiveness on one aspect of the disease, frequency or more comfortable mode of administration, etc.

What are the main improvements expected compared to current treatments?

Answer box (you can enlarge)

1.3.3.2. Your fears about the drug studied in this review

What are the main fears about this drug, especially compared to current treatments?

As patient, and speaking also knowing the ideas of many other patients and families, there are not fears regarding this treatment : in fact, Zokinvy/Lonafarnib is used since more than 15 years, without dangerous side effects, and without any kind of side effects not reversible with a simple sospension of the drug. The scientific reports are enlightening good results and we are seeing patients living better and longer than in the past. So, no fears to report.

2. Questionnaire – Part B /// /// SKIP THIS PART FOR ZOKINVY (Lonafarnib) /// /// IGNORE PARAGRAPHS IN PINK

This part only applies to requests for early access authorization

If your contribution concerns a notice for refund, please go directly to Part C "Summary".

The decision taken by the HAS to allow or not to allow early access is based on four criteria:

1. the rare, severe or disabling nature of the disease treated by the medicinal product for which the application for early authorisation is made.
2. lack of appropriate treatment available.
3. the presumed innovative nature of the medicinal product, in particular with regard to any clinically relevant comparator.
4. the impossibility of postponing processing.

This is why we invite you in this section to position yourself on these issues.

You can use the "other" fields in a free way to express yourself.

2.1. Your position on the criteria for early access authorization

What are the arguments that would allow you to say that the disease for which this drug is being evaluated is disabling and/or severe?

Answer box (you can enlarge)

What are the arguments that would allow you to say that the treatments currently offered in this indication are not appropriate?

Answer box (you can enlarge)

What are the main arguments that allow you to say that the drug studied seems innovative compared to current treatments?

This question concerns the innovative nature of the use of the product for which the request for early access authorisation is requested.

The innovative nature of the product in the indication requested is based in particular on two points:2

- the introduction of a substantial change in efficacy, including quality of life, tolerance, practicality or convenience of use or care pathway;
- coverage for a medical need not or insufficiently covered (e.g. use adapted for children).

Answer box (you can enlarge)

2.2. Your position on what data to collect by patients in case early access to the medicine is granted

It is essential during early access to carefully observe the use and effects of the drug to better understand it and evaluate its effectiveness and adverse effects in "real life".

Data on the use and effects of the drug are collected from patients in two ways:

- by the doctor during consultations: the prescribing doctor of this medicine will ask patients questions about the condition in which they feel with the treatment;
- by the patients themselves between consultations: patients (and/or their relatives in some cases) will receive one or more online or paper questionnaires in order to collect health data themselves and more particularly quality of life data. These quality-of-life questionnaires must be completed by the patients themselves, without interpretation by the doctor or third parties.

How this monitoring and data collection is organized is described in detail in a specific document called "Therapeutic Use Protocol – Data Collection", or: PUT-RD.

We invite you to give us your opinion on what data or information would be relevant to collect from the perspective of patients and/or caregivers.

In this section, we ask you to express the types of data and how to collect them that are most relevant to you. It is not useful to mention purely medical data such as biological parameters.

[2] For more details, see § 2.4.2 of the document: Authorization of early access to medicines: HAS evaluation doctrine

2.2.1. The data and information that is important to collect

What is the essential information that patients could collect themselves to help better understand (qualitatively and/or quantitatively) the efficacy and safety of the treatment being evaluated?

Answer box (you can enlarge)

What are the conditions to be met so that patients can best collect the requested information (collection at home, with the help of a caregiver in the hospital, collection by relatives, collection with the help of an expert patient, combination of several collection methods, etc.?)

Answer box (you can enlarge)

2.2.2. Your opinion on the therapeutic use protocol - Data collection

The submission of a "Therapeutic Use and Data Collection Protocol" (PUT-RD) is a legal requirement for the pharmaceutical company submitting an early access request. These usage data will strengthen knowledge about the drug in routine clinical practice.

The PUT-RD aims in particular at data collection and patient monitoring; it must mention what will be collected for this purpose.3

The PUT-RD is not published on our site. The HAS may decide to transmit it as it was drafted by the manufacturer when submitting its file to patient associations constituted as a legal person.

