Pharmacy Practice Communicator

An Official Newsletter of the Department of Pharmacy Practice

Volume - 10 | Issue - 1 | January - March 2022

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Published by

NITTE (Deemed to be University)
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A SHORT REVIEW ON ONASEMNOGENE ABEPARVOVEC

Akshay Abraham Thomas*

Spinal muscular atrophy (SMA) is a genetic (inherited) neuromuscular disease that causes muscles to become weak and waste away. People with SMA lose a specific type of nerve cell in the spinal cord called motor neurons that control muscle movement. In the absence of these motor neurons, muscles don't receive nerve signals that are necessary for their movement. It is a ruinous neurodegenerative autosomal recessive disease that arises because of the survival of motor neuron 1 (SMN1) gene mutation or deletion. Patients with spinal muscular atrophy type 1 utilize supportive care, which focuses on symptom management. They can never sit unassisted, and 75% die or require permanent ventilation by the age of 13.6 months. Approximately 10,000 to 25,000 children and adults live with SMA in the United States. It's a rare disease that affects one out of 6,000 to 10,000 children. The quality of life and life expectancy for people with SMA varies depending on the type. Infants with type 1 SMA usually die before their second birthday. Children with type 2 or type 3 SMA may live full lives depending on the severity of symptoms. People who develop SMA during adulthood (type 4) often remain active and enjoy a normal life expectancy.[1]

On Dec. 23, 2016, the U.S. Food and Drug Administration (FDA) approved Spinraza (nusinersen) for the treatment of SMA. It is a disease modifying therapy that is designed to treat the underlying defect in SMA, which means it potentially may be effective at slowing, stopping, or perhaps reversing the symptoms of SMA. In May 2019, the FDA approved Zolgensma (onasemnogene abeparvovac-xioi), the first gene-replacement therapy for a neuromuscular disease. Zolgensma is mainly available in the United States, and it is marketed by AveXis, a Novartis company. Onasemnogene abeparvovec (Zolgensma, formerly AVXS-101) comprises of an adeno-associated viral vector containing the human SMN gene under the control of the chicken beta-actin promoter. This therapy addresses the genetic root cause of the disease by increasing functional SMN protein in motor neurons and preventing neuronal cell death, resulting in improved neuronal and muscular function as previously demonstrated in transgenic animal models.[2]

Before starting the treatment of spinal muscular atrophy, one day prior to infusion, the patient is administered with oral corticosteroids (e.g., prednisolone 1 mg/kg/dose once daily or equivalent) and should be continued for at least 30 days. This is done because taking corticosteroids with Zolgensma treatment helps prevents serious liver damage by reducing a significant rise in liver enzymes.

Note: May be administered to preterm neonates once PMA (Post Menstrual Age) reaches full term.

Term Neonates: IV infusion: 1.1×10^{14} vector genomes/ kg as a single dose.

Infants and Children <2 years: IV infusion: 1.1×10^{14} vector genomes/ kg as single dose.[3]

Route of administration for this therapy is IV, which is stated to be slow IV infusion only; do not administer as IV push or bolus. It is recommended to flush with saline before and after administration. Finally infuse onasemnogene abeparvovec slowly over 60 minutes. The recommended storage conditions for Zolgensma is 2°C to 8°C (36°F to 46°F) for ≤14 days. Do not refreeze.

Dose volume based on weight range:

Weight range (kg)	Dose Volume (ml)	Population
2.6 to 3	16.5	NEONATAL & PAEDIATRIC
3.1 to 3.5	19.3	
3.6 to 4	22	
4.1 to 4.5	24.8	
4.6 to 5	27.5	
5.1 to 5.5	30.3	
5.6 to 6	33	
6.1 to 6.5	35.8	
6.6 to 7	38.5	
7.1 to 7.5	41.3	
7.6 to 8	44	
8.1 to 8.5	46.8	PAEDIATRIC
8.6 to 9	49.5	
9.1 to 9.5	52.3	
9.6 to 10	55	
10.1 to 10.5	57.8	
10.6 to 11	60.5	
11.1 to 11.5	63.3	
11.6 to 12	66	
12.1 to 12.5	68.8	
12.6 to 13	71.5	
13.1 to 13.5	74.3	
≥13.6	Multiple kits will be required.	

