פברואר 2022

EVRYSDI® (Risdiplam 0.75mg/ml)
אוורייסדי
Powder for oral solution

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת רוש פרמצבטיקה (ישראל) בע"מ מבקשת להודיעכם על מספר עדכונים בעלון לרופא ובעלון לצרכן של התכשיר המצויין מעלה. בהודעה זו מצויניים רק עדכונים מהותיים ועדכונים אשר מהווים החמרה.

ההתוויה הרשומה לתכשירים בישראל:

EVRYSDI is indicated for the treatment of spinal muscular atrophy (SMA) types 1, 2 and 3 in patients 2 months of age and older.

הסבר:
טקסט עם קו תחתי מציין טקסט שהוסף לעלון.
~~טקסט עם קו חוצה~~ מציין טקסט שהוסר מן העלון.

למידע נוסף יש לעיין בעלון לרופא ובעלון לצרכן כפי שאושרו ע"י משרד הבריאות.

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על-ידי פנייה לבעל הרישום: רוש פרמצבטיקה (ישראל) בע"מ, ת.ד 6391 , הוד השרון 4524079 טלפון 09-9737777. כתובתנו באינטרנט: www.roche.co.il.

ב ב ר כ ה,

מאי קדים
מחלקת רישום

לילי אדר
רוקחת ממונה

עדכונים מהותיים בעלון לרופא

בסעיף 4.8 Undesirable effects עודכן המידע הבא:

Summary of the safety profile
In infantile-onset SMA patients, the most common adverse reactions observed in Evrysdi clinical studies were pyrexia **(**~~48.4~~ 54.8%), rash **(**~~27.4~~ 29.0%) and diarrhoea (~~16.1~~ 19.4%).

[…]

Post-marketing experience

Cutaneous vasculitis was reported during post-marketing experience. Symptoms recovered after permenant discontinuation of Evrysdi. The frequency cannot be estimated based on available data.

[…]

בסעיף 5.1 Pharmacodynamic properties עודכן המידע הבא:

[…]

Pharmacodynamic effects

In clinical studies, risdiplam led to an increase in SMN protein in blood with a greater than 2-fold median change from baseline within 4 weeks of treatment initiation across all SMA types studied. The increase was sustained throughout the treatment period (of at least ~~12~~ 24 months).

[…]

FIREFISH Part 2

[…]

Table 3. Summary of key efficacy results at month 12 and month 24 (FIREFISH Part 2)

Efficacy Endpoints	**Proportion of Patients N=41 (90% CI)**	
	Month 12	**Month 24**
Motor function and development milestones		
BSID-III: sitting without support for at least 5 seconds	29.3% (17.8%, 43.1%) p <0.0001[a]	61.0% (46.9%, 73.8%)
CHOP-INTEND: score of 40 or higher	56.1% (42.1%, 69.4%)	75.6% (62.2%, 86.1%)
CHOP-INTEND: increase of ≥4 points from baseline	90.2% (79.1%, 96.6%)	90.2% (79.1%, 96.6%)
HINE-2: motor milestone responders[b]	78.0% (64.8%, 88.0%)	85.4% (73.2%, 93.4%)
HINE-2: sitting without support[c] ~~HINE-2: supports weight or stands with support[d]~~	24.4% (13.9%, 37.9%) ~~22.0% (12.0%, 35.2%)~~	53.7% (39.8%, 67.1%)
Survival and event-free survival		
Event-free survival[d]	85.4% (73.4%, 92.2%)	82.9% (70.5%, 90.4%)
Alive	92.7% (82.2%, 97.1%)	92.7% (82.2%, 97.1%)
Feeding		
Ability to feed orally[e]	82.9% (70.3%, 91.7%)	85.4% (73.2%, 93.4%)

Abbreviations: CHOP-INTEND=Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; HINE-2=Module 2 of the Hammersmith Infant Neurological Examination.

[a] p-value is based on a one-sided exact binomial test. The result is compared to a threshold of 5%.

[b] According to HINE-2: ≥2 point increase [or maximal score] in ability to kick, OR ≥1 point increase in the motor milestones of head control, rolling, sitting, crawling, standing or walking, AND improvement in more categories of motor milestones than worsening is defined as a responder for this analysis.

[c] Sitting without support includes patients that achieved "stable sit" (~~15~~ 24%, ~~6~~10/41) and "pivots (rotates)" (~~10~~ 29%, ~~4~~12/41) as assessed by the HINE-2 at Month 24.

