INVITATION

Join us in the live webinar
with a faculty of international experts to discuss the importance of long-term management of MPS and the clinical impact of treatment interruptions on MPS patients

Live webinar

Optimising MPS patient care during challenging times

Wednesday, 15 July 2020

15:00-16:00 hrs GMT

- 08:00-09:00 hrs Pacific Daylight Time (PDT) GMT-7
- 11:00-12:00 hrs Eastern Daylight Time (EDT) GMT-4
- 12:00-13:00 hrs Brasília Time (BRT) GMT-3
- 16:00-17:00 hrs British Summer Time (BST) GMT+1
- 17:00-18:00 hrs Central European Summer Time (CEST) GMT+2

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Programme

Chairman: Christian J. Hendriksz, MD - *Pretoria, South Africa*

15 min. **Long-term care in MPS: A look at real-world evidence**
Christian J. Hendriksz, MD - *Pretoria, South Africa*

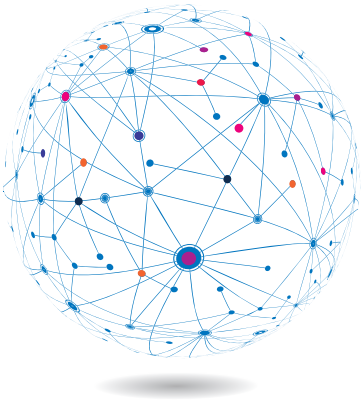
15 min. **Overcoming barriers in MPS management: Impact of treatment interruption and restart**
Charles M. Lourenço, MD, PhD - *Ribeirão Preto, SP, Brazil*

15 min. **Experience of the Advanced Practice Provider with MPS treatment interruptions**
Colleen P. Ditro, NP - *Wilmington, DE, USA*

15 min. **Concluding remarks & discussion**
Faculty & audience

What you will learn

HCPs will learn about long-term treatment outcomes in MPS based on real-world evidence and the management of treatment interruptions during challenging times.



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Faculty

Christian J. Hendriksz, MD - Pretoria, South Africa

Christian J. Hendriksz is CEO of FYMCA Medical Ltd and extraordinary Professor of Paediatrics and Child Health at the Steve Biko Academic Unit, University of Pretoria, Pretoria, South Africa. Prof. Hendriksz established a national reference centre for lysosomal storage disorders at the Birmingham Children's Hospital and developed the adult inherited metabolic disorders service at the Salford Royal NHS Foundation Trust, Manchester, UK until 2018. He spent more than 18 years managing patients with rare disorders in major reference centres and now focusses on sharing his years of experience in the rare disorders field to help healthcare professionals managing these patients.

Charles M. Lourenço, MD, PhD - Ribeirão Preto, SP, Brazil

Charles M. Lourenço is a Professor of Clinical Genetics and Applied Medical Research at the Faculty of Medicine, Centro Universitário Estácio de Ribeirão Preto, São Paulo, Brazil. He is part of a multidisciplinary clinic at his hospital, which focuses on investigation of childhood neurodegenerative disorders. Dr. Lourenço is a member of various professional societies, including the American Society of Human Genetics, International Skeletal Dysplasia Society, and the Society for the Study of Inborn Errors of Metabolism. His interests include the clinical and molecular aspects of several inherited disorders, including lysosomal storage disorders.

Colleen P. Ditro, NP - Wilmington, DE, USA

Colleen P. Ditro is a Lead Nurse Practitioner (NP) at the Nemours Children's Health System Alfred I. duPont Hospital for Children, Wilmington, DE, USA, where serves as an Orthopedic Nurse and Skeletal Dysplasia Coordinator. She has been Board Certified in Pediatric Nursing and is a Certified Lactation Consultant. Currently, she is also an Adjunct Faculty at West Chester University, West Chester, PA, USA and a Pediatric NP at the Abington Memorial Hospital, Abington, PA, USA. Ms. Ditro has served as the President of the Pediatric Orthopedic Practitioners Society and National Association of Pediatric Nurse Practitioners and is still an active member of the latter society.

Abbreviated Prescribing Information (PI) (INTL): NAGLAZYME® (galsulfase)