Some of the adverse reactions that have been reported in neonates, infants and young children are increased serum alanine aminotransferase, increased serum aspartate aminotransferase and vomiting.

Monitoring parameters to be taken note of during treatment with Zolgensma (Basic): Liver function (clinical exam, AST, ALT, total bilirubin and prothrombin time [PT]), CBC (Hgb, platelet count), troponin I and anti-AAV9 antibody test.

It is important to note that Zolgensma isn't marketed or available in India and has to be imported from the US if prescribed by a medical practitioner. At $2.125 million, it is touted to be the world's most expensive drug. When it comes to India, the price is approximately 16 crores. [4]

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DARIDOREXANT: TREATMENT OF INSOMNIA

Varshini Sathish*

Insomnia is defined as a dissatisfaction with sleep either qualitatively or quantitatively.[1] It is a condition characterized by difficulty in initiation, maintenance and early awakening resulting in subjectively reduced daily functioning.[2] Benzodiazepine sedatives, non-benzodiazepine sedatives, melatonin receptor agonists, antidepressants, and orexin receptor antagonist are the commonly recommended pharmacological therapies.[3]

Daridorexant is a dual orexin receptor antagonist. It is a new, potent and selective compound being evaluated for the treatment of insomnia that blocks the action of the orexin neuropeptides of both orexin 1 and orexin 2 receptors [4]. Oral administration is characterized by quick absorption (bioavailability of 62%) and elimination, with a median value to reach maximum concentration (t_{max}) of 1-2 h and a mean terminal half-life ($t_{1/2}$) of approximately 8 h for a dose range of 5-50mg.[5] It has a high plasma protein binding of 99.7% as well. [6]

The recommended dosage is 25 mg to 50 mg once per night, taken orally within 30 minutes before going to bed, with at least 7 hours remaining prior to planned awakening [6]. Daridorexantwas noted to improve both sleep latency variables and Wake after sleep onset (WASO), whereas Zolpidem only improved the former and had a null effect on the WASO.[7] Common side effects associated with the drug are headache (7%), somnolence (5%) and dizziness (3%). [6]

There is no available data on the use of this drug among pregnant women, However, fetal toxicity or malformation in animal reproduction studies was not observed. In the case of lactating women, monitoring infants for excessive sedation should be considered. The safety of daridorexant has not been established in the pediatric population. Even though no dose adjustment is required during its use among geriatric patients, one should monitor for an increased risk of falls. This novel drug is contraindicated in patients with narcolepsy. Currently, there is no specific antidote in case of an overdosing with daridorexant. General symptomatic, supportive and medical care accompanied with gastric lavage and close monitoring of vitals and symptoms can help alleviate the toxicities of poisoning.[6]

References:

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2. Ditmer M, Gabryelska A, Turkiewicz S, Białasiewicz P, Małecka-Wojciesko E, Sochal M. Sleep problems in chronic inflammatory diseases: prevalence, treatment, and new perspectives: a narrative review. Journal of clinical medicine. 2022; 11(1): 67.
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4. Berger B, Muehlan C, Klein G, Dingemanse J. Pharmacokinetics of daridorexant, a dual orexin receptor antagonist, are not affected by renal impairment. Clinical and Translational Science. 2021; 14(6): 2132-8.
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Adverse Drug Reaction Reported to AMC (January– March 2022)

