Making the most of

Upstaza™▼ (eladocagene exuparvovec)

A multidisciplinary approach to post-treatment care

This booklet provides an overview of the roles and responsibilities of each multidisciplinary team member involved in the post-treatment care of patients who have received Upstaza gene therapy, with the aim of facilitating a successful and coordinated post-treatment care plan.

Upstaza Prescribing Information can be found at the end of this document.

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Post-treatment care: A coordinated approach

Post-treatment care of patients following Upstaza gene therapy for AADC deficiency is essential for monitoring recovery and promoting developmental improvements.[1,2] It requires a coordinated approach between the treatment centre's neurosurgeon, a local referring neurologist and a multidisciplinary team to ensure patients have access to the necessary programmes, facilities and tools in order to reach their full potential after gene therapy.[1,2]

The post-treatment care team should partner with the caregiver to develop a personalised treatment plan, incorporating therapy strategies that are most appropriate for each patient as they progress after gene therapy.[2]

Therapy strategies recommended for post-treatment care:

Inpatient/intensive physical therapy

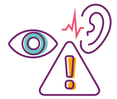
In-home therapy

Facilitating active movements

Functional use of active movement

Age-appropriate experiences

Play therapy



Sensory-based interventions/sensory integration therapy

Assistive technology

Aquatic therapy

Hippotherapy

Music therapy

Cognitive and communication training

Adapted from Lee H-M, *et al.* 2024.[2]

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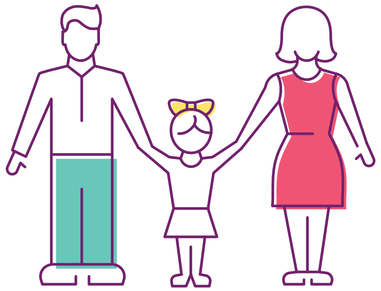
Collaborative post-treatment care: Roles and responsibilities



Caregivers

Caregivers play a crucial role in the post-treatment care of patients with AADC deficiency treated with Upstaza gene therapy.[2] The post-treatment care team should regularly communicate with caregivers and coach them on how to interact with the patient to maximise improvements after treatment. Caregivers should provide opportunities for their child to develop new skills, incorporating play and in-home therapy into daily routines, and explore therapy strategies that may suit post-treatment goals and patient needs.[2]

An information sheet for caregivers with an overview of the post-treatment care multidisciplinary team is also available and can be requested.

Local team:

After gene therapy and post-procedure approval, the patient will return home to their referring neurologist and local care team for post-treatment care[1,2]

Local healthcare professionals (referring neurologist and local physician)[1–3]
After leaving the treatment centre, the referring neurologist or a local physician in communication with the referring neurologist will be the main point of contact for caregivers regarding post-treatment care.[1,2] They will collaborate with the treatment centre neurosurgeon to lead a post-treatment care multidisciplinary team.[1,2]

Treatment centre:

Specialised in stereotactic neurosurgery, the treatment centre is where gene therapy surgery takes place[1,3]

Neurosurgeon
The neurosurgeon at the treatment centre will perform neurological assessments, monitor for adverse events and collaborate with the patient's referring neurologist to oversee the post-treatment care multidisciplinary team.[1,3]

Neurosurgical team
This team will perform the stereotactic neurosurgery. Led by the neurosurgeon, it will consist of specialists trained in neurosurgery and may include a neurologist, anaesthesiologist, pharmacist and radiologist.[3]

Post-treatment care multidisciplinary team

The post-treatment care multidisciplinary team, led by the patient's referring neurologist, may include specialists from their regular AADC deficiency management team in addition to post-gene therapy rehabilitation therapists.[1–4] This is because autonomic and serotonergic symptoms of AADC deficiency may persist after gene therapy.[1]

The composition of the multidisciplinary team may vary for each patient and could be adjusted throughout the post-treatment care journey based on their changing needs, abilities and local conditions.[2,3]

- **Physical therapist or occupational therapist**
- **Psychologist or social worker**
- **Speech therapist**
- **Dietitian or gastroenterologist**

Prescribing Information can be found at the end of this document.

Post-treatment care multidisciplinary team: The specialists

Physical therapist or occupational therapist

Due to the severe motor impairments and potential for accelerated skill acquisition by the patient post treatment, physical therapy and functional testing procedures are essential. These should be performed by a physical therapist or occupational therapist.[1–4]

Psychologist or social worker

Caregivers of children with chronic diseases are at risk of poorer quality of life, and psychological care for patients and caregivers should be provided throughout the post-treatment period.[2–4] Counselling and psychological testing should take place after gene therapy, conducted by a social worker or psychologist with experience in children with movement disorders or rare diseases.[1–4]

Speech therapist

Delayed speech development is a typical symptom of AADC deficiency.[1,4] After gene therapy, speech and communication training is critical as it may enhance development of cognition and help the patient comprehend therapy instructions.[1,2]

Dietitian or gastroenterologist

Gastrointestinal problems, including feeding difficulties, are common in patients with AADC deficiency and may initially remain or worsen after gene therapy.[1,2,4] Patients may benefit from seeing a gastroenterologist after gene therapy who will perform feeding and nutritional assessments to monitor weight and support with feeding difficulties.[1,2,4]

AADC, aromatic L-amino acid decarboxylase.

References

1. Upstaza (eladocagene exuparvovec) Summary of Product Characteristics. PTC Therapeutics. 2025.
2. Lee H-M, *et al. Orphanet J Rare Dis.* 2024;19(1):17.
3. Roubertie A, *et al. J Inherit Metab Dis.* 2023. doi: 10.1002/jimd.12649. Online ahead of print.
4. Wassenberg T, *et al. Orphanet J Rare Dis*. 2017;12(1):12.

