PRESCRIBING INFORMATION

NAME OF THE MEDICINAL PRODUCT

DAYBUE®

Oral solution.

COMPOSITION

Each ml of oral solution contains 200 mg of trofinetide.

Excipient(s) with known effect
This medicine contains maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
This medicine contains methylparaben sodium, propylparaben sodium, propylene glycol, and FD&C Red No. 40.
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'.

For the full list of excipients, see section 11.

1 THERAPEUTIC INDICATIONS

DAYBUE is indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older and weighing at least 9 kg.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

Administer DAYBUE orally twice daily, in the morning and evening, according to patient weight as shown in **Table 1**. DAYBUE can be taken with or without food.

Table 1 Recommended Dosage of DAYBUE in Patients 2 Years of Age and Older

Patient Weight	DAYBUE Dosage	DAYBUE Volume
9 kg to less than 12 kg	4,000 mg twice daily	20 ml twice daily
12 kg to less than 20 kg	6,000 mg twice daily	30 ml twice daily
20 kg to less than 35 kg	8,000 mg twice daily	40 ml twice daily
35 kg to less than 50 kg	10,000 mg twice daily	50 ml twice daily
50 kg or more	12,000 mg twice daily	60 ml twice daily

Recommended Titration Dosing Schedule of DAYBUE
- Start with 50% of the recommended dose (see **Table 1** or **Table 2**) taken twice daily.
- Increase the dose over 4 to 8 weeks until the recommended dose is reached.

A longer titration period may be required if patients are experiencing side effects and/or are not able to tolerate DAYBUE.

2.2 Administration Information

Administer DAYBUE orally or via gastrostomy (G) tube; doses administered via gastrojejunal (GJ) tubes must be administered through the G-port.

Using a dosing cup provided with the medicinal product, measure the appropriate volume (ml) of oral solution corresponding to the prescribed dose of DAYBUE.

Administer the entire contents of the dosing cup orally. After the administration, the dosing cup should be rinsed under running cold water and air dry. Store the cleaned dosing cup with the bottle until next use.

Discard any unused DAYBUE oral solution after 14 days of first opening the bottle *[see How Supplied/Storage and Handling (16.2)]*.

2.3 Dose Modification for Diarrhea or Weight Loss

Advise patients to stop laxatives before starting DAYBUE. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs, if dehydration is suspected, or if significant weight loss occurs *[see Warnings and Precautions 5.1, 5.2)]*.

2.4 Dose Modification for Vomiting After Administration

If vomiting occurs after DAYBUE administration, an additional dose should not be taken. Instead, continue with the next scheduled dose. Interrupt, reduce dose, or discontinue DAYBUE if vomiting is severe or occurs despite medical management *[see Warnings and Precautions (5.3)]*.

2.5 Dosage Recommendations in Patients with Renal Impairment

No dosage adjustment is required in patients with mild renal impairment with an estimated glomerular filtration rate (eGFR) of 70 to 89 ml/min/1.73 m^2. However, as the degree of renal impairment increases so does trofinetide exposure. Consider a 20% to 30% dose reduction for those with a high degree of mild renal impairment with eGFR 60 to 70 ml/min/1.73 m^2.

The recommended dose of DAYBUE for patients with moderate renal impairment (eGFR 30 to 59 ml/min/1.73 m^2) is described in **Table 2**.

Table 2 Recommended Dosage of DAYBUE in Patients with Moderate Renal Impairment

Patient Weight	DAYBUE Dosage	DAYBUE Volume
9 kg to less than 12 kg	2,000 mg twice daily	10 ml twice daily
12 kg to less than 20 kg	3,000 mg twice daily	15 ml twice daily
20 kg to less than 35 kg	4,000 mg twice daily	20 ml twice daily
35 kg to less than 50 kg	5,000 mg twice daily	25 ml twice daily
50 kg or more	6,000 mg twice daily	30 ml twice daily

Consider a 20% to 30% further dose reduction for those with a high degree of moderate renal impairment.

DAYBUE is not recommended in patients with severe renal impairment (eGFR 15 to 29 ml/min/1.73 m^2) or with end stage renal disease (see 12.3 Pharmacokinetics).

2.6 Patients With Hepatic Impairment

The pharmacokinetics in patients with hepatic impairment have not been studied. However, hepatic impairment is not expected to impact the exposure of trofinetide because hepatic metabolism is not a significant route of trofinetide elimination.