Refer to Summary of Product Characteristics for full information.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. **Presentation:** Vials containing 5 mg galsulfase in 5 ml for solution for single use. Galsulfase is a recombinant form of human N-acetylgalactosamine 4-sulfatase and is produced by recombinant DNA technology. **Therapeutic indications:** NAGLAZYME® is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of mucopolysaccharidosis VI (MPS VI; N-acetylgalactosamine 4-sulfatase deficiency; Maroteaux–Lamy syndrome). **Dosage and administration:** NAGLAZYME® treatment should be supervised by a physician experienced in the management of patients with MPS VI or other inherited metabolic diseases. Administration of NAGLAZYME® should be carried out in an appropriate clinical setting where resuscitation equipment to manage medical emergencies would be readily available. The recommended dosage regimen for galsulfase is 1 mg/kg body weight administered once every week as an intravenous infusion over 4 hours. The initial infusion rate is adjusted so that approximately 2.5% of the total solution is infused during the first hour, with infusion of the remaining volume (approximately 97.5%) over the next 3 hours. **Contraindications:** Severe or life-threatening hypersensitivity to the active substance or to any of the excipients, if hypersensitivity is not controllable. **Special warnings and precautions:** Caution must be exercised in the management and treatment of patients with compromised airways by limitation or careful monitoring of antihistamine and other sedative medication use. Institution of positive-airway pressure during sleep as well as potential tracheostomy in clinically appropriate situations should also be considered. Consider delaying NAGLAZYME® infusions in patients who present with an acute febrile or respiratory illness. The safety and efficacy of NAGLAZYME® in patients older than 65 years have not been established. The safety and efficacy of NAGLAZYME® in patients with renal or hepatic insufficiency have not been evaluated. Based on data obtained during NAGLAZYME® clinical trials, the majority of patients are expected to develop IgG antibodies to galsulfase within 4–8 weeks of treatment initiation. It is recommended that patients be administered pretreatment medications (antihistamines with or without antipyretics) approximately 30–60 minutes prior to the start of the infusion to minimise the potential occurrence of infusionassociated reactions (IARs). In the case of a mild or moderate IAR, treatment with antihistamines and paracetamol should be considered and/or a reduction in the infusion rate to half the rate at which the reaction occurred. In case of a single severe IAR, the infusion should be stopped until the symptoms are resolved and treatment with antihistamines and paracetamol should be considered. The infusion can be restarted with a reduction of the infusion rate to 50%–25% of the rate at which the reaction occurred. In case of a recurrent moderate IAR or rechallenge after a single severe IAR, pretreatment should be considered (antihistamines and paracetamol and/or corticosteroids) and a reduction of the infusion rate to 50%–25% of the rate at which the previous reaction occurred. As with any intravenous protein product, severe allergic-type hypersensitivity reactions are possible. If these reactions occur, immediate discontinuation of NAGLAZYME® is recommended and appropriate medical treatment should be initiated. The current medical standards for emergency treatment are to be observed. In patients who have experienced allergic reactions during infusion with NAGLAZYME®, or who are resuming treatment after prolonged interruption, caution should be exercised upon rechallenge/readministration. Appropriately trained personnel and equipment for emergency resuscitation (including epinephrine) should be available during infusions. Spinal/Cervical cord compression (SCC) with resultant myelopathy is a known and serious complication that can be due to MPS VI. There have been post-marketing reports of patients treated with NAGLAZYME® who experienced the onset or worsening of SCC, requiring decompression surgery. Patients should be monitored for signs and symptoms of spinal/cervical cord compression (including back pain, paralysis of limbs below the level of compression, urinary and faecal incontinence) and given appropriate clinical care. **Interaction:** No interaction studies have been performed. **Pregnancy and lactation:** No clinical data on exposed pregnancies are available. NAGLAZYME® should not be used during pregnancy unless clearly necessary. It is not known whether galsulfase is excreted in milk; therefore, breastfeeding should be stopped during NAGLAZYME® treatment. **Undesirable effects:** The most common adverse reactions were pyrexia, rash, pruritus, urticaria, chills/rigours, nausea, headache, abdominal pain, vomiting and dyspnoea. Serious adverse reactions included laryngeal oedema, apnoea, pyrexia, urticaria, respiratory distress, angioedema, asthma and anaphylactoid reaction. Infusion reactions, defined as adverse reactions occurring during NAGLAZYME® infusions or until the end of the infusion day, were observed in 33 (56%) of the 59 patients treated with NAGLAZYME® across five clinical studies. Infusion reactions began as early as Week 1 and as late as Week 146 of NAGLAZYME® treatment, and occurred during multiple infusions, though not always in consecutive weeks. Very common symptoms of these infusion reactions were pyrexia, chills/rigours, rash, urticaria and dyspnoea. Common symptoms of infusion reactions were pruritus, vomiting, abdominal pain, nausea, hypertension, headache, chest pain, erythema, cough, hypotension, angioedema, respiratory distress, tremor, conjunctivitis, malaise, bronchospasm and arthralgia. Other adverse events include anaphylaxis, shock, pharyngitis, gastroenteritis, areflexia, paraesthesia, corneal opacity, bradycardia, tachycardia, cyanosis, ear pain, hearing impaired, pallor, nasal congestion, hypoxia, tachypnoea and umbilical hernia. **Overdose:** No case of overdose with NAGLAZYME® has been reported. **List of excipients:** Sodium chloride. Sodium phosphate monobasic, monohydrate. Sodium phosphate dibasic, heptahydrate. Polysorbate 80. Water for injections. **Incompatibilities:** This medicinal product must not be mixed with other medicinal products. **Storage and use:** Store in a refrigerator (2–8 °C). Do not freeze. Diluted NAGLAZYME® should be used immediately. If not used immediately, in-use storage times and conditions should normally not be longer than 24 hours at 2–8 °C followed up to 24 hours at room temperature (23–27 °C) during administration. **Preparation of NAGLAZYME® infusion:** See full Summary of Product Characteristics. **Legal category:** POM. **Marketing authorisation holder:** BioMarin International Limited, Shanbally, Ringaskiddy, County Cork, P43 R298, Ireland. **Marketing authorisation number(s):** EU/1/05/324/001. EU/1/05/324/002. **Date of first authorisation:** 24 January 2006. **Date of revision of the text:** July 2018. NAGLAZYME® is a trademark of BioMarin Pharmaceutical Inc. Further information is available from BioMarin International Limited, Shanbally, Ringaskiddy, County Cork, P43 R298, Ireland.