Suspected Drug	Adverse Drug Reaction	Number (%) (n=64)
Clonazepam + Imipramine	Constipation	1 (1.5%)
Mirtazapine		1 (1.5%)
Tramadol		5 (7.8%)
Olanzapine		1 (1.5%)
Diclofenac		1 (1.5%)
Tramadol + Acetaminophen		1 (1.5%)
Clozapine		1 (1.5%)
Hyoscyamine		1 (1.5%)
Lorazepam		1 (1.5%)
Lithium	Tremor	1 (1.5%)
Olanzapine		1 (1.5%)
Sodium Valproate		1 (1.5%)
Lorazepam		1 (1.5%)
Clonazepam		1 (1.5%)
Furosemide	Hypokalemia	2 (3.12%)
Meropenem	Seizures	1 (1.5%)
Amoxicillin + Clavulanic Acid	Thrombocytopenia	1 (1.5%)
Dabigatran	Hemorrhage	1 (1.5%)
Meropenem	Acute Kidney Injury	1 (1.5%)
Sodium Valproate	Insomnia	1 (1.5%)
Ceftriaxone	Diarrhea	1 (1.5%)
Piperacillin + Tazobactam		1 (1.5%)
Gliclazide		1 (1.5%)
Clindamycin		1 (1.5%)
Lorazepam	Drowsiness	2 (3.12%)
Olanzapine		2 (3.12%)
Levetiracetam		1 (1.5%)
Sodium Valproate		1 (1.5%)
Clonazepam		1 (1.5%)
Quetiapine		1 (1.5%)

Suspected Drug	Adverse Drug Reaction	Number (%) (n=64)
Dexamethasone	Psychosis	1 (1.5%)1
Quetiapine + Imipramine	Restlessness	(1.5%)1
Quetiapine + Lithium		(1.5%)1
Dosulipin	Weight Gain	(1.5%)1
Dosulipin	Xerostomia	(1.5%)1
Quetiapine	Extrapyramidal Symptoms	(1.5%)2
Risperidone		(3.12%)1
Quetiapine	Irritability	(1.5%)1
Linezolid	Increased Blood Urea	(1.5%)1
Amphotericin B	Dyselecrtolytemia	(1.5%)1
Eplerenone	Hyperkalemia	(1.5%)1
Amoxicillin + Clavulanic Acid		(1.5%)1
Cefuroxime	Vomiting	(1.5%)1
Amlodipine	Pedal Edema	(1.5%)1
Ceftriaxone	Increased Serum Creatinine Level	(1.5%)1
Sodium Valproate	Nausea	(1.5%)1
Clindamycin	Maculopapular Rash	(1.5%)1
Cisplatin	Thrombophlebitis	(1.5%)2
Human Insulin	Hypoglycemia	(3.12%)1
Risperidone	Gastritis	(1.5%)1
Clonazepam	Bradycardia	(1.5%)1
Docetaxel	Neutropenia	(1.5%)1
Methotrexate	Skin Eruption	(1.5%)1
Acetaminophen	Skin Rash	(1.5%)1
Olanzapine	Itching	(1.5%)

NEW DRUGS APPROVED BY U.S. FOOD AND DRUG ADMINISTRATION (FDA)

(January - March 2022)

Megha Sunny*

Generic Name	Brand Name	Uses	Approved (Month, Year)
Sutimlimab-jome	Enjaymo	To decrease the need for red blood cell transfusion due to hemolysis in cold agglutinin disease	February 2022
Mitapivat	Pyrukynd	To treat hemolytic anemia in pyruvate kinase deficiency	February 2022
Pacritinib	Vonjo	To treat intermediate or high-risk primary or secondary myelofibrosis in adults with low platelets	February 2022
Ztalmy	Ztalmy	To treat seizures in cyclin-dependent kinase-like 5 deficiency disorder	March 2022
Nivolumab and relatlimab-rmbw	Opdualag	To treat unresectable or metastatic melanoma	March 2022

Reference : *Available from: https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2022(Last accessed on 28 March 2022)*

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NEW DRUGS APPROVED BY CENTRAL DRUGS STANDARD CONTROL ORGANISATION (CDSCO)
(January - March 2022)