2.7 Missed Dose

If a dose of DAYBUE is missed, the next dose should be taken as scheduled. Doses should not be doubled.

3 DOSAGE FORMS AND STRENGTHS

200 mg/ml of a pink to red, strawberry flavored oral solution.

4 CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed in section 11.

5 WARNINGS AND PRECAUTIONS

5.1 Diarrhea

In Study 1 *[see Clinical Studies (14)]* and in long-term studies, 85% of patients treated with DAYBUE experienced diarrhea. In those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy. Diarrhea severity was of mild or moderate severity in 96% of cases. In Study 1, antidiarrheal medication was used in 51% of patients treated with DAYBUE.

Advise patients to stop laxatives before starting DAYBUE . If diarrhea occurs, patients should notify their healthcare provider, consider starting antidiarrheal treatment, and monitor hydration status and increase oral fluids, if needed. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs or if dehydration is suspected *[see Dosage and Administration (2.4)]*.

5.2 Weight Loss

In Study 1, 12% of patients treated with DAYBUE experienced weight loss of greater than 7% from baseline, compared to 4% of patients who received placebo. In long-term studies, 2.2% of patients discontinued treatment with DAYBUE due to weight loss.

Monitor weight and interrupt, reduce dose, or discontinue DAYBUE if significant weight loss occurs *[see Dosage and Administration (2.4)]*.

5.3 Vomiting

In Study 1, vomiting occurred in 29% of patients treated with DAYBUE and in 12% of patients who received placebo *[see Adverse Reactions (6.1)]*.

Patients with Rett syndrome are at risk for aspiration and aspiration pneumonia. Aspiration and aspiration pneumonia have been reported following vomiting in patients being treated with DAYBUE. Interrupt, reduce dose, or discontinue DAYBUE if vomiting is severe or occurs despite medical management *[see Dosage and Administration (2.5)]*.

5.4 QT Prolongation

Patients with Rett syndrome are at increased risk of QT prolongation. A dedicated QT study using single doses of either 12, 18, or 24 g trofinetide in healthy adults did not provide evidence of QT prolongation. In the clinical trials, patients with Rett syndrome with baseline QTc prolongation (QTc > 450 ms) were excluded. Some patients in the trofinetide studies experienced QT prolongation while on trofinetide; however, causality was unknown. Consider baseline and more frequent electrocardiogram monitoring in patients with Rett syndrome.

5.5 Monitoring and Laboratory Tests

All patients should have baseline testing for serum potassium, calcium and magnesium levels as hypokalemia, hypocalcemia and hypomagnesemia are established risk factors for torsades de pointes in patients with underlying QTc prolongation. If a patient develops the adverse event of diarrhea, electrolyte abnormalities are more likely, thus more frequent monitoring of electrolytes is recommended. Any abnormalities should be promptly corrected. Additional ECG monitoring may also be considered in these patients.

5.6 Effects on ability to drive and use machines
There is no data on the effect of trofinetide on driving or using machines.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in labeling:

- Diarrhea *[see Warnings and Precautions (5.1)]*
- Weight Loss *[see Warnings and Precautions (5.2)]*
- Vomiting *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In controlled and uncontrolled trials in patients with Rett syndrome, 260 patients ages 2 to 40 years were treated with DAYBUE, including 112 patients treated for more than 6 months, 92 patients treated for more than 1 year, and 44 patients treated for more than 2 years.

Adult and Pediatric Patients with Rett Syndrome 5 Years of Age and Older
The safety of DAYBUE was evaluated in a randomized, double-blind, placebo-controlled, 12-week study of patients with Rett syndrome (Study 1) *[see Clinical Studies (14)]*. In Study 1, 93 patients received DAYBUE and 94 patients received placebo. All patients were female, 92% were White, and the mean age was 11 years (range 5 to 20 years).

Adverse Reactions Leading to Discontinuation of Treatment
Eighteen patients (19%) receiving DAYBUE had adverse reactions that led to withdrawal from the study. The most common adverse reaction leading to discontinuation of treatment with DAYBUE was diarrhea (15%).

Common Adverse Reactions
Adverse reactions that occurred in Study 1 in at least 5% of patients treated with DAYBUE and were at least 2% more frequent than in patients on placebo are presented in **Table 5**.

