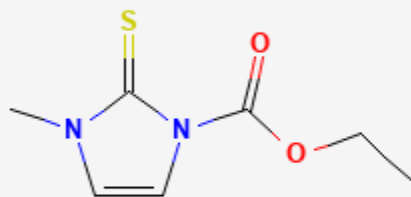




Carbimazole

Revised: June 20, 2022.

CASRN: 22232-54-8



Drug Levels and Effects

Summary of Use during Lactation

Carbimazole is not approved for marketing in the United States by the U.S. Food and Drug Administration, but is available in other countries. Doses of carbimazole of 30 mg daily or 50 mg weekly have not adversely affected the few breastfed infants studied. Carbimazole is a prodrug for methimazole which has been studied extensively during breastfeeding; maternal methimazole therapy does not affect thyroid function or intellectual development in breastfed infants with doses up to 20 mg daily. Some experts now recommend that methimazole should be considered the antithyroid drug of choice in nursing mothers.[1-3]

The American Thyroid Association recommends only monitoring infants for appropriate growth and development during routine pediatric health and wellness evaluations and routine assessment of serum thyroid

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function in the child is not recommended.[4] Rare idiosyncratic reactions (e.g., agranulocytosis) might occur, and the infant should be watched for signs of infection. Monitoring of the infant's complete blood count and differential is advisable if there is a suspicion of a drug-induced blood dyscrasia.

Drug Levels

Carbimazole is a prodrug that is rapidly converted to the active drug methimazole. The methimazole dose is 61% of the carbimazole dose after conversion.

Maternal Levels. Five lactating women who were 2 to 6 weeks postpartum were given a single dose of carbimazole 40 mg orally, equivalent to 24.5 mg of methimazole. Methimazole milk concentrations were measured every hour for 8 hours. The average milk concentration was 182 mcg/L at 1 hour after the dose and decreased to 83 mcg/L at 8 hours after the dose. The average total amount of methimazole excreted into milk over 8 hours was 34 mcg (range 29 to 47 mcg).[5]

Four women were receiving 10 to 20 mg of carbimazole daily. Milk samples were obtained on days 4, 7, 10, and 42 and at 3 and 6 months postpartum. The highest methimazole milk level was 75 mcg/L in a woman taking carbimazole 5 mg 4 times daily. The average milk level in all samples was 43.5 mcg/L.[6]

A mother with twins began taking carbimazole 30 mg daily 2 months postpartum. The dosage was lowered as she became euthyroid. Free methimazole was measured in breastmilk 10 times between weeks 2 and 16 of therapy. The mean milk methimazole concentration was 43 mcg/L (range 0 to 92 mcg/L), although the exact dosage the mother was taking during all of these measurements was not stated. The peak milk methimazole concentration occurred about 4 hours after the dose.[7]

Five mothers received carbimazole 10 to 20 mg daily during pregnancy and for 2 to 26 weeks of lactation. Steady-state concentrations of carbimazole (assayed as methimazole) in milk were 6 to 51 mcg/L. The estimated quantity of carbimazole ingested by the infants in milk was 0.5 to 3.2% of the weight-adjusted maternal daily dose.[8]

A woman (time postpartum not stated) given a single dose of 10 mg of carbimazole excreted a total of 0.47% of the dose in her breastmilk in 24 hours.[9]

Infant Levels. A mother with twins began taking carbimazole 30 mg daily 2 months postpartum. The dosage was lowered as she became euthyroid. The infants were breastfed (extent not stated) and plasma methimazole concentrations were measured between weeks 1 and 16 of therapy. The highest plasma levels occurred between 2 and 4 hours after a maternal dose. Average serum level in one twin averaged 45 mcg/L (range 0 to 105 mcg/L) over a 15 week period and the average serum level in the other twin was 52 mcg/L (range 0 to 156 mcg/L) over 14 weeks, with the highest values reported with a maternal dose of 30 mg daily.[7]

Effects in Breastfed Infants

Eleven mothers were taking oral carbimazole in dosages ranging from 5 to 20 mg daily during pregnancy and 5 to 15 mg daily during breastfeeding (extent not stated). None of the 12 infants, including one set of twins, had a serum thyroxine (T4) concentration below the lower limit of normal on day 4 of life. Thyrotropin (TSH) concentrations were normal in all infants when measured at various times over the first 21 days postpartum.[10]

Four women were receiving 10 to 20 mg of carbimazole daily. Infant blood samples were obtained on days 4, 7, 10, and 42 and at 3 and 6 months postpartum. Thyroid function was normal in 3 infants. In one infant, the TSH was elevated for the first 10 days of life.[6]

A mother with twins began taking carbimazole 30 mg daily 2 months postpartum. The dosage was lowered as she became euthyroid. The infants were breastfed (extent not stated) and clinical and laboratory examinations were performed over the following 4 months. There was no evidence of alterations in thyroid function.[7]

Fifteen mothers received carbimazole 10 to 20 mg daily for 12 to 40 weeks during pregnancy and 9 continued to take the drug during 2 to 26 weeks of lactation. Their infants were monitored for up to 18 months. Infant thyroid function was within normal over this period, the range of mean values for individual infants being TSH 1.4 to 5.9 milliunits/L, free T3 6.2 to 9.3 pmol/L and T4 104 to 189 nmol/L. Physical examination at intervals for 2 to 18 months was normal in all infants who received carbimazole and Griffiths mental development scales were normal in all 6 infants who were assessed at 18 months.[8]

A mother was taking carbimazole 50 mg once weekly during pregnancy and postpartum. Her infant was exclusively breastfed for the first 84 days of life and had clinical and laboratory examinations performed over the first 4 months of life. Although the infant's tone and deep tendon reflexes were slightly increased and she was easily irritable, serum thyroid hormone levels were normal as was her growth. No symptoms or signs of hypothyroidism were observed.[11]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

Methimazole, Propylthiouracil

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Substance Identification

Substance Name

Carbimazole

CAS Registry Number

22232-54-8

Drug Class

Breast Feeding

Lactation

Milk, Human

Antithyroid Agents

Thionamides