# Common Drug Review
## *Pharmacoeconomic Review Report*

**January 2018**

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| **Drug** | taliglucerase alfa (Elelyso) (30 to 60 U/kg intravenous infusion) |
| **Indication** | Long-term enzyme replacement therapy for adults and children (2 to 17 years old) with a confirmed diagnosis of type 1 Gaucher disease and for hematological manifestations in pediatric patients with a confirmed diagnosis of type 3 Gaucher disease. |
| **Listing request** | As per indication |
| **Manufacturer** | Pfizer Canada Inc. |

This review report was prepared by the Canadian Agency for Drugs and Technologies in Health (CADTH). In addition to CADTH staff, the review team included a clinical expert in pediatric inherited metabolic diseases who provided input on the conduct of the review and the interpretation of findings.



**Redactions:** Confidential information in this document has been redacted at the request of the manufacturer in accordance with the *CADTH Common Drug Review Confidentiality Guidelines.*

**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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# ABBREVIATIONS

| | |
|---|---|
| **AE** | adverse event |
| **CCA** | cost-consequence analysis |
| **CDR** | CADTH Common Drug Review |
| **CEA** | cost-effectiveness analysis |
| **ERT** | enzyme replacement therapy |
| **GD** | Gaucher disease |
| **OCCI** | Ontario Case Costing Initiative |
| **PE** | pharmacoeconomic |
| **TALI** | taliglucerase alfa |

# EXECUTIVE SUMMARY

# 1. BACKGROUND

Taliglucerase alfa (TALI) (Elelyso) is a recombinant form of human glucocerebrosidase, indicated for long-term enzyme replacement therapy (ERT) for adults and children (aged two to 17 years) with a confirmed diagnosis of type 1 Gaucher disease (GD) and for the hematological manifestations in pediatric patients with type 3 neuropathic GD.[1] TALI is available as a 13.5 mL single-use vial containing 200 units (U), at the submitted price of $648.36 per vial. The manufacturer is requesting for provinces that already fund ERTs to list TALI for patients with a confirmed diagnosis of type 1 GD, and for the hematological manifestations in pediatric patients with a confirmed diagnosis of type 3 GD.[2]

# 2. SUMMARY OF THE ECONOMIC ANALYSIS SUBMITTED BY THE MANUFACTURER

The manufacturer submitted a cost-consequence analysis (CCA) over a one-year time horizon from the perspective of the publicly funded health care system in Canada. For the primary analysis, the manufacturer compared TALI with other available ERTs (imiglucerase and velaglucerase) and no treatment with ERT, in patients with a confirmed diagnosis of type 1 GD or type 3 GD. This differs slightly from the Health Canada–approved indication. The CCA considered the following costs: drug acquisition, adverse events (AEs), and surgery. Although it is not specified in the manufacturer's pharmacoeconomic (PE) submission, the manufacturer's cover letter indicates that it is requesting listing from provinces that already list ERTs.

Data on the comparative effectiveness and safety of the treatments were based on two systematic reviews of the evidence: one presented in abstract format that identified seven studies in which ERT was used for up to 12 months; and a second that identified 13 papers that fulfilled the manufacturer's search criteria (ERT for GD with 36 months' duration). Data from both clinical registries and clinical trials were included to inform the efficacy for the ERTs and no treatment. AE data were based on the relevant product monographs for the three ERTs, as well as TALI data on file. The manufacturer identified two cost-effectiveness analyses (CEAs) of ERT in GD;[3,4] however, the manufacturer did not use this information to present its own CEA.

Drug costs for imiglucerase and velaglucerase alfa were sourced from the CADTH Common Drug Review (CDR) recommendation for velaglucerase alfa.[5] The cost of TALI was provided by the manufacturer as a confidential price. Administration costs were assumed equal among all ERTs. Costs associated with AEs were incorporated based on AE rates from product monographs and published trials (unspecified), and direct medical costs for the treatment of AEs were obtained from the Ontario Case Costing Initiative (OCCI) cost analysis tool, weighting between inpatient and ambulatory care case costs. Costs were reported in 2014 Canadian dollars, converted using the Canadian Consumer Price Index. Costs associated with non–ERT-treated patients were estimated based on data from published reports[3,4] using costing information from the OCCI cost analysis tool.