Table 5 Adverse Reactions in at Least 5% of Patients Treated with DAYBUE and at Least 2% Greater than Placebo in Study 1

Adverse Reaction	DAYBUE (N=93) %	Placebo (N=94) %
Diarrhea	82	20
Vomiting	29	12
Fever	9	4
Seizure	9	6
Anxiety	8	1
Decreased appetite	8	2
Fatigue	8	2
Nasopharyngitis	5	1

Pediatric Patients with Rett Syndrome 2 to 4 Years of Age
In an open-label study in pediatric patients 2 to 4 years of age with Rett syndrome (N=15), a total of 13 patients received DAYBUE for at least 12 weeks and 10 patients received DAYBUE for at least 12 months. Adverse reactions in pediatric patients 2 to 4 years of age treated with DAYBUE were similar to those reported in adult and pediatric patients 5 years of age and older with Rett syndrome in Study 1.

6.2 Postmarketing Experience
The following adverse reactions have been identified during postapproval use of DAYBUE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Aspiration and aspiration pneumonia secondary to vomiting *[see Warnings and Precautions (5.3)]*.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

7 DRUG INTERACTIONS

7.1 Effect of DAYBUE on Other Drugs
CYP3A and/or P-gp Substrates
Closely monitor patients when DAYBUE is administered concomitantly with sensitive CYP3A and/or P-gp substrates where minimal increases in the plasma concentration of these substrates may lead to serious adverse reactions. Trofinetide, a weak inhibitor of CYP3A and an inhibitor of P-gp, increased the plasma concentrations of CYP3A and/or P-gp substrates *[see Clinical Pharmacology (12.3)]*, which may increase the risk of adverse reactions associated with these substrates.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
There are no adequate data on the developmental risks associated with the use of DAYBUE in pregnant women. No adverse developmental effects were observed following oral administration of trofinetide to pregnant animals at doses associated with plasma exposures below those used clinically *[see Animal Data]*.

Data
Animal Data
Oral administration of trofinetide (0, 150, 450, or 1000 mg/kg twice daily; 0, 300, 900, or 2000 mg/kg/day) to pregnant rats during the period of organogenesis resulted in no adverse effects on embryofetal development. At the highest dose tested, plasma exposure (AUC) was less than that in humans at the maximum recommended human dose (MRHD) of 12,000 mg twice daily (24,000 mg/day).

Oral administration of trofinetide (0, 75, 150, or 300 mg/kg twice daily; 0, 150, 300, or 600 mg/kg/day) to pregnant rabbits during the period of organogenesis resulted in no adverse effects on embryofetal development. At the highest dose tested, plasma exposure (AUC) was less than that in humans at the MRHD.

Oral administration of trofinetide (0, 150, 450, or 1000 mg/kg twice daily; 0, 300, 900, or 2000 mg/kg/day) to rats throughout pregnancy and lactation resulted in no adverse effects on pre- and postnatal development. At the highest dose tested, plasma exposure (AUC) was less than that in humans at the MRHD.

8.2 Lactation

Risk Summary

There is no information regarding the presence of trofinetide or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for DAYBUE and any potential adverse effects on the breastfed infant from the treatment or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of DAYBUE for the treatment of Rett syndrome have been established in pediatric patients aged 2 years and older. The safety and effectiveness of DAYBUE for the treatment of Rett syndrome in pediatric patients 5 years of age and older was established in a randomized, double-blind, placebo-controlled, 12-week study (Study 1), which included 108 pediatric patients age 5 to less than 12 years of age and 47 pediatric patients age 12 to less than 17 years of age *[see Adverse Reactions (6.1) and Clinical Studies (14)]*. Use of DAYBUE in patients 2 to 4 years of age is supported by evidence from Study 1 and pharmacokinetic and safety data in 15 pediatric patients 2 to 4 years of age treated with DAYBUE *[see Dosage and Administration (2.1), Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]*.

Safety and effectiveness in pediatric patients less than 2 years of age have not been established.

Juvenile Animal Data

Oral administration of trofinetide (0, 150, 300, or 1000 mg/kg twice daily; 0, 300, 600, or 2000 mg/kg/day) to rats from postnatal day (PND) 13-14 through 28 weeks of age resulted in no adverse effects on growth or neurobehavioral function. Plasma exposures at the highest dose tested were similar to those in pediatric patients at recommended doses.