Melja Joseph*

Sl.No.	Name of Drug	Uses	Date of Issue
1	Triamcinolone Hexacetonide injectable suspension 20mg/ml	For intraarticular, intra-synovial or periarticular use in adults and adolescents for the symptomatic treatment of subacute and chronic inflammatory joint diseases including rheumatoid arthritis and Juvenile Idiopathic Arthritis (JIA), Osteoarthritis and post-traumatic arthritis, Synovitis, tendinitis, bursitis and epicondylitis.	20.01.2022
2	Gimeracil bulk & Oteracil potassium bulk and Tegafur 15mg/20mg, Gimeracil 4.35mg/5.8mg and Oteracil 11.8mg/ 15.8mg capsules	Indicated in adults for the treatment of advanced gastric cancer when given in combination with cisplatin.	01.02.2022
3	Nitric oxide nasal spray	For treatment of adult high-risk patients with mild Covid-19 having risk of progression of the disease.	08.02.2022
4	Vericiguat tablets 2.5mg/ 5mg/ 10mg	Indicated to reduce the risk of cardiovascular death and heart failure (HF) hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics, in adults with symptomatic chronic HF and an ejection fraction less than 45%	25.02.2022
5	Inosine pranobex bulk and Inosine pranobex 500mg tablet	As an add on therapy for the treatment of mild Covid-19 patients with co-morbidities and moderate Covid-19 patients.	02.03.2022
6	Desidustat bulk and Desidustat tablets 25mg and 50mg	For treatment of Anemia in adult patients with chronic kidney disease (CKD) not on Dialysis and on Dialysis.	03.03.2022

Reference : https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=ODIzOA==(Last accessed on 28 March 2022)22)

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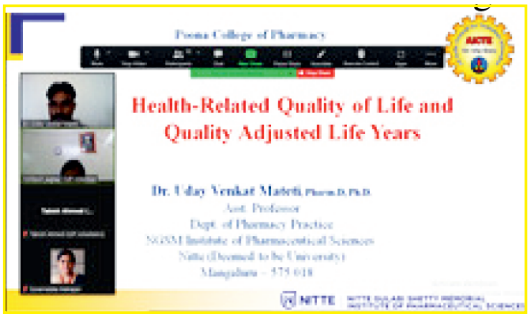
DEPARTMENT OF PHARMACY PRACTICE NEWS

PAPER PRESENTATION : Students Mr. Shijas Ahammed P.P. (M. Pharm), Mrs. Zainabath Mahnoora (M. Pharm) and Ms. S. Dhanya Nayak (Fifth Pharm. D) each presented a paper in the scientific poster session in the 7th International Conference on Clinical Pharmacy organized by Centre for Pharmaceutical Care, Department of Pharmacy Practice conducted during 6-8th January 2022 by Manipal College of Pharmaceutical Sciences, a constituent unit of MAHE, Manipal.

GUEST LECTURE ON "REMINISCING TREATMENT OPTIONS DURING THE COVID-19 PANDEMIC: A PHYSICIAN'S EXPERIENCE" : The Department of Pharmacy Practice of NGSM Institute of Pharmaceutical Sciences organized a guest lecture on "Reminiscing treatment options during the COVID-19 pandemic: A Physician's Experience" on the 21st of March 2022 at Justice K.S. Hegde Charitable Hospital, Deralakatte, Mangaluru. The guest speaker for the event was Dr. Adithi Shetty, Associate Professor, Department of General Medicine, K. S. Hegde Medical Academy, Nitte (DU).

GUEST LECTURE ON "TUBERCULOSIS- PAST, PRESENT AND FUTURE" : The Department of Pharmacy Practice of NGSM Institute of Pharmaceutical Sciences organized a guest lecture on "Tuberculosis – Past, Present and Future" to commemorate World Tuberculosis Day on 24th of March 2022 at Justice K.S. Hegde Charitable Hospital, Deralakatte, Mangaluru. The guest speaker for the event was Dr. Rajesh V, Associate Professor, Department of Pulmonary Medicine, Justice K.S. Hegde Charitable Hospital, K. S. Hegde Medical Academy, Nitte (DU), Mangaluru.