The manufacturer estimated that the total costs associated with treatment were $337,725 for TALI, $510,627 for velaglucerase alfa, $640,178 for imiglucerase, and $1,578 for no ERT; the manufacturer also indicated that point estimates for four outcomes (changes in spleen volume, liver volume,

hemoglobin count, and platelet count) indicate TALI is similar to velaglucerase alfa and imiglucerase. The manufacturer reported that TALI was cost-saving compared with the other ERTs.

# 3. KEY LIMITATIONS

CDR identified the following limitations in the manufacturer's PE submission:

- **Lack of comparative data:**
  - There are no studies comparing TALI with another treatment for GD, even though there are two other ERTs available for patients in this population.
  - The manufacturer briefly reported the results of two systematic reviews, but the results were poorly reported and no details were provided regarding the parameters of the search and data interpretation.
  - The manufacturer did not include all TALI trials in the comparative analysis, focusing on Study PB-06-001 (Study 001) and Study PB-06-003 (extension; Study 003) while ignoring two primary studies (PB-06-002 [Study 002] and PB-06-005 [Study 005]), and another extension study (PB-06-004 [Study 004]). No justification for this was provided.
  - Given the lack of comparable clinical trials, the manufacturer attempted to compare AE data from the product monographs of the ERTs, which report different AE parameters for the various ERTs (all-cause versus treatment-related).
  - The comparative clinical effectiveness of TALI versus ERT, surgery, or no treatment is not known, which limits the confidence in the results presented in both the primary analysis (CCA) and sensitivity analysis (cost-minimization analysis).
- **Uncertainty regarding costing of comparative harms data**: As noted above, AEs are reported differently for the various treatments (all-cause AE, treatment-related AEs). In addition to the lack of comparative harms information, the different reported harms outcome limits comparisons among treatments; thus, the application of costs to the AE rates increases the uncertainty of the PE evaluation.
- **Reimbursement criteria:** Although the manufacturer's cover letter indicated the manufacturer requested listing of TALI in jurisdictions that currently fund ERTs, this was not referenced at all within the PE submission. The manufacturer should have been more clear about this in its economic submission to account for all participating public drug plans.
- **Short time horizon:** The manufacturer assessed costs over a one-year time frame. The product monograph states that TALI is indicated for long-term treatment; however, there is little information on the long-term clinical effectiveness of the ERTs. The CDR clinical expert indicated that when patients deteriorate, they generally remain on the same ERT, but with an increased dose. The manufacturer did not assess any of these possibilities in sensitivity analyses.
- **No data presented for pediatric patients or patients with type 3 GD:** While both TALI and velaglucerase alfa are indicated for type 1 GD, TALI is also indicated for patients with type 3 GD. Two patients with type 3 GD were included in Study PB-06-005. This study was not included as part of the clinical evidence base in the manufacturer's PE submission; as such, pediatric or type 3 GD patients were not accounted for in the manufacturer's PE submission. CDR clinical reviewers concluded that evidence for efficacy and safety is very limited for TALI in patients with type 3 GD.
- **Uncertainty regarding data for no medication:** The true costs associated with GD patients not treated with ERT are unknown; however, given associated hospitalizations, the cost reported ($1,578) may be an underestimate. In addition, appropriate efficacy data in untreated patients are not available relative to TALI given the lack of placebo-controlled trial or appropriate comparison of registry patient data with trial patients.

# 4. ISSUES FOR CONSIDERATION

- The CDR clinical expert and patient groups reported that cost is an important factor when choosing the ERT for an individual.
- The manufacturer indicated that it has set up a patient support program that covers the cost of a nurse providing infusion services in the patients' home, so no extra costs will be incurred for the infusion of TALI in patients' homes. If this patient support program is not operationalizable by the participating plans, the total costs associated with TALI will be underestimated.

# 5. RESULTS / CONCLUSIONS

There is no comparative clinical information available for TALI and compared with the other available ERTs. Consequently, whether TALI is clinically similar to other ERTs could not be assessed. Cost-effectiveness could not be assessed for jurisdictions not currently reimbursing ERTs, given the submitted economic evaluation.

At the submitted price of $3.24 per U, TALI is less costly than the other ERTs ($4.89 per U to $6.15 per U).

# 6. COST COMPARISON TABLE

Clinical experts have deemed the comparator treatments presented in Table 1 to be appropriate. Comparators may be recommended (appropriate) practice versus actual practice. Comparators are not restricted to drugs, but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified.