If you wish to consult this document to comment on it in this section, please send us a request email to contact.contribution@has-sante.fr. Consultation of the document is subject to the signing of a confidentiality agreement, and will only be approved for incorporated associations. The document is generally sent within 72 hours.

Have you consulted the draft Therapeutic Use Protocol – Data Collection?

☐ Yes

☐ No

Do you have any comments or additions related to the Therapeutic Use Protocol – Data Collection?

Answer box (you can enlarge)

[3] Isalso called "variables of interest"

3. Questionnaire – Part C: Request for Hearing

The Transparency Committee may decide to hear one or more associations or groups of users during the examination of the application.

Here you can express your interest in such a hearing (in addition to this written contribution).

ATTENTION: Hearings before the Transparency Committee are usually granted within the framework of early access authorisations; They are exceptional in the context of reimbursement.

Would you like to be auditioned?

☒ Yes

☐ No

For what reasons?

I think that the voice of the patients is so important on the evaluation of a drug. I am a patient and a scientist both, so my perspective could be quite complete, and as spokesperson of the Associazione Italiana Progeria Sammy Basso APS Onlus and International Ambassador of the Progeria Research Foundation I had the possibility to share so many useful infomration from families, patients and these associations as well.

4. Questionnaire – Part D: Summary

List the most important points of your contribution, such as:

- *The greatest difficulties of living with the disease are ...*
- *The therapies currently available are (in)adequate because...*
- *The drug studied responds (little) to the needs and expectations of patients because ...*
- *The most important unmet therapeutic needs are ...*

This list is of course not exhaustive.

The greatest difficulties of living with the disease are the reduced lifespan ; the unability to conduce a normal life, especially phisically speaking ; not to be autonomous ; to be often in pain and limitated in the daily activity ; to live with consciousness to be different.

The therapies currently available are inadequate because they are just symptom pad and not a real treatment, sot hey are not able to contrast efficacely Progeria.

The drug studied responds little to the needs and expectations of patients because we are seeing always more patients able to survive the teenhood, able to life in a better condition, and able to become adult, studying and working (with limitations of course, but able to do that).

The most important unmet therapeutic need is that we are not able to reverse the progression of this disease, so in any case, treated or not, progeria contiues to be a degenerative disease.

5. Questionnaire – Part E: Your other comments

If you wish to complete the information that you consider useful for the Transparency Commission, please use this part freely.

Answer here (no lenght limit)

6. Questionnaire – Part F: Methods

Methods used to complete this questionnaire

Please explain the method used to inform the different parts of this questionnaire (e.g. survey, social networks, working group, testimonials, qualitative interviews of patients or relatives who have had access to treatments during clinical trials, telephone calls, number of participants, international exchanges with associations in countries where the treatment is already marketed, with the periods concerned).

How did you fill in the chapters on the impact of the disease and the treatments currently available?

I fill this chapter starting from my personal experience, but I based my answers also hearing : *testimonials, qualitative interviews of patients or relatives who have had access to treatments during clinical trials, telephone calls and meeting with the families, international exchanges with associations in countries where the treatment is already used during the Clinical Trial.*

How did you collect patients' experiences with this treatment?

I did not use any specific survey for collecting patients' experience, but I tried to summarize everything I know from my personal experience and from my personal relationship with patients, families, and foundations.

Who contributed significantly to the writing of the contribution?

I di dit by myself.

Has the association received external aid to support its contribution? If so, which ones?

I wrote everything on my behalf, and I did not receive any external aid on doing that.

Can you give us an estimate of the time it took to write this contribution?

More or less 2 hours

Did you encounter any difficulties in completing this questionnaire, and if so, which ones?

I did not ecounter any difficulties, I was not able to fill only the first part, not being a legal representative of any foundations, but being just an Ambassador of them.

Thanks

Thank you very much for your input and your time. We know they are important. Your contribution will be taken into account by the Transparency Commission. *It will be distributed to all members of the latter in the same way as the other documents in the file and will be presented orally by the members of the commissions appointed as adherent members of a users' association before the deliberations.*

Questionnaire design

This questionnaire was built in collaboration with associative representatives via a dedicated working group. For more information, click here.