ספטמבר 2019

הנדון: RABIPUR / רביפור
Powder and solvent for solution for injection

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

חברת גלקסוסמיתקליין ישראל בע"מ (GSK) מבקשת להודיע על עדכון העלון לרופא של התכשיר
RABIPUR / רביפור. עדכון העלון כולל גם את הבאים:
-עדכון נוסח התווית התכשיר לצורך פישוט הניסוח בלבד
-הוספת משטר מינון: Accelerated PrEp (pre-exposureprophylaxis)

חומר פעיל:

-RABIES, INACTIVATED, WHOLE VIRUS 2.5 IU/ML

ההתוויה העדכנית המאושרת לתכשיר בישראל:

Rabipur is indicated for active immunization against rabies in individuals of all ages. See Sections 4.2 and 5.1 for detailed information about pre- and post-exposure prophylaxis.
Rabipur should be used in accordance with official recommendations.

בהודעה זו מצויינים השינויים שבוצעו לעלון .

מקרא לעדכונים המסומנים:
תוספת – כתב אדום
מחיקה-כתב כחול עם קו מחיקה

להלן העידכונים המהותיים שנעשו בעלון לרופא:

Section	Marked update
4.1 Therapeutic indications	Rabipur is indicated for Active immunization against Rabies in individuals of all ages. ~~This includes~~See Sections 4.2 and 5.1 for detailed information about pre-~~exposure prophylaxis (i.e. before possible risk of exposure to rabies), in both primary series and booster dose,~~ and post-exposure prophylaxis ~~(i.e. after suspected or proven exposure to rabies).~~ Rabipur ~~is to~~should be used ~~on the basis of~~in accordance with official recommendations.
4.2 Posology and method of administration	~~*Dosage in adults and children*~~ The recommended ~~single intramuscular (IM)~~ dose for both primary immunization and boosters is 1.0 ml ~~in individuals of all ages.~~ *Pre-exposure prophylaxis* ~~(PrEP)~~ *Primary immunization* In previously unvaccinated individuals, ~~an initial course of pre-exposure prophylaxis consists of~~ three doses ~~(each of 1.0 ml)~~should be administered ~~IM on~~according to the conventional or rapid regimen as shown in Table 1. Table 1 Primary immunization regimens | | *Conventional regimen* | *Rapid regimen** |

1st dose	Day 0	Day 0
2nd dose	Day 7	Day 3
3rd dose	Day 21 (or 28)	Day 7

The conventional regimen of days 0,7,21 (or 28) is the preferable regimen.

*The rapid regimen should only be considered for adults aged 18-65 years not able to complete the conventional pre-exposure prophylaxis regimen within 21 or 28 days ~~0, 7, and 21 (or 28).~~before protection is required.

Booster doses

~~The individual IM booster dose is 1.0 ml.~~
~~Rabipur may be used~~Booster doses are generally recommended every 2-5 years. Timing for booster after vaccination ~~after prior immunization~~ with ~~a human diploid cell rabies vaccine (HDCV).~~
~~The need of intermittent serological~~rapid regimen has not yet been established (see also section 5.1). Serological testing for the presence of antibody ≥ 0.5 IU/ml ~~and~~to assess the ~~administration of~~need for booster doses should be ~~assessed~~conducted in accordance with official recommendations.

~~Experience shows that reinforcing doses are generally required every 2-5 years.~~
Rabipur may be used to boost individuals previously immunized with any human diploid cell rabies vaccine.

Post-exposure prophylaxis ~~(PEP)~~

Post-exposure prophylaxis ~~consists of:~~
~~local treatment of the wound~~should commence as soon as possible after exposure~~.~~.
- ~~a course of rabies vaccine and~~
- ~~administration of rabies immunoglobulin, if indicated~~

~~The indication~~Table 2 summarises recommendations for post-exposure prophylaxis ~~depends on the type of contact with the suspected rabid animal, as provided in Table 1, *Recommended post-exposure prophylaxis*~~, including immunization, according to the type of exposure. ~~Post-exposure immunisation should begin as soon as possible after exposure.~~

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~~*Post*~~In post-exposure prophylaxis of previously unvaccinated individuals, the vaccine should be administered according to Table 3.