**TABLE 1: COST COMPARISON TABLE FOR ENZYME REPLACEMENT THERAPIES FOR GAUCHER DISEASE**

| Drug/Comparator | Strength | Dosage Form | Price ($) | Recommended Dose | Average Annual Drug Cost ($) |
|---|---|---|---|---|---|
| Taliglucerase alfa (Elelyso) | 200 U/vial | IV | 648.3600[a] | 60 U/kg every other week | 286,575 |
| Imiglucerase (Cerezyme) | 400 U/vial<br>200 U/vial | IV | 2,460.0000[b]<br>1,230.0000[b] | 60 U/kg every other week | 575,640<br>543,660 |
| Velaglucerase alfa (VPRIV) | 400 U/vial | IV | 1,955.0000[b] | 60 U/kg every other week | 457,470 |

CDR = CADTH Common Drug Review; IV = intravenous; U = unit.
[a] Manufacturer-submitted price.
[b] Price based on CDR recommendation report for velaglucerase.[5]
Note: A patient weight of 55 kg has been used, based on a weighted average of the patient weights reported in the CDR Clinical Report (total units: 55 x 60 = 3,300. 9 x 400 U vials per infusion, or 17 x 200 U vials per infusion). Vials are single-use only; wastage has been accounted for. At a lower body weight, any cost savings associated with taliglucerase alfa may be reduced.

# APPENDIX 1: REVIEWER WORKSHEETS

**TABLE 2: SUMMARY OF MANUFACTURER'S SUBMISSION**

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|---|---|
| **Drug Product** | Elelyso (TALI) |
| **Treatment** | TALI, 60 U/kg |
| **Comparator(s)** | No treatment, ERT (imiglucerase, velaglucerase alfa) |
| **Study Question** | "The study was designed to evaluate the costs of long-term ERT for patients with a confirmed diagnosis of type 1 and type 3 GD, comparing taliglucerase alfa to the commercially available ERT (imiglucerase and velaglucerase alfa), imiglucerase is currently reimbursed by the majority of provincial drug programs, and velaglucerase alfa in Ontario and British Columbia, under the various Exceptional Access Programs" (manufacturer submission, page 8).<br>"This report also provides an estimate of the costs and consequences associated with the management of clinical complications of uncontrolled GD when patients are not treated with ERT" (manufacturer submission, page 8). |
| **Type of Economic Evaluation** | Cost-consequence analysis (vs. no treatment) |
| **Target Population** | Patients with a confirmed diagnosis of type 1 or 3 GD |
| **Perspective** | Publicly funded health care system (provincial Ministry of Health) |
| **Outcome(s) Considered** | Costs, AEs |
| **Key Data Sources** | |
| **Cost** | Drug acquisition costs are based on manufacturer's internal sources (TALI) and previous CDR documents for other ERTs.<br>Administration costs were assumed equal and therefore not included.<br>Direct medical costs for AEs were obtained from the OCCI database.<br>Costs associated with no treatment sourced from published papers |
| **Clinical Efficacy** | TALI: Study 001 and Study 003<br>Velaglucerase alfa: Gonzalez et al. and Zimran et al.<br>Imiglucerase: Grigorescu-Sido et al. (2010) and Grabowski et al. (1995) |
| **AEs** | Product monographs |
| **Time Horizon** | One year |
| **Results for Base Case** | Treatment and AE costs associated with the different treatment options were reported to be:<br>• TALI = $337,725;<br>• Velaglucerase alfa = $510,627;<br>• Imiglucerase = $640,178;<br>• No ERT = $1,578<br>Clinical results for change from baseline to 9 months for hemoglobin, liver, spleen, and platelet count (point estimates) were reported separately for the each comparator and reported to be similar. |

AE = adverse event; CDR = CADTH Common Drug Review; ERT = enzyme replacement therapy; GD = Gaucher disease; OCCI = Ontario Case Costing Initiative; TALI = taliglucerase alfa; U = unit; vs. = versus.