TALK ON "HEALTH-RELATED QUALITY OF LIFE AND QUALITY ADJUSTED LIFE YEARS" : Dr. Uday Venkat Mateti, Asst. Professor, Dept. of Pharmacy Practice, NGSM Institute of Pharmaceutical Sciences delivered a talk on "Health-Related Quality of Life and Quality Adjusted Life Years" in the AICTE sponsored STC on Newer Horizons in Pharmacy Practice held from 7-12 March 2022 organized by Poona College of Pharmacy, Poona.

NGSM Institute of Pharmaceutical Sciences

Nitte Institutions

Health Science Institutions, Hospitals and Research Centres

1. K.S. Hegde Medical Academy, Mangaluru
2. A.B. Shetty Memorial Institute of Dental Sciences, Mangaluru
3. Nitte Gulabi Shetty Memorial Institute of Pharmaceutical Sciences, Mangaluru
4. Nitte Usha Institute of Nursing Sciences, Mangaluru
5. Nitte Institute of Physiotherapy, Mangaluru
6. Nitte Institute of Medical Laboratory Sciences, Mangaluru
7. Nitte Institute of Speech and Hearing, Mangaluru
8. Justice K. S. Hegde Charitable Hospital, Mangaluru
9. Nitte Meenakshi Institute of Craniofacial Surgery, Mangaluru
10. Leela Narayana Shetty Memorial Cancer Institute, Mangaluru
11. Nitte-Gajria Hospital, Karkala
12. Kshema-IVF: Fertillity & Reproductive Medicine Centre, Mangaluru
13. Nitte Rural Psychiatry Centre, Nitte.
14. Kowdoor Gopal Hegde & Smt. Manorama Hegde Hospital, Bailur.
15. Nitte University Centre for Science Education & Research (NUCSER), Mangaluru
16. Nitte University Centre for Animal Research & Experimentation (NUCARE), Mangaluru
17. Nitte University Centre for Stemcell Research & Regenerative Medicine (NUCSReM), Mangaluru

Engineering Institutions

18. Nitte Mahalinga Adyanthaya Memorial Institute of Technology, Nitte
19. Nitte Meenakshi Institute of Technology, Bengaluru
20. Nitte Institute of Architecture, Mangaluru

Management Institutions

21. Justice K. S. Hegde Institute of Management (Dept. of Nitte Management Studies, NMAMIT, Nitte)
22. Nitte School of Management, Bengaluru
23. Sarosh Institute of Hotel Administration, Mangaluru
24. Nitte Institute of Banking & Finance, Mangaluru
25. Nitte Institute Communication, Mangaluru

Technical Instituions

26. Nitte Rukmini Adyanthaya Memorial Polytechnic, Nitte
27. Mulki Ramakrishna Punja Industrial Training Institute, Thokur

Science and Commerce Institutions

28. Dr. Nitte Shankara Adyanthaya Memorial First Grade College, Nitte
29. Dr. Nitte Shankara Adyanthaya Memorial First Grade College, Bengaluru
30. Dr. Nitte Shankara Adyanthaya Memorial Pre-University College, Nitte
31. Dr. Nitte Shankara Adyanthaya Memorial Pre-University College, Mangaluru
32. Dr. Nitte Shankara Adyanthaya Memorial Pre-University College, Bengaluru

Schools

33. Dr. Nitte Shankara Adyanthaya Memorial Senior Secondary School, Nitte
34. Dr. Mundkur Ramanna Shetty Memorial English Medium High School, Thokur
35. Nitte International School, Bengaluru
36. Dr. Nitte Shankara Adyanthaya Memorial Higher Primary School, Bolakodi

Satellite Health Centres:

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