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דצמבר 2019

הנדון: עדכון עלון לצרכן ולרופא עבור התכשיר Nuedexta

ההתוויה המאושרת: NUEDEXTA is indicated for the treatment of pseudobulbar affect (PBA).

החומר הפעיל: 10 mg quinidine sulfate and 20 mg dextromethorphan hydrobromide

רופא/ה, רוקח/ת נכבדים,

חברת מדיסון פארמה מבקשת ליידע על עדכון העלון לצרכן ולרופא לתכשיר *Nuedexta*
העדכון כולל עדכוני נוסח ופורמט משה"ב לאורך כל העלון (צרכן/רופא).
כמו כן, נעשה עדכון לגבי שימוש בהריון/הנקה/אצל קשישים בעלון לרופא בסעיף 8.5 /8.2 /8.1.
להלן השינויים המהותיים, מסומנים בעקוב אחר שינויים:

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

~~Pregnancy Category C:~~
Risk Summary

There are no adequate ~~and well-controlled studies~~data on the developmental risk associated with the use of NUEDEXTA in pregnant women. In oral studies conducted in rats and rabbits, a combination of dextromethorphan/quinidine demonstrated developmental toxicity, including teratogenicity (rabbits) and embryolethality, when given to pregnant animals~~. NUEDEXTA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.~~ *(see Data).*

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown.

Data

Animal Data
When dextromethorphan/quinidine was administered orally (0/0, 5/100, 15/100, and 50/100 mg/kg/day) to pregnant rats during the period of organogenesis, embryo-fetal deaths were observed at the highest dose tested and reduced skeletal ossification was observed at all doses. The lowest dose tested (5/100 mg/kg/day) is approximately 1/50 times the recommended human dose (RHD) of 40/20 mg/day on a mg/m^2 basis.

Oral administration ~~(0/0, 5/60, 15/60, and 30/60 mg/kg/day)~~ to pregnant rabbits during organogenesis in two separate studies (0/0, 5/60, 15/60, and 30/60 mg/kg/day; 0/0, 5/100, 15/100, and 50/100 mg/kg/day) resulted in an increased incidence of fetal malformations at all but the lowest dose tested. The no-effect dose (5/~~60~~100 mg/kg/day) is approximately 2/~~60~~100 times the RHD on a mg/m^2 basis.

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When dextromethorphan/quinidine was orally administered ~~(0/0, 5/100, 15/100, and 30/100 mg/kg/day)~~ to female rats during pregnancy and lactation~~,~~ in two separate studies (0/0, 5/100, 15/100, and 30/100 mg/kg/day; 0/0, 5/100, 15/100, and 50/100 mg/kg/day), pup survival and pup weight were decreased at all doses, and developmental delay was ~~seen~~observed in offspring at the mid~~-~~ and high~~-doses.~~ doses. A no-effect dose for adverse developmental effects was not identified. The lowest dose tested (5/100 mg/kg/day) is approximately 1/50 times the RHD on a mg/m^2 basis.

~~**8.2 Labor and Delivery**~~

~~The effects of NUEDEXTA on labor and delivery are unknown.~~

~~**8.3 Nursing Mothers**~~

When dextromethorphan/quinidine was orally administered (0/0, 5/50, 15/50, 25/50 mg/kg) to male and female rats on postnatal day (PND) 7, the highest dose resulted in neuronal death in brain (thalamus and medulla oblongata). PND 7 in rat corresponds to the third trimester of the gestation through the first several months of life but may extend to approximately three years of age in humans.

8.2 Lactation

Risk Summary

Quinidine is excreted in human milk. It is not known whether dextromethorphan ~~and/or quinidine are excreted in human milk. Because many drugs are~~is excreted in human milk~~, caution~~. There are no data on the effects of quinidine or dextromethorphan on the breastfed infant or the effects on milk production. The development and health benefits of breastfeeding should be ~~exercised when~~considered along with the mother's clinical need for NUEDEXTA and any potential adverse effects on the breastfed infant from NUEDEXTA ~~is administered to a nursing mother~~or from the underlying material condition.

8.5 Geriatric Use

Of the total number of patients with PBA in clinical studies of NUEDEXTA, 14 percent were 65 years old and over, while 2 percent were 75 and over. Clinical ~~study~~studies of NUEDEXTA did not include sufficient number of patients aged 65 and over to determine whether they respond differently than younger patients.

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

העלון לרופא ולצרכן נמצאים בקישור וכן נשלחו לפרסום במאגר התרופות באתר משרד הבריאות וניתן לקבלם מודפס על ידי פניה לבעל הרישום.

בברכה,
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