



Switching and Monitoring Best Practice for Gaucher Disease

A consensus document

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1 Introduction

Recently, patients living with Gaucher disease, their caregivers and families, and patient organisations, have increasing concerns about the circumstances of switching medicines used to treat this rare condition.

In many countries, medicines are available that have had their safety and efficacy formally demonstrated, through clinical research programs and decades of real-world evidence. These medicines supported may improve both physical functioning and quality of life and give confidence to families and patients who are using a medicine supported by robust clinical evidence.

It is to be expected that healthcare providers will seek to acquire expensive medicines at the most competitive price, however cost should not take precedence over safety and effectiveness.

Some medicines which have recently been made available to patients in some parts of the world may not have sufficient levels of clinical evidence available. As healthcare advocates, both physicians and patient organisations have a responsibility to address the standards of clinical evidence we would expect for new medicines. The terminology used to describe medicines considered similar to predecessors and therefore not subject to equivalent level of evidence generation differ. For the purpose of this consensus document, we have used the word “non-comparables” to describe those medicines which do not have the same level of clinical evidence as the established medicines.

In this consensus document we have listed the points that decision-makers should consider prior to approving a new medicine purely on economic grounds.

2 Methods

The consensus was developed by a joint meeting of the six IWGGD representatives and 13 IGA board members held in September 2022. Participants were divided into three groups with a facilitator and discussed what does the global Gaucher community expect when the health authority in a country is engaging in a procurement process for a new medicine that could result in patients being switched to this new medicine. Each group fed back the discussion points to the main group and the themes for the statements were developed. The draft statements were then distributed to the eight IWGGD representatives and eleven IGA board members for their final comments and approval.

The survey with the statements was sent to the membership of the IWGGD and IGA. A total of 60 responses from physicians and patient advocates were received from 34 countries. The survey was provided in English, Spanish and French and open for 7 weeks (January - March 2023). Participants were asked to mark each statement with “agree”, or “disagree”, and were given the opportunity to make a comment.

This consensus document was developed through the results obtained from this survey.

In this consensus process, a number of sections were skipped. Those ‘skipped’ responses were excluded from the group response to ensure that the reported percentage agreement or disagreement for each statement represented the consensus among only those who felt they knew the answer. This was done according to Vogel et al.: Reference: Vogel, C., Zwolinsky, S., Griffiths, C. et al. A Delphi study to build consensus on the definition and use of big data in obesity research. *Int J Obes* **43**, 2573–2586 (2019). <https://doi.org/10.1038/s41366-018-0313-9>

3 Results

3.1 Patient information standards

The national government agency/agencies responsible for the procurement of medicines must:

- ✓ Ensure that criteria of minimum standards relating to the safety and effectiveness of the medicine are developed by Gaucher expert physicians in consultation with national patient organisation(s) in order to ensure the highest level of safety for patients. (100% consensus)
- ✓ Collaborate with the Gaucher expert physicians and national patient organisation(s) to produce a lay patient leaflet (in the national language, and in paper and digital format) to inform the patients/caregivers about the medicine(s) they are registering and approving in the country. (100% consensus)
- ✓ Use the World Health Organisation (WHO) definitions when procuring medicines to ensure transparency. The definition used must be clearly recorded as, original biological product, biosimilar, non-quality assured biologics. (96% consensus)

Comment:

Definitions are not universally understood and should be explained in any document ensuing them.

Treating physicians should be responsible for:

- ✓ Informing patients/caregivers of the medicine that they are being prescribed and being vigilant to ensure that the correct WHO definition of the medicine is given to the patient. (96% consensus)
- ✓ Informing patients/caregivers, where requested, about the different medicine options available in their country. (96% consensus)
- ✓ Informing patients/caregivers, where requested, about safety and efficacy information on the different medicine options. (98% consensus)

Comment:

Local or national registries may be considered to collect evidence of safety and efficacy.

3.2 Standards of engagement

The national government/insurance agency/agencies responsible for the procurement of medicines should be in a timely manner.

- ✓ Inform the relevant national patient organisation(s) in writing that a procurement process of medicines for the patient community they represent is taking place. (96% consensus)
- ✓ Consult and actively involve the relevant national patient organisation(s) when decisions are made about the treatment of patients that they represent. Patient advocates should be invited to attend all meetings when procurement is being discussed, as active participants, and their contribution should be included in the meeting minutes. (94% consensus)
- ✓ The national patient organisation(s) will offer a contribution by actively engaging the government in a conversation about the procurement and decisions made about new treatments. (98% consensus)
- ✓ Consult all Gaucher expert physicians that a procurement process of medicines for the patient community they treat is taking place and invite them to attend any meeting where procurement is being discussed. They should be at the meeting as an active participant and their contribution should be included in the meeting minutes. (94% consensus)

Comment:

Ideally, notice of procurement should occur at the planning stage. Those involved may elect to attend in full or send representatives.