Oral administration of trofinetide (0, 150, 300, or 1000 mg/kg twice daily; 0, 300, 600, or 2000 mg/kg/day) to juvenile rats for 10 weeks beginning on PND 13-14 resulted in no adverse effects on sexual maturation or reproductive function. Plasma exposures at the highest dose tested were similar to those in pediatric patients at recommended doses.

8.5 Geriatric Use

Clinical studies of DAYBUE did not include patients 65 years of age and older to determine whether or not they respond differently from younger patients. This drug is known to be substantially excreted by the kidney. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function.

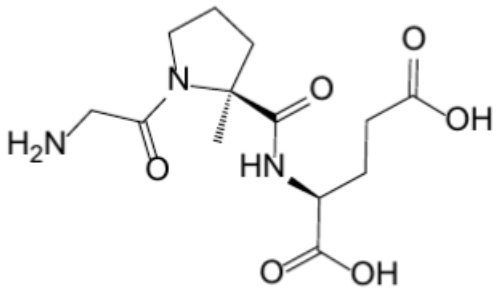
8.6 Renal Impairment

Mild renal impairment is not expected to impact the exposure of trofinetide; therefore, dosage adjustment is not necessary. Dosage adjustment of DAYBUE is recommended in patients with moderate renal impairment (adult: eGFR 30 to 59 ml/min; pediatric: eGFR 30 to 59 ml/min/1.73 m^2) *[see Dosage and Administration (2.6), Clinical Pharmacology (12.3)]*. Administration of DAYBUE to patients with severe renal impairment (eGFR less than 30 ml/min for adults or less than 30 ml/min/1.73 m^2 for pediatrics) is not recommended.

11 DESCRIPTION

DAYBUE oral solution contains the active moiety trofinetide. The chemical name of trofinetide is (2S)-2-{[(2S)-1-(2-aminoacetyl)-2-methylpyrrolidine-2-carbonyl]amino}pentanedioic acid (IUPAC). The molecular

formula of trofinetide is $C_{13}H_{21}N_3O_6$ and its molecular weight is 315.33 g/mol. The chemical structure is shown below.



Trofinetide is a white to off-white solid and is freely soluble in water.

DAYBUE oral solution is pink to red in color and contains 1 g of trofinetide in each 5 ml of solution (200 mg/ml). The oral solution also contains maltitol, strawberry flavor (contains propylene glycol), sucralose, methylparaben sodium, propylparaben sodium, FD&C Red No. 40 and purified water, as excipients.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
The mechanism by which trofinetide exerts therapeutic effects in patients with Rett syndrome is unknown.

12.2 Pharmacodynamics
Cardiac Electrophysiology
At the maximum recommended dose in healthy adult subjects, trofinetide does not prolong the QT interval to any clinically relevant extent.

12.3 Pharmacokinetics
Trofinetide exhibits linear kinetics with no time- or dose-dependent effect on pharmacokinetic parameters. Systemic exposure to trofinetide was dose-proportional across the studied dose range. Minimal to no accumulation was observed following multiple-dose administration.

Absorption
The time to maximum drug concentration (T_{max}) is about 2 to 3 hours after administration. Based on the mass balance study, at least 84% of the administered dose was absorbed following oral administration of 12,000 mg trofinetide.

Effect of Food
Coadministration of trofinetide with a high-fat meal had no impact on the total exposure ($AUC_{0\text{-}inf}$) of trofinetide and reduced the peak plasma concentration (C_{max}) by approximately 20% *[see Dosage and Administration (2.1)]*.

Distribution
Following oral administration, the apparent volume of distribution of trofinetide in adult healthy subjects was approximately 80 L. Trofinetide protein binding in human plasma is less than 6%.

Elimination

The effective elimination half-life of orally administered trofinetide in healthy subjects is about 1.5 hours.

Metabolism

Trofinetide is not significantly metabolized by CYP450 enzymes. Hepatic metabolism is not a significant route of trofinetide elimination.

Excretion

Trofinetide is primarily excreted unchanged (approximately 80% of the dose) in urine, with minor excretion in feces.

Specific Populations

Pediatric Patients

The drug exposure of trofinetide in pediatric patients ages 2 to 4 years of age is similar to children older than 4 years and adults when following the recommended dosage *[see Dosage and Administration (2.1)]*.