~~[d] Supports weight or stands with support includes patients that achieved "supports weight" (17%, 7/41) and "stands with support" (5%, 2/41) as assessed by the HINE-2.~~

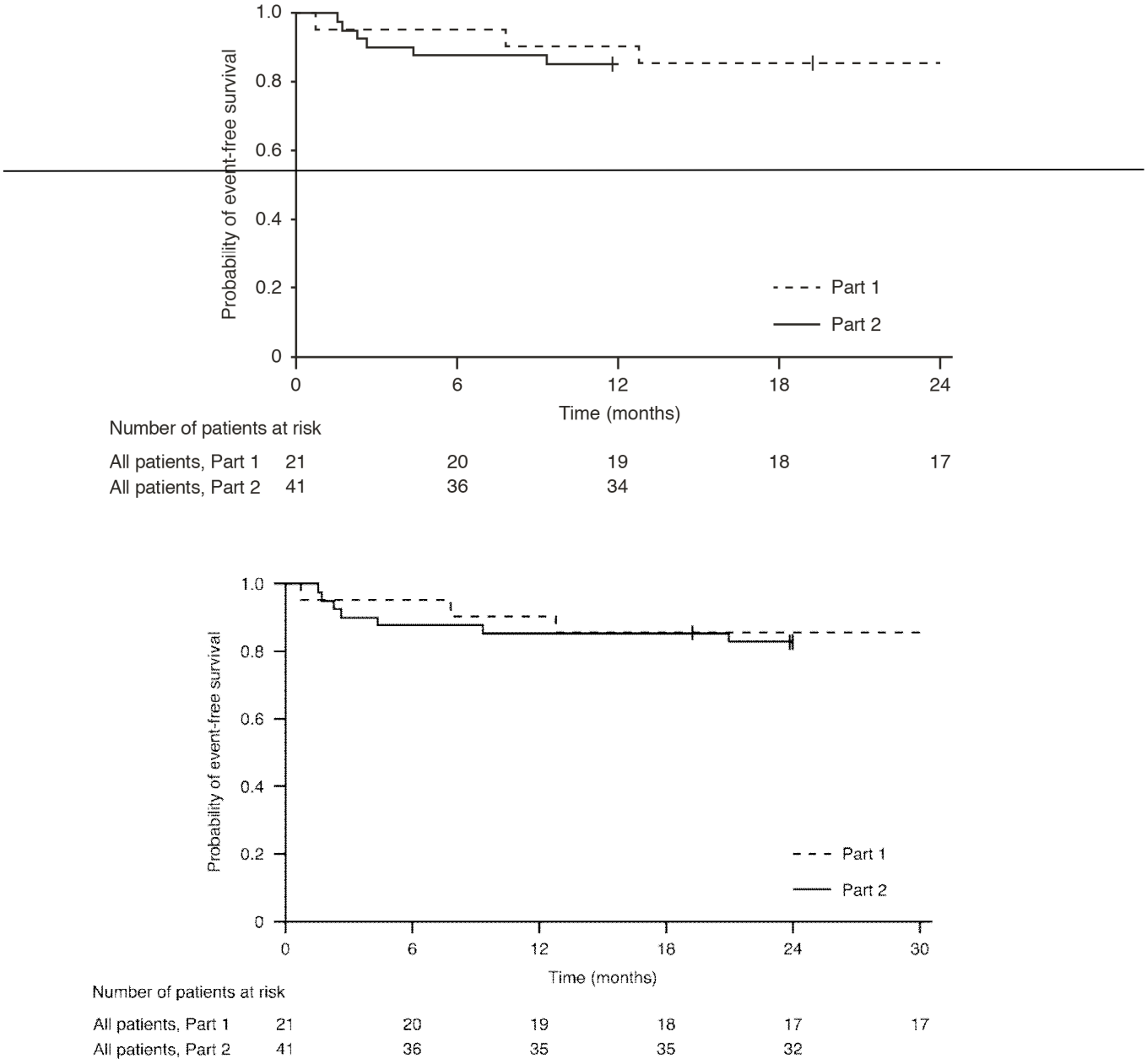
[d] An event is meeting the endpoint of permanent ventilation defined as tracheostomy or ≥16 hours of non-invasive ventilation per day or intubation for > 21 consecutive days in the absence of, or following the resolution of, an acute reversible event. Three patients died within the first 3 months following study enrolment and 4 patients met the endpoint of permanent ventilation before Month ~~12~~ 24. ~~All~~ These 4 patients achieved an increase of at least 4 points in their CHOP-INTEND score from baseline.

[e] Includes patients who were fed exclusively orally (~~28~~29 patients overall) and those who were fed orally in combination with a feeding tube (6 patients overall) at Month ~~12~~24.

At Month 24, 44% of patients achieved sitting without support for 30 seconds (BSID-III, Item 26). Patients continued to achieve additional motor milestones as measured by the HINE-2; 80.5% were able to roll and 27% of patients achieved a standing measure (12% supporting weight and 15% standing with support).