## Manufacturer's Results

Although the manufacturer identified two cost-effectiveness analyses (CEAs) of enzyme replacement therapy (ERT) in Gaucher disease (GD),[3,4] it did not use this information to present its own CEA. Instead, the manufacturer submitted a cost-consequence analysis (CCA) for taliglucerase alfa (TALI). Although the manufacturer indicated that the CCA compared TALI with no ERT treatment, the analysis did also indirectly compare TALI with the other available ERTs (imiglucerase and velaglucerase alfa).[6]

The manufacturer did not identify any randomized clinical trials comparing TALI with other ERTs, and thus undertook various literature searches to identify relevant information. The manufacturer identified one review of ERTs for GD, which was presented as a poster abstract. The authors indicated that six high-quality studies (five publications and one abstract) of imiglucerase or velaglucerase alfa were identified, as well as one publication on TALI. The studies themselves were not identified in the abstract. The authors stated that these studies reported spleen and liver volumes, and hemoglobin and platelet counts for the treatments at six, nine, and 12 months.

The manufacturer reported baseline characteristics for the three ERTs and two registries, as well as a comparison of study end points.[7-14] The manufacturer focused on two trials for TALI: studies 001 and 003 (an extension of the Study 001 clinical trial and the Study 002 clinical trial) to compare the results of TALI to imiglucerase and velaglucerase alfa. The authors concluded that the results indicated the magnitude of effect size was comparable between TALI and the other ERTs. The results of this analysis are reported in Appendix 6 of the CADTH Common Drug Review (CDR) Clinical Report.

The manufacturer also presented — as an appendix within the pharmacoeconomic (PE) submission[6] — a systematic review of long-term data as part of its post-marketing commitment to compare long-term safety and effectiveness data for TALI with the other available ERTs (imiglucerase and velaglucerase alfa). This review included only studies covering at least 36 months.

The manufacturer also reports AEs based on data available in the product monographs of the ERTs and data on file for TALI.[1,15,16] The product monographs for imiglucerase and velaglucerase alfa report all-cause AEs or treatment-emergent adverse events (TEAEs), respectively.

In the manufacturer's base case, the acquisition cost of the three ERTs was reported, along with costs associated with all-causality AEs; TEAEs were assumed to be representative of all-causality AEs for imiglucerase. The costs associated with no ERT were based on AE and surgery costs. The manufacturer assumed an average patient weight of 66 kg.

The manufacturer reported that following initial training, injections can be administered by caregivers, health care professionals, or the patients themselves; therefore, costs for administration were considered equal among all products.

Table 3 reports the results of the manufacturer's analysis, presenting the costs associated with each comparator and the clinical outcomes separately.

**TABLE 3: MANUFACTURER'S BASE-CASE RESULTS**

| Treatment | TALI 30 | TALI 60 | Velaglucerase | Imiglucerase | No Medication |
|---|---|---|---|---|---|
| **Parameter** | | | | | |
| **Total Costs** | $337,725 | | $510,627 | $640,178 | $1,578 |
| **Hemoglobin (g/dL)** | 1.4 (1.3) | 2.1 (1.5) | 2.2 (0.9) | 2.3 (1.2) | –0.20 (0.85) |
| **Liver (MN)** | –0.24 (0.21) | –0.26 (0.17) | –0.32 (0.21) | –0.34 (NR) | –0.14 (0.29) |
| **Platelets (x 1,000 $mm^3$)** | 12 (23) | 40 (52) | 41 (31) | 29 (22) | –0.5 (62) |
| **Spleen (MN)** | –4.2 (2.0) | –6.8 (6.0) | –9.5 (3.7) | –8.6 (NR) | –1.4 (2.95) |

MN = multiples of normal; NR = not reported; TALI = taliglucerase alfa.
Source: Adapted from the manufacturer's pharmacoeconomic submission.[6]
Note: An increase in hemoglobin and platelet counts indicates improvement. A decrease in liver and spleen volume indicates improvement.

The manufacturer also undertook a cost analysis of drug costs based on the assumption of comparative clinical benefit for TALI versus the other currently available ERTs (imiglucerase and velaglucerase alfa), using a base weight for patients of 66 kg. The manufacturer concluded that TALI was cost-saving under these assumptions.

## CADTH Common Drug Review Results

Due to the substantial uncertainty noted with the comparative clinical data identified in Section IV below and by the CDR clinical reviewers, the CDR PE reviewers determined that, given the information presented in the submission, it was not appropriate to assess the clinical comparability of TALI, velaglucerase alfa, and imiglucerase in an economic evaluation. CDR presented an analysis of the costs of treatment based on available drug acquisition prices, administration costs, and a revised average patient weight. Although a cost-minimization analysis was also submitted by the manufacturer, this is only appropriate when comparative efficacy and safety have been demonstrated, which — given the lack of appropriate comparative data — is not the case.

