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Zonisamide

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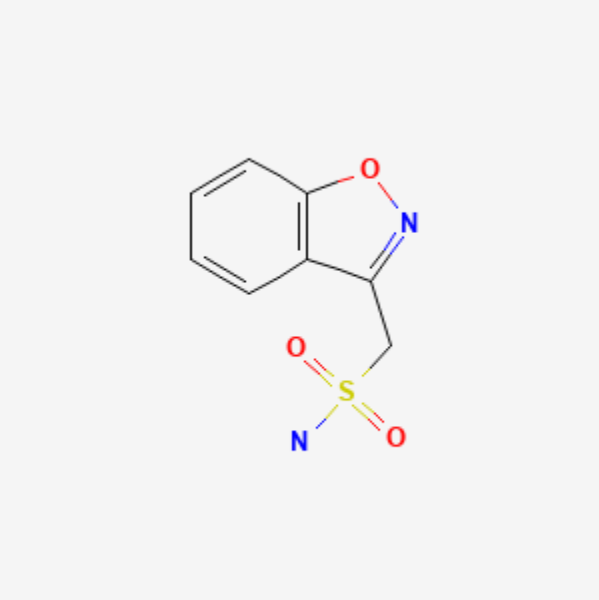
CASRN: 68291-97-4



Drug Levels and Effects

Summary of Use during Lactation

Limited information indicates that maternal doses of zonisamide up to 400 mg daily produce high levels in milk and infant serum, but infant serum levels in neonates decrease during the first month of life while nursing. Although no adverse reactions have been reported in breastfed infants, the number of infants reported have been small. Alternative drugs are preferred, but if it must be given, monitor the infant for drowsiness, adequate weight gain, and developmental milestones, especially in younger or exclusively breastfed infants and when using combinations of anticonvulsant drugs. Some clinicians recommend that mothers taking zonisamide only partially breastfeed in order to reduce the exposure of the infant to the drug and to consider monitoring infants' serum zonisamide concentrations.[1]

Drug Levels

In published reports of anticonvulsant use during breastfeeding, most women were taking a combination of anticonvulsants. Some other anticonvulsants (e.g., phenytoin, carbamazepine) stimulate the metabolism of other drugs including anticonvulsants, whereas others (e.g., valproic acid) inhibit the metabolism of other drugs. Therefore, the relationship of the maternal dosage to the concentration in breastmilk can be quite variable, making calculation of the weight-adjusted percentage of maternal dosage less meaningful than for other drugs in this database.

Maternal Levels. A woman took zonisamide monotherapy (dosage and regimen not specified) during pregnancy and postpartum. Two serum concentration were measured: 13.6 mg/L at 3 hours before delivery and 23.2 mg/L on day 17 postpartum. Milk samples were collected postpartum and measured for zonisamide using untreated breastmilk in an enzyme immunoassay. Milk levels were 4.6 mg/L at 58 hours postpartum, 13.6 at 61 hours postpartum, and 19.2 mg/L at 77 hours postpartum.[2]

A mother was taking oral zonisamide 300 mg daily. Milk levels measured 1.5 hours after her dose on days 6 and 30 postpartum were 9.75 and 10.5 mg/L, respectively. Milk levels measured 2.5 hours after her dose on days 3 and 15 postpartum were 8.25 and 9.12 mg/L, respectively.[3] The same authors reported that "patients" (number and time postpartum unspecified) taking oral zonisamide 300 mg daily had an average (+/- SD) breastmilk level of 9.41 +/- 0.95 mg/L.[4] These values are exactly the same as the average and standard deviation of the former patient's 4 milk levels. It is likely that these results are merely a duplicate of the above results.

A mother who was taking oral zonisamide 400 mg, carbamazepine 1 g, and clonazepam 1 mg daily had breastmilk whey levels of zonisamide measured 9 times from day 1 to day 10 postpartum. All of the levels were distributed (neither increasing nor decreasing) in the range of 8.9 to 10.9 mg/L.[5]

Using data from the 2 patients with relatively complete information on dosage and milk levels,[2,4] the average amounts in milk represent an infant dosage of about 23 to 28% of the maternal weight-adjusted dosage.

