IMMUNOTESTING SERVICES - HCP GUIDE

Nexviazyme® (avalglucosidase alfa)

Guidance for health care professionals on immunology testing services provided with Nexviazyme® administration

You are encouraged to report any suspected adverse events to Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

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ABBREVIATIONS

AE	Adverse Event
HCP	Health Care Professional
IAR	Infusion-Associated Reaction
ADA	Antidrug Antibodies
SmPC	Summary of Product Characteristics

1. OBJECTIVES AND GOALS

Aims of the Immunotesting services guide

Nexviazyme® (avalglucosidase alfa) treatment should be supervised by a physician experienced in the management of patients with Pompe disease or other inherited metabolic or neuromuscular diseases

The Nexviazyme® Immunotesting services guide is part of the educational materials provided to physicians involved in managing patients with Pompe disease treated with Nexviazyme®. Treating physicians may make this material available to other health care professionals (HCPs) involved in the management of the disease as required. The main purposes of the Immunotesting service guide are to:

1. Guide HCPs to carry out immunological testing which will help to further characterize the potential mechanism of infusion-associated reactions (IARs) and hypersensitivity reactions, and appropriately manage patients experiencing loss of treatment response due to antidrug antibodies (ADA).
2. Provides information on the Sanofi Rare Disease Specialty Testing program, for immunological testing practicalities.

2. KEY CONTACTS

- **To report adverse event(s) (AE) occurring in association with the use of Nexviazyme®:**

  Please contact the Ministry of Health by using an online form
  https://sideeffects.health.gov.il/

  Additionally suspected adverse events can be reported to Sanofi by calling 09-8633700

- **For information how to access Sanofi- Rare Disease Specialty Testing program or other test-related questions for Nexviazyme®**:

  Please contact Sanofi Medical Department:

  E-mail: Medical.Israel@Sanofi.com

- **For medical information regarding Pompe Disease or Nexviazyme®:**

  Please contact Medical Department:

  E-mail: Medical.Israel@Sanofi.com

3. Testing Recommendations

This current testing service described in this HCP guide is part of Sanofi Rare Disease Specialty Testing program through LabCorp. It provides a complimentary offer of testing: anti-drug IgG antibody, adverse event related immunogenicity testing and biomarker testing services for patients with Pompe Disease and other rare diseases. This is a service offered to the HCPs which can be also managed through a local laboratory for some of the testing.

Testing recommendations for Nexviazyme®:

- Baseline serum sample collection prior to the first infusion is strongly encouraged.
- IgG antibody titers should be regularly monitored, and IgG ADA testing should be considered if patients do not respond to therapy
    - Treated patients may be tested for inhibitory antibodies if they experience a decrease in clinical benefit despite continued treatment with Nexviazyme®
- Adverse-event (AE)-driven immunologic testing, including IgG and IgE ADA, should also be considered in patients who experience moderate/severe or recurrent IARs suggestive of hypersensitivity reactions, anaphylactic reactions.
- AE-driven immunologic testing should be considered for patients at risk for allergic reaction or previous anaphylactic reaction to Myozyme® (alglucosidase alfa).

Please see sections 4.4 and 4.8 of the SmPC for more information related to Nexviazyme® immunogenicity.

4. Testing practicalities

4.1 Description of the immunotesting services

A list of the immunogenicity testing offered (free of charge) with Nexviazyme® treatment through the Sanofi Rare Disease Specialty Testing program with Labcorp is provided in table 1. Detailed sample collection and submission information will be provided upon account set-up with LabCorp.

Table 1. Clinical immunology testing characteristics.