As noted in the manufacturer's cover letter, the manufacturer is requesting listing in provinces that currently fund ERTs. This creates uncertainty with regard to the applicability to the other plans, which do not list ERTs.

The manufacturer briefly reported results from a CEA of ERTs in GD in the Netherlands,[3] and a National Institute for Health and Clinical Excellence (NICE) health technology assessment (HTA).[4] These publications reported incremental cost-effectiveness ratios (ICERs) of €884,994 (C$1,586,062) per quality-adjusted life-year (QALY) and £380,000 (C$961,613) to £476,000 (C$1,229,600) per QALY, respectively. However, the generalizability of these results to the Canadian setting is highly uncertain. The manufacturer's assumption – derived from the studies[3,4] – that costs associated with no treatment over the long term could be broken down into annual costs that are equal from year to year is not appropriate given aforementioned generalizability issues."

The drug acquisition costs of the three ERTs are reported in the Table 1. Each ERT is administered via infusion every two weeks. The product monographs for the ERTs indicate that TALI and imiglucerase are administered over a period of between 1 and 2 hours, while velaglucerase alfa is administered over a period of 60 minutes. None of the product monographs present information on subsequent monitoring.

There is no information presented as to who should monitor patients over the infusion time. Given that the monitoring costs are relatively small in relation to the drug acquisition cost, CDR hasn't undertaken reanalyses based on assumptions around monitoring costs. If TALI were to require substantially more monitoring during and post-infusion than velaglucerase alfa and imiglucerase, then the potential for TALI to be cost-saving would be reduced. The manufacturer later indicated that a patient support program had been set up to cover the cost of a nurse providing infusion services in the patients' home, so there will be no extra costs incurred for the infusion of TALI in patients' homes. If this patient support program is not operationalizable to the plans, the administration and monitoring costs associated with TALI would increase.

**TABLE 4: KEY LIMITATIONS**

| Identified Limitation | Description | Implication |
|---|---|---|
| Lack of comparative efficacy data | No studies compared TALI with other treatment, although there are 2 other ERTs available for patients in this population. The previous ERT (velaglucerase) presented a head-to-head trial against the standard of care (imiglucerase). A head-to-head trial against a comparator treatment would have been preferred. | Increases difficulty in assessing comparative effectiveness and safety. |
| | Manufacturer briefly reported the results of 2 systematic reviews, but the results were poorly reported; little data interpretation and justification were provided despite the obvious heterogeneity of the data. | The information in the Clinical Summary for studies 001 and 003 differed from the information reported in the PE submission. The CDR clinical reviewers undertook an appraisal of the comparative effectiveness and safety of TALI and the other ERTs based on available systematic reviews. In addition to the information provided by the manufacturer, the CDR clinical reviewers identified a more recent systematic review, though this also included data on available SRTs.[17] The CDR clinical reviewers found that there was a substantial amount of uncertainty regarding the assessment of comparative efficacy (see CDR Clinical Report, Appendix 6). |
| | The manufacturer did not include all TALI trials in the comparative analysis in the PE submission. The focus was on two trials for TALI – studies 001 and 003 (an extension of 001 and 002 clinical trials) – while ignoring two primary studies (002 and 005) and another extension study (004). No justification for this was provided. In additional information received from the manufacturer, it was indicated that relevant information was located in the submitted Clinical Summary. | |
| Comparator treatment indications/ patient populations | TALI and imiglucerase are indicated for patients with types 1 and 3 GD.<br>Velaglucerase alfa is indicated only for type 1 GD.<br>The manufacturer included only studies 001 and 003, which did not include cohorts of patients with type 3 GD, or pediatric patients. | In provinces that currently fund other ERTs, imiglucerase and velaglucerase are the appropriate comparators.<br>Imiglucerase is the most appropriate comparator for patients with type 3 GD, although there is little appropriate information on comparative effectiveness of treatments in this population.<br>The manufacturer's exclusion of these studies effectively meant it did not consider patients with type 3 GD or |