In one report, two mothers took zonisamide during pregnancy and breastfeeding. One mother was taking 300 mg (6.2 mg/kg) zonisamide daily as 100 mg in the morning and 200 mg in the evening. On days 4 and 5 postpartum, milk zonisamide levels were 16.2 mg/L at 10 hours after a 100 mg dose and 18 mg/L at 12.5 hours after a 200 mg dose. Using the larger value, the authors estimated the maximum infant dosage to be 2.7 mg/kg daily corresponding to 44% of the weight-adjusted maternal dosage. Another woman was taking 100 mg (2.1 mg/kg) of zonisamide daily. On day 3 postpartum, a trough milk levels was 3.4 mg/L; on day 5, a level taken at 4.5 hours after the dose (approximately the peak) was 5.1 mg/L. Using the larger value, the authors estimated the maximum infant dosage to be 0.77 mg/kg daily corresponding to 36% of the weight-adjusted maternal dosage. [1]

Two breastfeeding women who were taking zonisamide had zonisamide levels measured in their milk. One woman who was taking a dose of 500 mg daily and levetiracetam had milk levels of 15.2, 13.2 and 11.3 mg/L at 3, 7 and 12 days postpartum, respectively, after one pregnancy. After a subsequent pregnancy, when she was taking a dose of 550 mg daily and levetiracetam she had a milk level of 13.3 mg/L at 3 days postpartum. The second woman was taking zonisamide 400 mg daily had a milk level of 10.3 mg/L at 3 days postpartum.[6]

Infant Levels. The serum zonisamide levels were measured in a breastfed infant whose mother was taking zonisamide 400 mg, carbamazepine 1 g, and clonazepam 1 mg daily. In this infant and in another breastfed infant whose mother was taking zonisamide 400 mg and carbamazepine 800 mg daily, high transplacentally acquired plasma levels of about 14 and 11 mg/L, respectively, fell over a 6- to 7-day monitoring period despite intake via breastmilk. The first infant's plasma level on day 24 was 3.9 mg/L.[5]

An infant whose mother was taking zonisamide (dose not specified) during pregnancy and breastfeeding had a serum zonisamide concentration that was 3.6 mg/L or 17% of the maternal serum concentration at 9 days postpartum. The half-life of zonisamide in this infant and one other was estimated to be about 100 hours.[7]

An infant whose mother was taking zonisamide 300 mg (6.2 mg/kg) daily was exclusively breastfed for 9 days postpartum, then breastfed twice daily and supplemented with formula 7 to 8 times daily, resulting in an estimated zonisamide dose of 0.54 mg/kg daily or 8% of the maternal weight-adjusted dosage. At birth, the infant's serum zonisamide concentration was 14.4 mg/L, but on day 34 postpartum, zonisamide was undetectable (<0.5 mg/L) in the infant's serum.[1]

In a multicenter study of nursing mother-infant pairs, 4 infants had blood samples taken at about the same time as maternal blood samples. Two of the infants had blood levels of zonisamide above the lower limit of quantification (1 mg/L). The authors estimated the average infant zonisamide serum concentration to be 6.5 mg/L (range 3.9 to 18.7 mg/L), assuming unquantifiable serum concentrations to be 50% of the lower limit of quantification. Median infant blood levels were 44.2% (range 35.2 to 125.3%) of their mothers' blood levels.[8]

A breastfeeding woman who was taking zonisamide had zonisamide levels measured in both her and her infants' serum in two pregnancies. While taking a dose of 500 mg daily and levetiracetam, her infant had serum levels of 13.1, 7.3 and 6.4 mg/L at 2, 6 and 12 days postpartum, respectively. The infant-to-maternal serum concentration ratio 0.44 at 12 days postpartum. After a subsequent pregnancy, the same mother was taking a dose of 550 mg daily plus levetiracetam and the second infant had a serum level of 13.9 mg/L at 4 days postpartum.[6]

Effects in Breastfed Infants

A patient taking zonisamide 300 mg orally 3 times daily as well as other unspecified antipsychotics was followed at 0, 3, 14 and 30 days postpartum. Her infant exhibited no behavioral problems.[3]

Two infants were breastfed postpartum by their mothers. One was exclusively breastfed for 9 days postpartum, then breastfed twice daily and supplemented with formula 7 to 8 times daily. The maternal zonisamide dose was 300 mg (6.2 mg/kg) daily. On day 34, the infant was healthy, had gained weight and had experienced no observable adverse effects. The second infant was partially breastfed by a mother taking zonisamide 100 mg (2.1 mg/kg) daily. No adverse reactions were noted in the infant during the first 2 weeks postpartum, at which time breastfeeding was discontinued because of a low milk supply.[1]

Effects on Lactation and Breastmilk

Relevant published information was not found as of the revision date.

Alternate Drugs to Consider

(Seizure Disorder) Carbamazepine, Divalproex, Gabapentin, Lamotrigine, Oxcarbazepine, Phenytoin, Valproic Acid

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Substance Identification

Substance Name

Zonisamide

CAS Registry Number

68291-97-4

Drug Class

Breast Feeding

Lactation

Milk, Human

Anticonvulsants