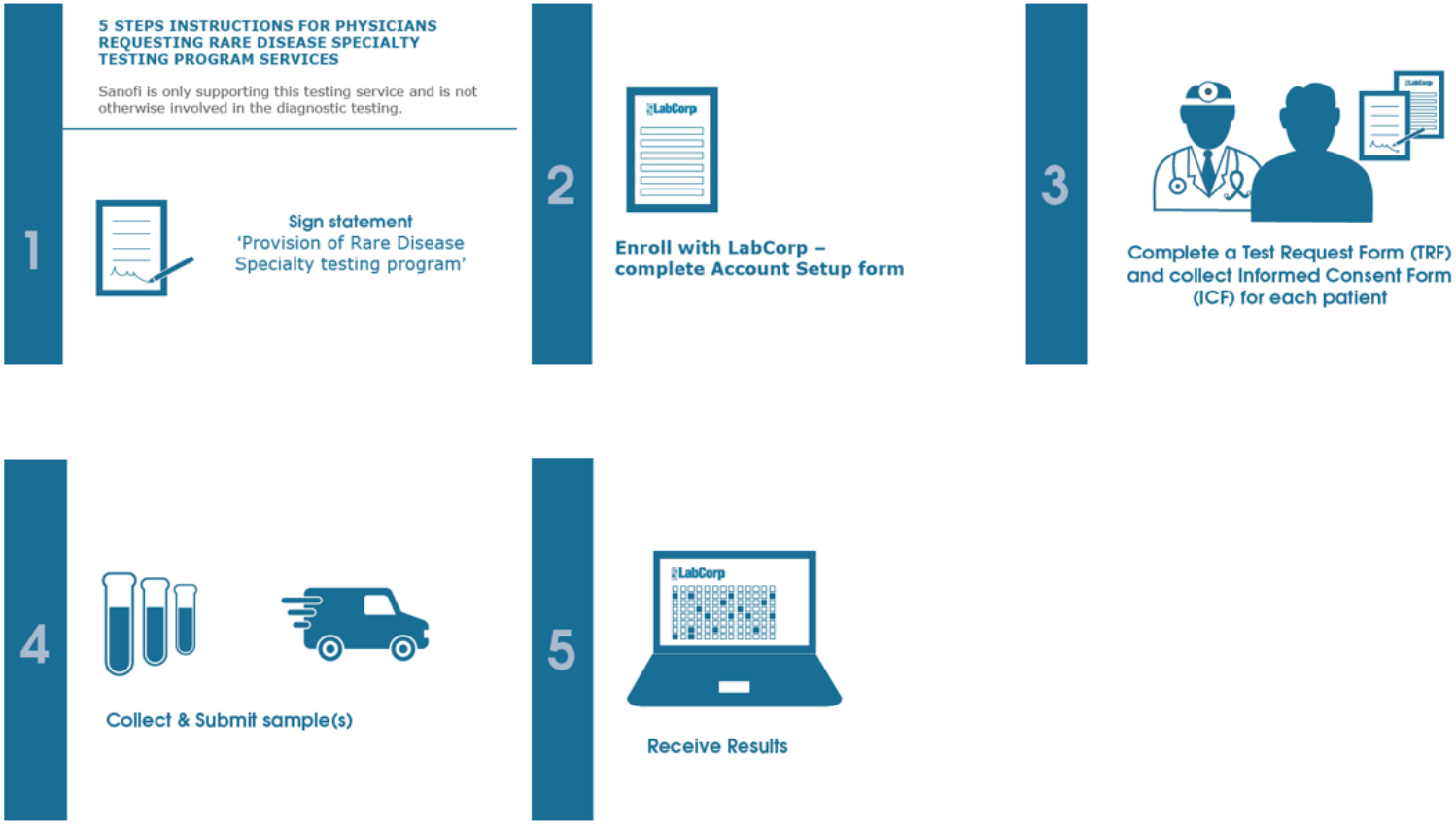
Test	Indication for testing	Sample Type	Frequency	Collection Time[a]
IgG	Routine monitoring	Serum-Frozen Whole blood (received within 24 hours of collection)	Routine monitoring	Sample should be Pre-infusion or ≥3 days post infusion
IgG/inhibitory antibody	Decreased response to treatment or lack of effect	Serum-Frozen Whole blood (received within 24 hours of collection)	Ad hoc (as needed)	Sample should be Pre-infusion or ≥3 days post infusion
IgG/IgE antibody	Moderate/severe or recurrent IARs suggestive of hypersensitivity reactions, anaphylactic reactions	Serum-Frozen Whole blood (received within 24 hours of collection)	Ad hoc (as needed)	Pre-infusion or at least ≥3 days post infusion
Serum Tryptase	Moderate/severe or recurrent IARs suggestive of hypersensitivity reactions, anaphylactic reactions	Serum-Frozen	Ad hoc (as needed)	1-3 hours post infusion reaction
Complement Activation	Moderate/severe or recurrent IARs suggestive of hypersensitivity reactions, anaphylactic reactions	EDTA Plasma-Frozen	Ad hoc (as needed)	1-3 hours post infusion reaction

[a]Document the time and date when the sample was taken.

4.2 Procedure for testing

The procedure described in Figure 1 applies to all tests performed as part of an adverse event investigation (including IgG antibody, IgE antibody, inhibitory antibody, complement activation), and to all samples for routine IgG monitoring. Please contact your local Sanofi representative via e-mail at Medical.Israel@Sanofi.com for further information how to access Sanofi Rare Disease Specialty Testing program.

Figure 1. Procedure to use the Sanofi Rare Diseases Specialty testing program



The immunogenicity testing is performed through LabCorp (California, United States). Follow the link https://www.labcorp.com/account-setup-international-providers in order to create an account.

5. Reporting adverse events

Reporting AE after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. HCP are asked to report any suspected adverse reactions to Israeli Ministry of Health or to contact Sanofi Pharmacovigilance department. For full contact details on reporting adverse reactions please refer to ***KEY CONTACTS.***