Patients with Renal Impairment

Based on population PK analysis of clinical trials data, patients with mild renal impairment (eGFR 60 to 89 ml/min/1.73 m^2) showed no significant impact on the exposure of trofinetide compared to patients with normal renal function. Based on a renal impairment study in adult subjects, the effect of moderate renal impairment (eGFR 30 to 59 ml/min) increases the exposure ($AUC_{0\text{-}inf}$) of trofinetide approximately 80% compared to patients with normal renal function administered the same dose *[see Dosage and Administration (2.6)]*. The effect of severe renal impairment on the exposure of trofinetide has not been investigated *[see Use in Specific Populations (8.6)]*.

Patients with Hepatic Impairment

The pharmacokinetics in patients with hepatic impairment have not been studied. However, hepatic impairment is not expected to impact the exposure of trofinetide because hepatic metabolism is not a significant route of trofinetide elimination.

Drug Interaction Studies

Clinical Studies

CYP3A and/or P-gp Substrates:

Coadministration of trofinetide 12,000 mg twice daily with 4 mg of loperamide (a moderately sensitive CYP3A substrate and a P-gp substrate) increased the AUC of loperamide by 1.73-fold and the C_{max} by 1.95-fold *[see Drug Interactions (7.1)]*. Administration of trofinetide 2 hours prior to loperamide increased the AUC of loperamide by 1.22-fold and the C_{max} by 1.44-fold.

In Vitro

Trofinetide is not a substrate of CYP450 enzymes, uridine diphosphate glucuronosyltransferase (UGT), or major drug transporters.

Cytochrome P450 (CYP450) Enzymes:

Trofinetide inhibits CYP3A *[see Drug Interactions (7.1)]. T*rofinetide inhibits CYP1A2, 2B6, 2C8, 2C19, and 2D6, but is not expected to result in clinically significant drug interactions. Trofinetide does not inhibit CYP2C9.

UDP-Glucuronosyltransferase (UGT):

Trofinetide inhibits UGT enzymes, UGT1A9, 2B7, and 2B15.

Transporter Systems:

Trofinetide inhibits P-gp *[see Drug Interactions (7.1)]*, BCRP, and BSEP. Trofinetide inhibits OAT1, OCT2, OATP1B1, OATP1B3, MATE1, and MATE2-K, but is not expected to result in clinically significant drug interactions. Trofinetide does not inhibit OAT3.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Studies to evaluate the carcinogenic potential of trofinetide have not been conducted.

Mutagenesis

Trofinetide was negative in in vitro (bacterial reverse mutation, chromosomal aberration in Chinese hamster ovary cells) and in vivo (mouse micronucleus) assays.

Impairment of Fertility

Oral administration of trofinetide (0, 150, 450, or 1000 mg/kg twice daily; 0, 300, 900, or 2000 mg/kg/day) to male and female rats prior to and throughout mating and continuing in females through gestation day 7 resulted in no adverse effects on fertility or reproductive function. Plasma exposures at the highest dose tested were less than that in humans at the maximum recommended human dose of 12,000 mg/dose (24,000 mg/day).

14 CLINICAL STUDIES

The efficacy of DAYBUE for the treatment of Rett syndrome was established in a 12-week randomized, double-blind, placebo-controlled study in patients with Rett syndrome 5 to 20 years of age (Study 1; NCT04181723).

Patients (N=187) had a diagnosis of typical Rett syndrome according to the Rett Syndrome Diagnostic Criteria with a documented disease-causing mutation in the *MECP2* gene. Patients were randomized to receive DAYBUE (N=93) or matching placebo (N=94) for 12 weeks. The DAYBUE dosage was based on patient weight to achieve similar exposure in all patients *[see Dosage and Administration (2.1)]*.

The co-primary efficacy measures were change from baseline after 12 weeks of treatment in the total score of the Rett Syndrome Behaviour Questionnaire (RSBQ) and the Clinical Global Impression-Improvement (CGI-I) score. The RSBQ is a 45-item rating scale completed by the caregiver that assesses a range of symptoms of Rett syndrome (breathing, hand movements or stereotypies, repetitive behaviors, night-time behaviors, vocalizations, facial expressions, eye gaze, and mood). Each item is scored as 0 (not true), 1 (somewhat or sometimes true), or 2 (very true or often true), with a maximum possible score of 90 points. Lower scores reflect lesser severity in signs and symptoms of Rett syndrome. The CGI-I is rated by clinicians to assess whether a patient has improved or worsened on a 7-point scale (1=very much improved to 7=very much worse) in which a decrease in score indicates improvement.