| Identified Limitation | Description | Implication |
|---|---|---|
| | | children in its PE submission.<br>Where ERTs are not funded, no treatment (including surgery) is an appropriate comparator. |
| Short time horizon | The manufacturer assessed costs over a 1-year period. The TALI product monograph states that it is indicated for long-term treatment. The CDR clinical expert noted that when patients deteriorate, they would generally remain on the same ERT with an increased dose. | ERT is recommended for long-term use; thus, a less costly product would reduce the cost to the payer. However, the CDR clinical expert indicated that if ERT didn't have the desired effect initially, the dose (therefore cost) would be increased, making efficacy even more important. |
| Uncertainty regarding comparative harms | The manufacturer's PE submission did not report the AE rate consistently for all treatments (all-causes for TALI and velaglucerase alfa, but only TEAEs for imiglucerase). AE rates are based on data from product monographs. Cost of AEs were assigned based on these AE rates using codes assumed to best represent the AE and costs from the OCCI database.[18] | Limited by the available data. The CDR clinical reviewers indicated that, although the systematic reviews concluded there was no difference in safety, there is substantial uncertainty with the conclusions. Applying costs to these rates increases uncertainty in the results of the PE evaluation. |
| Weight-based dosing | Each of the comparator treatments use weight-based dosing. | The weight of patients has an impact on any annual cost differences between the drugs. |
| Uncertainty regarding data for no medication | The true cost associated with not treating a patient with type 1 GD or type 3 GD with ERT is unknown; however, given the expected risk factors and potential for hospitalization, the reported cost associated with no ERT of $1,578 may be an underestimate given the way the number was derived. Equally, appropriate efficacy data in untreated patients are not available relative to TALI. | The potential underestimate of costs associated with no ERT may bias the results against TALI (compared with no ERT); however, the uncertainty regarding the efficacy differences means that this cannot be definitively stated. |
| Administration costs were assumed equal among all ERTs and assumed to be given at home | The manufacturer reported TALI could be given as injection by a caregiver, health care professional, or the patient at home; therefore, administration costs were assumed equal among all ERTs. | ERTs are administered via infusion; therefore, the manufacturer's statement isn't applicable. |
| | Each ERT is administered via infusion every 2 weeks. The product monographs report different infusion times for the ERTs: TALI and imiglucerase are administered over 1 to 2 hours; velaglucerase is administered over 60 minutes. There is no information on subsequent monitoring. | No drug administration program was referred to in the submission to CDR, although the manufacturer indicated in its comments to the report that a patient support program that covers the cost of a nurse providing infusion services in the patients' home had been set up. Based on the assumption that the manufacturer's patient support program is operationalizable, this is appropriate.<br>However, if the public health care system was not able to operationalize the program and pays for |

| Identified Limitation | Description | Implication |
|---|---|---|
| | | administration, the potential for TALI to be cost-saving would be reduced. |
| Assumed average patient weight | The average patient weight assumed for the analysis was 66 kg. No appropriate rationale for using this weight for the analysis was provided. | Based on the demographics of the trial reported in the CDR Clinical Report, the weighted average weight of patients was 55 kg. |
| Calculation errors | The manufacturer reported total costs associated with treatment, including drug acquisition, AE costs, and surgery costs. | The sum of the drug acquisition, AE, and surgery costs does not equal the total cost. The differences are negligible and do not alter the overall conclusions of the manufacturer's analysis. |

AE = adverse event; CDR = CADTH Common Drug Review; ERT = enzyme replacement therapy; GD = Gaucher disease; OCCI = Ontario Case Costing Initiative; PE = pharmacoeconomic; SRT = substrate reduction therapy; TALI = taliglucerase alfa; TEAEs = treatment-emergent adverse events.