Treating Gaucher expert physicians should:

- ✓ Inform their patients/caregivers when there is a possibility of a change of medicine. (100% consensus)
- ✓ Support their patients during the time of change of medicine by adhering to the recommended monitoring standards as set out in the clinical standards of this document (see next chapter). (100% consensus)
- ✓ Provide information to the patients/caregivers if a new medicine is to be prescribed and be prepared to answer questions about the medicine. (98% consensus)

Comment:

Whilst it is not the responsibility of treating physicians to check the appropriateness of definitions used for medicines in question, they may wish to review this when a new medicine becomes available.

Pharmaceutical companies should:

- ✓ Contact the relevant national patient organisation(s) when they are considering entering the country with their medicine to inform them of this decision and be open to meeting with them and answering questions on the safety and efficacy of the medicine. (94% consensus)
- ✓ Provide a patient information leaflet in the national language and in paper and digital format. (94% consensus)
- ✓ Use the WHO definitions of medicines, original biological product, biosimilar, and non-quality assured biologics, to ensure transparency. (96% consensus)
- ✓ Make available up to date safety and efficacy data on their product. (98% consensus)

3.3 Clinical standards

- ✓ For biosimilars, clinical data should prove the bio similarity to the reference product. For non-comparables, a robust programme of clinical trials should be prepared to prove safety and efficacy of the product. (100% consensus)
- ✓ Clinical recommendations/guidelines of preferred product should be based on the best available clinical evidence. Where local recommendations of preferred product are based on cost negotiations then this recommendation should only apply to drugs within groups with the same mechanism of action (i.e., Enzyme Replacement Therapy (ERT) or Substrate Reduction Therapy (SRT)). (98% consensus)

- ✓ Consider published evidence of side effects and potential drug interactions. (98% consensus)
- ✓ Usage of one ERT medicine should be for a minimum period of 2 years to avoid high frequency of switches to another ERT (unless there is an overriding clinical reason to switch the medicine) (98% consensus)
- ✓ Recognise that whilst the dose of ERT medicines may be adjusted according to the individualised goals and response, there is currently no individualising the dose of SRT beyond the requirement of metaboliser status of the patient (96% consensus)
- ✓ Recognise that the two SRT medicines (i.e., miglustat and eliglustat) are not equivalent or generics of other medicines and should not be used interchangeably. (98% consensus)

Comment:

- A personalised approach should be used when treating patients. Guidelines are a tool to support clinicians, any decision regarding switching treatment must be made in the patients' best interest between the patient and the treating clinician.

Treating Gaucher expert physicians should:

- ✓ Monitor clinical effects of any treatment initiation or switch (haematological, visceral, bone, neurological, biomarkers etc.) according to the guidelines available from the IWGGD (<https://www.ewggd.com/publications/#guidelines>) (100% consensus)
- ✓ Discuss and establish individualised goals of treatment established for each patient according to their clinical characteristics. (100% consensus)
- ✓ Be aware of potential side effects of any medicine that they are prescribing. (98% consensus)
- ✓ Collect data to support ongoing evidence of safety and efficacy, specifically of new medicines. (98% consensus)
- ✓ Collaborate in local, national, and international networks (e.g., registries) to collect data to support ongoing evidence of safety and efficacy of medicines. (98% consensus)

Comments:

- Physicians are obliged to collect and report safety data on all licensed medicines.
- An academic, product-agnostic registry should be a goal.
- The collection of safety and efficacy is desirable but can be difficult to impose due to the resources required by the registries.
- Data collection (e.g., registries) should be mandatory to the pharmaceutical industry entering the market, not an obligation of the physicians.

4 General comments

- Biosimilars are an accepted way to reduce costs of therapies.
- Some respondents to the consensus felt the patients should be able to switch back immediately to the original medicine if there were any concerns.
- Any proposed changes to the patient's medicine must be reported to the patient timely through the treating physician.
- Decisions for a preferred product can be made on an individual basis, in consultation with the patient, considering potential adverse events and personal choice and cost.
- Cooperation between pharmaceutical companies, Gaucher expert physicians and patient organisations has historically been effective and important for advances in treating Gaucher disease, therefore they should be encouraged or mandated to continue.
- SRT is not for everybody, and some patients have risked their lives taking this drug. If a patient worsens rather than gets better, he/she should be immediately taken off SRT.