Healthcare professionals should report adverse events in accordance with their local requirements.
Adverse events should also be reported to BioMarin on +1 415 506 6179 or drugsafety@bmrn.com

Abbreviated prescribing information (INTL): VIMIZIM® (elosulfase alfa)

Refer to Summary of Product Characteristics for full information.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Please refer to section 4.8 of the full Summary of Product Characteristics for how to report adverse reactions. **Name of product:** VIMIZIM® (elosulfase alfa) 1 mg/ml concentrate for solution for intravenous infusion. **Presentation:** Vials containing 5 mg elosulfase alfa in 5 ml for solution for single use. Elosulfase alfa is a recombinant form of human N-acetylgalactosamine-6-sulphatase (rhGALNS) and is produced in mammalian Chinese Hamster Ovary (CHO) cell culture by recombinant DNA technology. **Therapeutic indications:** VIMIZIM® is indicated for the treatment of mucopolysaccharidosis, type IVA (Morquio A syndrome, MPS IVA) in patients of all ages. **Dosage and administration:** Administration of VIMIZIM® should be carried out by an appropriately trained healthcare professional with the ability to manage medical emergencies. Home administration under the supervision of an appropriately trained healthcare professional may be considered for patients who are tolerating their infusions well. The recommended dose of elosulfase alfa is 2 mg/kg of body weight administered once a week. The total volume of the infusion should be delivered over approximately 4 hours (see Table 1). When diluted in 100 ml, the initial infusion rate should be 3 ml/hr. The infusion rate may be increased as tolerated, every 15 minutes as follows: first increase the rate to 6 ml/hr, then increase the rate every 15 minutes by 6 ml/hr increments until a maximum rate of 36 ml/hr is reached. When diluted in 250 ml, the initial infusion rate should be 6 ml/hr. The infusion rate may be increased as tolerated, every 15 minutes as follows: first increase the rate to 12 ml/hr, then increase the rate every 15 minutes by 12 ml/hr increments until a maximum rate of 72 ml/hr is reached.

Table 1: Recommended infusion volumes and rates*

Patient weight (kg)	Total infusion volume (ml)	Step 1 Initial infusion rate 0 – 15 mins (ml/hr)	Step 2 15 – 30 mins (ml/hr)	Step 3 30 – 45 mins (ml/hr)	Step 4 45 – 60 mins (ml/hr)	Step 5 60 – 75 mins (ml/hr)	Step 6 75 – 90 mins (ml/hr)	Step 7 90+ mins (ml/hr)
< 25	100	3	6	12	18	24	30	36
≥ 25	250	6	12	24	36	48	60	72

* Infusion rate may be increased as tolerated by patient.