~~5-dose Essen regimen (~~Table 3: Post-exposure immunization regimens for previously unvaccinated individuals

	Essen regimen (5 doses)	*Zagreb regimen (4 doses)*	*Reduced Essen regimen (4 doses)*[2]
1st dose	Day 0	Day 0, 2 doses[1]	Day 0
2nd dose	Day 3		Day 3
3rd dose	Day 7	Day 7	Day 7
4th dose	Day 14	Day 21	Day 14
5th dose	Day 28		

- [1] ~~1-1-1-1):~~ one ~~1.0 ml IM~~ injection ~~on each of days 0, 3, 7, 14 and 28~~
- ~~4 dose modified Essen regimen (1-1-1-1): one 1.0 mL IM injection on each of days 0, 3, 7 and 14, for healthy, immunocompetent persons only.~~
  ~~4 dose Zagreb regimen (2-1-1): two 1.0 ml IM injections on day 0 (one~~ in each of the two deltoids or thigh sites~~) followed by one 1.0 ml IM injection on each of days 7 and 21.~~

~~*Post-exposure prophylaxis in previously vaccinated individuals*~~

[2] this shortened Essen regimen may be used as an alternative for healthy, immunocompetent individuals provided they receive wound care plus rabies immunoglobulin in category III as well as in category II exposures and a WHO-prequalified rabies vaccine

In previously vaccinated individuals, post-exposure prophylaxis consists of two doses ~~(each of 1.0 ml)~~ administered ~~IM~~ on days 0~~,~~ and 3. Rabies immunoglobulin is not indicated in such cases.

~~Paediatric patients~~

~~Paediatric individuals receive the same 1.0 ml IM dose as adults.~~

~~Geriatric patients~~
~~Geriatric individuals receive the same 1.0 ml IM dose as adults.~~

~~Immunocompromised individuals~~
In immunocompromised individuals~~, a complete series of~~ with category II and III exposures, 5 doses ~~according to the Essen (1-1-1-1-1) on days 0, 3, 7, 14 and 28) regimen~~should be given in combination with comprehensive wound management and local infiltration of rabies immunoglobulin ~~is required for individuals with category II and III exposure~~as shown in Table 4.

~~Alternatively, two~~Table 4: Post-exposure immunization regimens for immunocompromised individuals

	Essen regimen	*Alternative to Essen*
1st dose	Day 0	Day 0, 2 doses[1]
2nd dose	Day 3	Day 3
3rd dose	Day 7	Day 7
4th dose	Day 14	Day 14
5th dose	Day 28	Day 28

[1] Two doses of vaccine may be given on day 0, that is, a single dose of 1.0 ml vaccine should be injected into the right deltoid and another single dose into the left deltoid muscle. In small children, one dose should be given into the anterolateral region of each thigh. This would result in a total of 6 doses ~~(2-1-1-1-1 on days 0, 3, 7, 14 and 28).~~ .

When feasible, the rabies virus neutralising antibody response should be measured 2 to 4 weeks (preferably on day 14) following the start of vaccination to assess the possible need for an additional dose of the vaccine. Immunosuppressive agents should not be administered during postexposure therapy unless essential for the treatment of other conditions (see section 4.5).

Paediatric population
Paediatric individuals receive the same dose as adults (1.0 ml).

Method of administration

Rabipur is for intramuscular administration only. For adults and children ≥ 2 years of age, the vaccine should be administered ~~intramuscular~~ into the deltoid~~; for~~ muscle. For children < 2 years, the anterolateral area of the thigh is recommended.
~~The vaccine must not be given by intravascular injection, see section 4.4.~~
~~Rabies vaccine must not be given by intra-gluteal injection or subcutaneously, see section 4.4.~~
For instructions on reconstitution of the vaccine before administration, see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

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Almost all adult subjects achieved an adequate immune response (Rabies Viral Neutralizing Antibodies (RVNAs) ≥ 0.5 IU/ml) within 7 days after the end of a primary series of three injections of Rabipur when given concomitantly with inactivated JE vaccine according to ~~the~~ to either a rapid or the conventional PrEP

	schedule by the intramuscular route. From day 57 after vaccination a faster decline in immune response to rabies was observed in individuals vaccinated concomitantly with JE vaccine according to the rapid PrEP schedule compared with the concomitant conventional PrEP schedule and the rabies only conventional PrEP schedule. At day 366, percentages of subjects with RVNA concentration ≥0.5 IU/mL were 68%, 76%, and 80% for vaccine groups ~~rabies~~rabies/JE accelerated, rabies/JE conventional, and rabies conventional, respectively. ~~PrEP schedule /JE, and rabies PrEP schedule respectively.~~ ……

קיימים עדכונים נוספים . למידע נוסף יש לעיין בעלון לרופא המעודכן.
העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://www.old.health.gov.il/units/pharmacy/trufot/index.asp?safa=h וניתן לקבלו מודפס על-ידי פניה לחברת גלקסוסמיתקליין רח' בזל 25 פתח תקוה בטלפון: 03-9297100.

בברכה,
ליליאנה בלטר
רוקחת ממונה