Treatment with DAYBUE demonstrated a statistically significant difference in favor of DAYBUE as compared to placebo on the co-primary efficacy endpoints, the change from baseline in RSBQ total score, and the CGI-I score at week 12 (**Table 6**, **Figure 1**, and **Figure 2**).

Table 6 Summary of Study 1 Efficacy Results

		Mean Baseline Score (SE)	Mean Week 12 Score (SE)	LS Mean Change from Baseline to Week 12 (SE)	DAYBUE-Placebo Treatment Difference, LS Mean (95% CI)[a]	p-value
RSBQ	DAYBUE	43.7 (1.21)	39.9 (1.38)	-4.9 (0.94)	-3.2 (-5.7, -0.6)	0.018
	Placebo	44.5 (1.26)	42.8 (1.42)	-1.7 (0.90)		
CGI-I	DAYBUE	--	3.5 (0.08)	--	-0.3 (-0.5, -0.1)	0.003
	Placebo	--	3.8 (0.06)			

CI=confidence interval; LS mean=least-squares mean; SE=standard error
[a] Difference in LS mean from the mixed-effect model for repeated measure analysis

Figure 1 Change From Baseline in RSBQ Total Score in Study 1

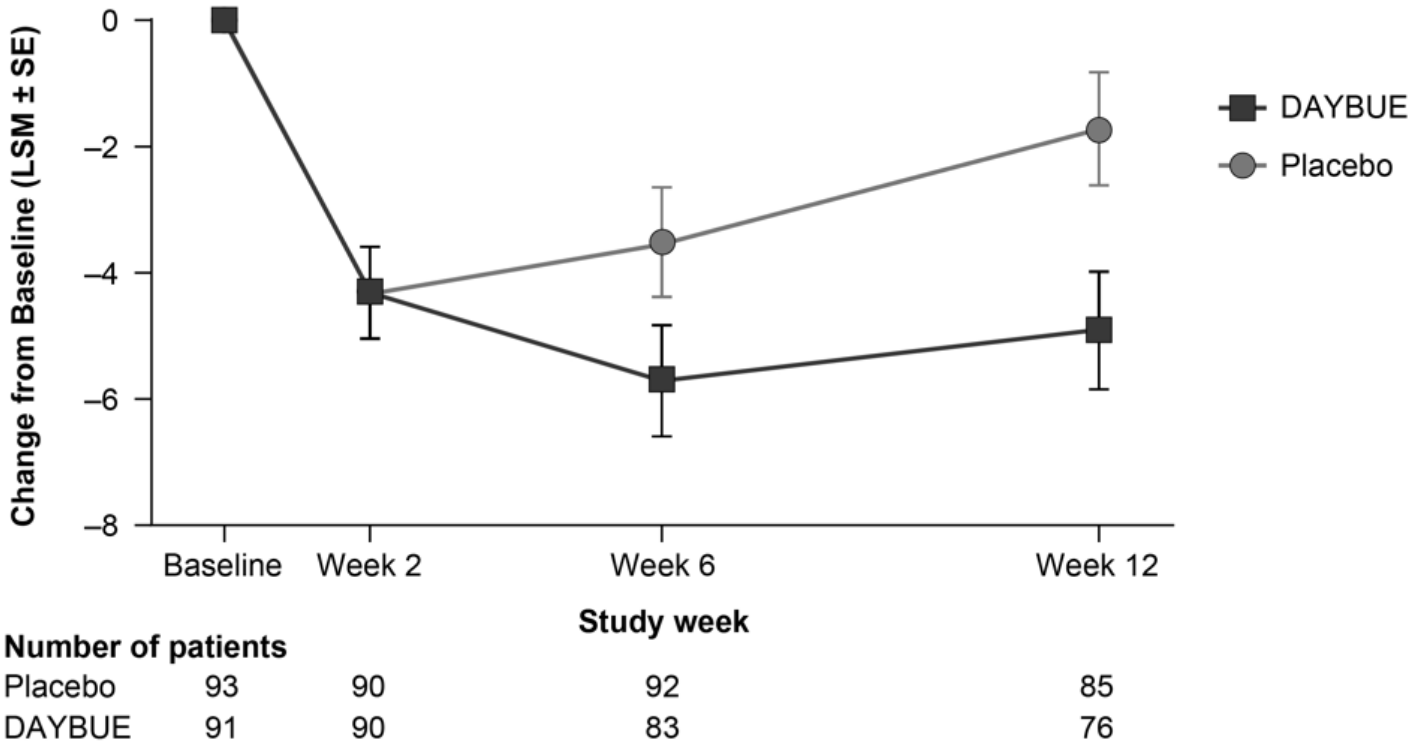
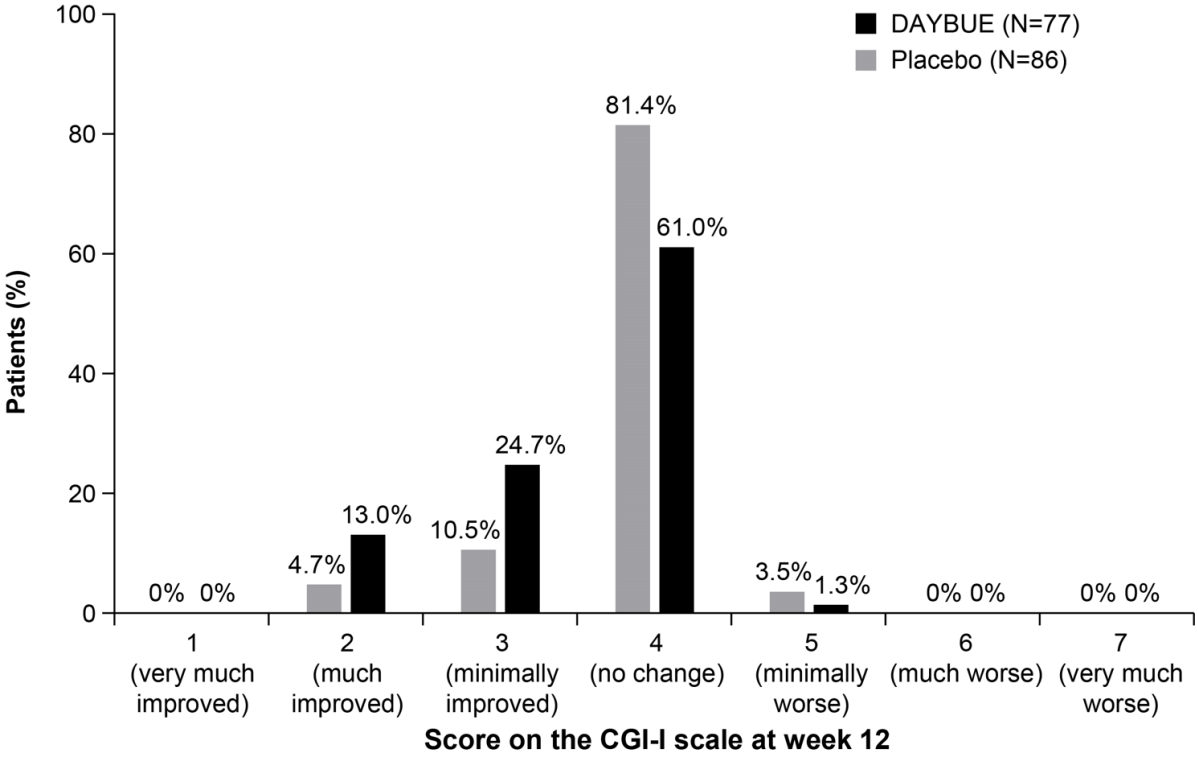


Figure 2 Distribution of CGI-I Scores for Patients Completing Study 1



16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

DAYBUE (trofinetide) 200 mg/ml oral solution is a pink to red, strawberry flavored solution supplied in a round high-density polyethylene (HDPE) multi-dose bottle with a child-resistant closure containing 450 ml of oral solution.

16.2 Storage and Handling

Store DAYBUE in an upright position refrigerated at 2°C to 8°C. Do not freeze.
Keep the child-resistant cap tightly closed.

Shelf life after first opening: 14 days at 2°C–8°C.

MANUFACTURER: Acadia Pharmaceuticals Inc. San Diego, CA 92130 USA

REGISTRATION HOLDER: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301, Israel.

Registration number: 181-58-38516-99

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