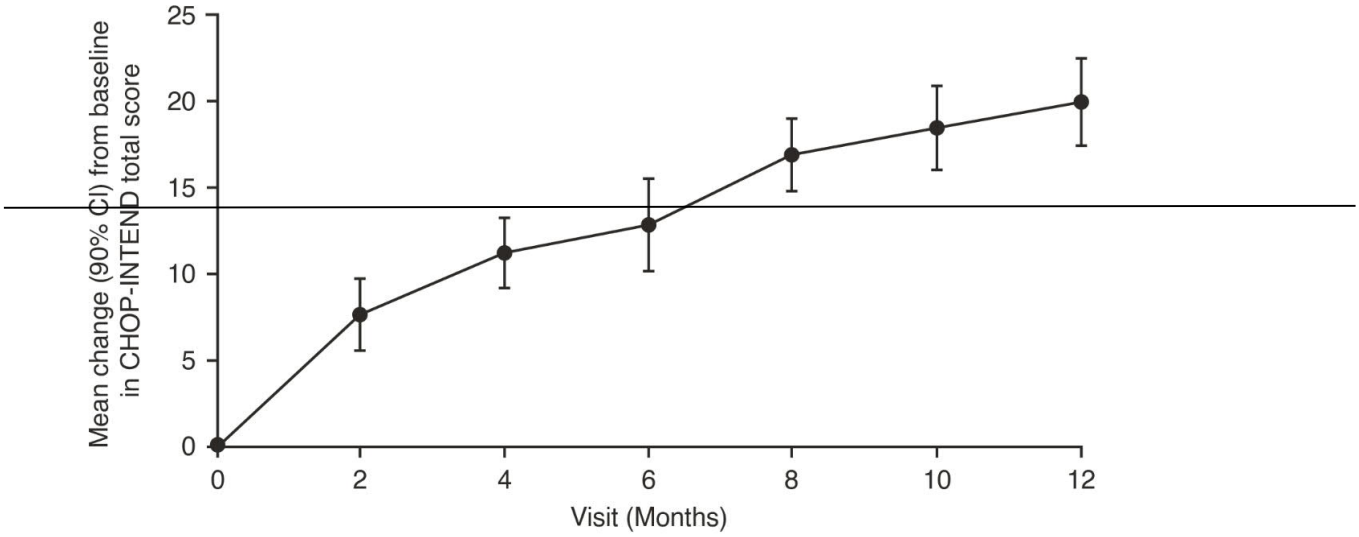
[…]

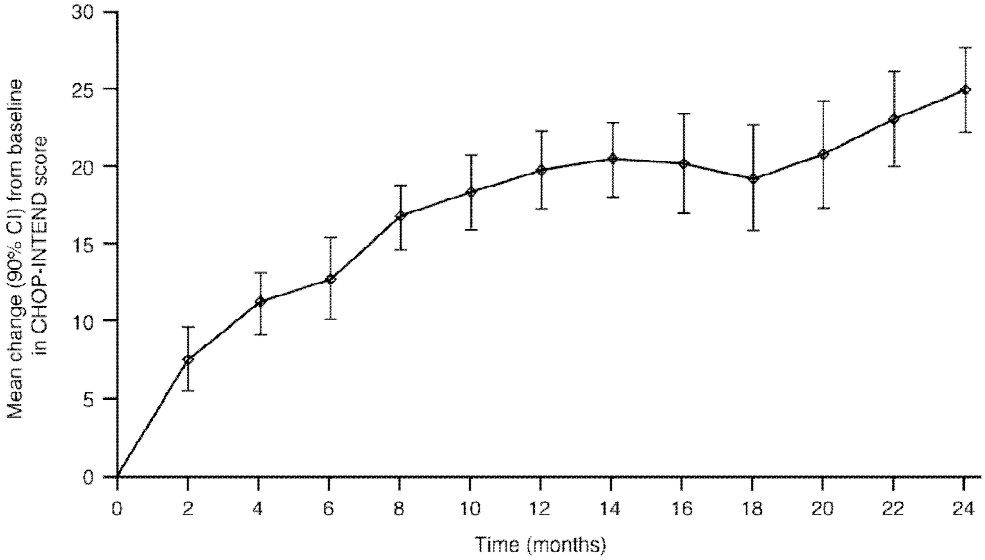
Figure 1. Kaplan-Meier plot of event-free survival (FIREFISH Part 1 and Part 2)



+ Censored: ~~one~~ two patients in Part 2 were censored because the patients attended the Month ~~12~~ 24 visit early, one patient in Part 1 was censored after discontinuing treatment and died 3.5 months later

Figure 2. Mean change from baseline in CHOP-INTEND total score (FIREFISH Part 2)





FIREFISH Part 1

[…]

After 12 months of treatment, 90% (19/21) of patients were alive and event-free (without permanent ventilation) and reached 15 months of age or older. After a minimum of ~~24~~ 33 months of treatment, 81% (17/21) of patients were alive and event-free and reached an age of ~~28~~ 37 months or older (median ~~32~~ 41months; range ~~28~~37 to ~~45~~53 months), see Figure 1. Three patients died during treatment and one patient died 3.5 months after discontinuing treatment

עדכונים מהותיים בעלון לצרכן

בסעיף 4. תופעות לוואי עודכן המידע הבא:

תופעות הלוואי הבאות דווחו מאז תחילת השיווק של אווריסדי, אך שכיחותן אינה ידועה:

- דלקת של כלי דם קטנים המשפיעה בעיקר על העור (וסקוליטיס עורית)