Contraindications: Life-threatening hypersensitivity (anaphylactic reaction) to the active substance or any of the excipients. **Special warnings and precautions:** Anaphylaxis and severe allergic reactions have been reported in clinical studies. Therefore, appropriate medical support must be readily available when elosulfase alfa is administered. If these reactions occur, immediately stop the infusion and initiate appropriate medical treatment. The current medical standards for emergency treatment are to be followed. For patients who have experienced allergic reactions during infusion, caution should be exercised upon re-administration. **Infusion reactions (IRs):** IRs were the most commonly observed adverse reactions in clinical studies. IRs may include allergic reactions. Patients should receive antihistamines with or without antipyretics prior to infusion. Management of IRs should be based on the severity of the reaction and include slowing or temporary interruption of the infusion and/or administration of additional antihistamines, antipyretics, and/or corticosteroids. If severe IRs occur, immediately stop the infusion and initiate appropriate treatment. Re-administration after a severe reaction should be carried out with caution and close monitoring by the treating physician. In clinical studies, spinal cord compression (SCC) was observed both in patients receiving VIMIZIM® and patients receiving placebo. Patients should be monitored for signs and symptoms of SCC (including back pain, paralysis of limbs below the level of compression, urinary and faecal incontinence) and given appropriate clinical care. This medicinal product contains 8 mg sodium per vial, equivalent to 0.4% of the WHO recommended maximum daily intake of 2 g sodium for an adult, and is administered in sodium chloride 9 mg/ml (0.9%) solution for injection. **Sorbitol:** This medicinal product contains 100 mg sorbitol per vial which is equivalent to 40 mg/kg. Patients with hereditary fructose intolerance (HFI) must not be given this medicinal product unless strictly necessary. Babies and young children (below 2 years of age) may not yet be diagnosed with hereditary fructose intolerance HFI. The treatment benefit to the child compared to the associated risks must be fully evaluated prior to treatment. A detailed history with regard to HFI symptoms has to be taken for each patient prior to being given this medicinal product. **Effects on ability to drive and use machines:** VIMIZIM® has minor influence on the ability to drive and use machines. Dizziness was reported during VIMIZIM® infusions; if dizziness occurs after the infusion, the ability to drive and use machines may be affected. Interaction: No interaction studies have been performed. **Fertility, pregnancy and lactation:** There are no data on the use of VIMIZIM® in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy or embryo–foetal development. As a precautionary measure, it is preferable to avoid the use of VIMIZIM® during pregnancy, unless clearly necessary. Available reproductive data in animals have shown excretion of elosulfase alfa in milk. It is not known whether elosulfase alfa is excreted in human breast milk, but systemic exposure via breast milk is not expected. Due to lack of human data, VIMIZIM® should only be administered to breast-feeding women if the potential benefit is considered to outweigh the potential risk to the infant. **Undesirable effects:** The majority of adverse reactions in clinical studies were Infusion Reactions (IRs), which are defined as reactions occurring after initiation of infusion until the end of the day following the infusion. Serious IRs were observed in clinical studies and included anaphylaxis, hypersensitivity and vomiting. The most common symptoms of IRs (occurring in ≥10% of patients treated with VIMIZIM® and ≥5% more when compared to placebo) were headache, nausea, vomiting, pyrexia, chills and abdominal pain. IRs were generally mild or moderate, and the frequency was higher during the first 12 weeks of treatment and tended to occur less frequently with time. Very common (≥1/10) reactions included hypersensitivity, headache, dizziness, dyspnoea, diarrhoea, vomiting, oropharyngeal pain, upper abdominal pain, abdominal pain, nausea, chills and pyrexia. Hypersensitivity and myalgia were common (≥1/100 to <1/10) adverse reactions – All patients developed antibodies to elosulfase alfa in clinical trials – Approximately 80% of patients developed neutralising antibodies capable of inhibiting the elosulfase alfa from binding to the cation-independent mannose- 6-phosphate receptor. Sustained improvements in efficacy measures and reductions in urine keratan sulphate (KS) over time were observed across studies, despite the presence of anti-elosulfase alfa antibodies. No correlations were found between higher antibody titres or neutralising antibody positivity and reductions in efficacy measurements or occurrence of anaphylaxis or other hypersensitivity reactions. IgE antibodies against elosulfase alfa were detected in ≤10% of treated patients and have not consistently been related to anaphylaxis or other hypersensitivity reactions and/or treatment withdrawal. In patients <5 years of age, the overall safety profile of VIMIZIM® at 2mg/kg/week was consistent with the safety profile of VIMIZIM® observed in older children. **Overdose:** In clinical studies, doses of elosulfase alfa were explored up to 4 mg/kg/week and adverse reactions similar to those in the pivotal trial were observed. **List of excipients:** Sodium acetate trihydrate, monobasic sodium phosphate monohydrate, arginine hydrochloride, sorbitol, polysorbate 20, water for injections. **Incompatibilities:** This medicinal product must not be mixed with other medicinal products. **Storage and use:** Store in a refrigerator (2–8°C). Do not freeze. **After dilution:** Chemical and physical inuse stability has been demonstrated for up to 24 hours at 2–8°C followed by up to 24 hours at 23–27°C. From a microbiological safety point of view, the diluted solution should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and should normally not be longer than 24 hours at 2–8°C followed by up to 24 hours at 23–27°C during administration. **Preparation of VIMIZIM® infusion:** See full Summary of Product Characteristics. **Legal category:** Prescription Only Medicine. **Marketing authorisation holder:** BioMarin International, Shanbally, Ringaskiddy, County Cork P43 R298 Ireland. **Marketing authorisation number(s):** EU/1/14/914/001 Date of first authorisation: 28 April 2014. **Date of revision of the text:** October 2018. VIMIZIM® is a trademark of BioMarin Pharmaceutical Inc. Further information is available from BioMarin International Limited, Shanbally, Ringaskiddy, County Cork, P43 R298, Ireland.

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