Prescribing Information can be found at the end of this document.

Abbreviated Prescribing Information

Upstaza™ (active ingredient: eladocagene exuparvovec) is indicated for the treatment of patients aged 18 months and older with a clinical, molecular, and genetically confirmed diagnosis of aromatic Lamino acid decarboxylase (AADC) deficiency with a severe phenotype. **Posology and administration**: Intraputaminal use. Upstaza is available as single dose vial containing 2.8×10^{11} vector genomes (vg)/ 0.5 mL solution for infusion. The patients will receive a total dose of 1.8×10^{11} vg delivered as four 0.08 mL (0.45×10^{11} vg) infusions (two per putamen). The posology is the same for the entire population covered by the indication. Treatment should be administered in a centre which is specialised in stereotactic neurosurgery, by a qualified neurosurgeon. There is limited experience in patients aged 12 years and older. The safety and efficacy of eladocagene exuparvovec in children aged below 18 months and with hepatic and renal impairment have not been evaluated. There is no safety or efficacy data for patients whose pre-treatment antibody levels to AAV2 was > 1:50. *Preparation:* Upstaza is a sterile solution for infusion that requires thawing and preparation by the hospital pharmacy prior to administration. For detailed instructions on preparation, administration, measures to take in case of accidental exposure and disposal of Upstaza, and on preparation of the surgical suite infusion, see the full prescribing information. **Ingredients**: Eladocagene exuparvovec; Upstaza is a gene therapy medicinal product that expresses the human aromatic Lamino acid decarboxylase enzyme (hAADC). It is a non-replicating recombinant adeno-associated virus serotype 2 (AAV2) based vector containing the cDNA of the human dopa decarboxylase (DDC) gene under the control of the cytomegalovirus immediate-early promoter. **Excipients**: potassium chloride, sodium chloride, potassium dihydrogen phosphate, disodium hydrogen phosphate, poloxamer 188, water for injections. **Contraindications**: Hypersensitivity to the active substance or to any of the excipients. **Special warnings and precautions for use**: Proper aseptic techniques should always be used for the preparation and infusion of Upstaza. Patients should be closely monitored for complications related to procedure (especially for cerebrospinal fluid (CSF) leaks, particularly in relation to the risk of meningitis and encephalitis), their underlying disease, and risks associated with general anaesthesia during the perioperative period. Patients may experience exacerbations of symptoms of their underlying AADC deficiency as a result of surgery and anaesthesia, and persistence of autonomic and serotonergic symptoms of AADC after treatment. AADC-deficient patients may have increased sensitivity to dopamine due to their chronic dopamine deficiency; the occurrence of dyskinesia is due to dopamine sensitivity and generally starts 1 month after the administration of gene therapy and gradually decreases over several months. Events of dyskinesia were managed with routine medical care, such as antidopaminergic treatment (risperidone). The risk of viral shedding is considered to be low due to very limited systemic distribution of eladocagene exuparvovec. As a precautionary measure, for 14 days after administration, patients/caregivers should be advised to handle waste material generated from dressings and/or any secretions (tears, blood, nasal secretions and CSF) appropriately, which may include storage of waste material in sealed bags prior to disposal and patients/caregivers wearing gloves for dressing changes and waste disposal, especially in case of pregnancy, breast-feeding, or immunodeficiency of caregivers. Patients treated with Upstaza must not donate blood, organs, tissues, and cells for transplantation. **Interactions**: No interaction is expected. No reported interactions between general vaccinations and gene therapy administration; the healthcare provider should determine the patient's vaccination schedule. **Fertility, pregnancy and lactation**: The risk for germline transmission is low. There are no data from the use of eladocagene exuparvovec in pregnant women and regarding the effect on fertility. No effect on the breastfed newborns/ infants are anticipated. **Effects on ability to drive and use machines:** Not relevant. **Adverse reactions**: Adverse events reported in at least 2 patients during 3 openlabel clinical studies with eladocagene exuparvovec according to frequency: Very common (≥1/10): initial insomnia, dyskinesia. Common (≥1/100 to <1/10): feeding disorders, irritability, salivary hypersecretion. Neurosurgery-related adverse reactions occurring in at least 2 patients: Very common (≥1/10): anaemia, CSF fluid leakage (may include pseudomeningocele). Anaesthesia and postoperative related adverse reactions in at least 2 patients within 2 weeks after administration: Very common (≥1/10): pneumonia, hypokalaemia, irritability, hypotension, upper gastrointestinal haemorrhage, diarrhoea, decubitus ulcer, pyrexia, breath sounds abnormal. Common (≥1/100 to <1/10): gastroenteritis, dyskinesia, cyanosis, hypovolaemic shock, respiratory failure, mouth ulceration, dermatitis diaper, rash, hypothermia, tooth extraction. **Overdose:** Symptomatic and supportive treatment, close clinical observation and monitoring of laboratory parameters for systemic immune response are recommended. **Marketing Authorisation number and holder**: EU/1/22/1653/001. PTC Therapeutics International Limited, 70 Sir John Rogerson's Quay, Dublin 2, Ireland. Please consult the SmPC before prescribing. **Classification for sale or supply**: Subject to restricted medical prescription. **Date of Preparation**: April 2024.

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system. Adverse events should also be reported to PTC at pharmacovigilance@ptcbio.com.

Registration conditions may differ internationally; always consult local Prescribing Information and/or Summary of Product Characteristics before prescribing any product. For additional information, please contact PTC Therapeutics Medical Information at medinfo@ptcbio.com.

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