# REFERENCES


1. Elelyso™ taliglucerase alfa for injection: lyophilized powder 200 units/vial [product monograph]. Kirkland (QC): Pfizer Canada Inc.; 2014 May 29.
2. CDR submission: Elelyso™ (taliglucerase alfa), 200 units/vial. Company: Pfizer Canada Inc. [**CONFIDENTIAL** manufacturer's submission]. Pointe-Claire/Dorval (QC): Pfizer Canada Inc.; 2015 Feb 26.
3. van Dussen L, Biegstraaten M, Hollak CE, Dijkgraaf MG. Cost-effectiveness of enzyme replacement therapy for type 1 Gaucher disease. Orphanet J Rare Dis [Internet]. 2014 [cited 2015 May 14];9:51. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4022049
4. Connock M, Burls A, Frew E, Fry-Smith A, Juarez-Garcia A, McCabe C, et al. The clinical effectiveness and cost-effectiveness of enzyme replacement therapy for Gaucher's disease: a systematic review. Health Technol Assess. 2006 Jul;10(24):iii-136.
5. Common Drug Review. CEDAC final recommendation: velaglucerase alfa (Vpriv - Shire Human Genetic Therapies Inc.) Indication: Gaucher disease [Internet]. Ottawa: CADTH; 2011 Apr 25. [cited 2015 May 14]. Available from: https://www.cadth.ca/sites/default/files/cdr/complete/cdr_complete_Vpriv_April-29-11.pdf
6. Pharmacoeconomic evaluation. In: CDR submission: Elelyso™ (taliglucerase alfa), 200 units/vial. Company: Pfizer Canada Inc. [**CONFIDENTIAL** manufacturer's submission]. Pointe-Claire/Dorval (QC): Pfizer Canada Inc.; 2015 Feb 26.
7. Weinreb NJ, Charrow J, Andersson HC, Kaplan P, Kolodny EH, Mistry P, et al. Effectiveness of enzyme replacement therapy in 1028 patients with type 1 Gaucher disease after 2 to 5 years of treatment: a report from the Gaucher Registry. Am J Med. 2002 Aug 1;113(2):112-9.
8. Giraldo P, Pocovi M, Perez-Calvo J, Rubio-Felix D, Giralt M. Report of the Spanish Gaucher's disease registry: clinical and genetic characteristics. Haematologica. 2000 Aug;85(8):792-9.
9. Grigorescu-Sido P, Drugan C, Alkhzouz C, Zimmermann A, Coldea C, Denes C, et al. Baseline characteristics and outcome in Romanian patients with Gaucher disease type 1. Eur J Intern Med. 2010 Apr;21(2):104-13.
10. Grabowski GA, Barton NW, Pastores G, Dambrosia JM, Banerjee TK, McKee MA, et al. Enzyme therapy in type 1 Gaucher disease: comparative efficacy of mannose-terminated glucocerebrosidase from natural and recombinant sources. Ann Intern Med. 1995 Jan 1;122(1):33-9.
11. Gonzalez DE, Turkia HB, Lukina EA, Kisinovsky I, Dridi MF, Elstein D, et al. Enzyme replacement therapy with velaglucerase alfa in Gaucher disease: Results from a randomized, double-blind, multinational, Phase 3 study. Am J Hematol. 2013 Mar;88(3):166-71.
12. Zimran A, Altarescu G, Philips M, Attias D, Jmoudiak M, Deeb M, et al. Phase 1/2 and extension study of velaglucerase alfa replacement therapy in adults with type 1 Gaucher disease: 48-month experience. Blood. 2010 Jun 10;115(23):4651-6.
13. Zimran A, Brill-Almon E, Chertkoff R, Petakov M, Blanco-Favela F, Munoz ET, et al. Pivotal trial with plant cell-expressed recombinant glucocerebrosidase, taliglucerase alfa, a novel enzyme replacement therapy for Gaucher disease. Blood. 2011 Nov 24;118(22):5767-73.
14. Zimran A, Heitner R, Mehta A, Giraldo P, Rosenbaum H, Giona F, et al. Long term safety and efficacy data of taliglucerase alfa, a plant cell expressed recombinant glucocerebrosidase, in treatment of naïve gaucher disease patients. Mol Genet Metab [abstract]. 2012 Jan 19;105(2):s68. (Presented at Lysosomal Disease Network's WORLD Symposium. San Diego (CA), 2012 Feb 8-10).

15. [Pr]Cerezyme® (recombinant human b-glucocerebrosidease analogue): lyophilized powder 200 units/vial and 400 units/vial [product monograph]. Mississauga (ON): Genzyme Canada, a division of Sanofi-Aventis Canada Inc.; 2014 Apr 15.

16. [Pr]Vpriv™ (velaglucerase alfa): powder for solution for injection 400 U/vial [product monograph]. Cambridge (MA): Shire Human Genetics Therapies, Inc.; 2011 Aug 12.

17. Shemesh E, Deroma L, Bembi B, Deegan P, Hollak C, Weinreb NJ, et al. Enzyme replacement and substrate reduction therapy for Gaucher disease. Cochrane Database Syst Rev. 2015;3:CD010324.

18. Ontario case costing initiative (OCCI) [Internet]. Toronto: OCCI; 2013. [cited 2015 May 26]. Available from: http://www.occp.com/