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IMPORTANT MEDICINE SAFETY INFORMATION

08 November 2019

Dear Healthcare Professional

Neomercazole® (carbimazole)-containing products: (1) Risk of acute pancreatitis and (2) Teratogenicity and foetal/neonatal hypothyroidism and/or goitre

Aspen Pharmacare Limited, in agreement with the South African Health Products Regulatory Authority (SAHPRA) would like to inform you about the risk of acute pancreatitis associated with carbimazole containing products including Neomercazole® and the need for strengthened advice on teratogenicity of Neomercazole®, use in pregnancy, lactation, foetal/neonatal hypothyroidism/goitre and contraception while on Neomercazole®.

SUMMARY

1. Risk of acute pancreatitis

- Acute pancreatitis has been reported following treatment with Neomercazole®.
- If acute pancreatitis occurs, treatment with Neomercazole® should be discontinued immediately and further use of carbimazole and/or its metabolite is contraindicated.
- Re-exposure may result in recurrence of acute pancreatitis, with decreased time to onset, therefore Neomercazole® and/or its metabolites must not be given to patients with a history of acute pancreatitis that occurred following administration of Neomercazole®.

2. Neomercazole® and/or its metabolites and teratogenicity, and foetal/neonatal hypothyroidism and/or goitre

- Neomercazole® and/or its metabolites are teratogenic.
- Women of childbearing potential must use effective contraception if treated with Neomercazole® and/or its metabolites.
- The use of Neomercazole® and/or its metabolites is contraindicated in women planning to become pregnant are pregnant or breastfeeding their babies.
- A medically/laboratory supervised pregnancy test should be done 24hours prior to starting treatment with Neomercazole® to exclude pregnancy.
- If a woman becomes pregnant whilst on treatment with Neomercazole® the possibility of termination of pregnancy (therapeutic abortion) should be considered if there is evidence of serious harm and/or abnormalities to the embryo/foetus.
- If termination of pregnancy is not an option and treatment is unavoidable and cannot be delayed until after the birth of the baby, and no safe or safer alternative is available or is not tolerable, is contraindicated or has failed, both partners should be counselled, and written consent be obtained to continue with treatment. In the aforementioned scenario the lowest effective dose should be used and if possible, not to be used in the first trimester of pregnancy. Thyroid functions should be frequently monitored.
- Neomercazole® crosses the placenta and may cause foetal and/or neonatal hypothyroidism and/or goitre with serious harm to the baby.
- Cases of congenital malformations have been observed following the use of Neomercazole® and/or its active metabolites.
- Reported malformations include aplasia cutis congenita (absence of a portion of skin [often localised on the head]), craniofacial malformations (choanal atresia: facial dysmorphism), defects of the abdominal wall and gastrointestinal tract (exomphalos, oesophageal atresia, omphalo-mesenteric duct anomaly), and ventricular septal defect.[1]

- Women on treatment with Neomercazole® and/or its metabolites should not breastfeed their infants as Neomercazole® and /or its metabolites appear in breastmilk and may cause hypothyroidism and/or goitre in their babies.

BACKGROUND ON THE SAFETY CONCERN

General information

Medicines containing carbimazole are used in the management of hyperthyroidism, preparation for thyroidectomy in hyperthyroidism and therapy prior to and post radioiodine treatment. Carbimazole is a prodrug which undergoes rapid metabolism to the active metabolite, thiamazole. Thiamazole is an antithyroid medicine that acts by blocking the production of thyroid hormones. It is teratogenic and crosses the placenta and may cause congenital abnormalities as already described, as well as foetal/neonatal hypothyroidism and/or goitre.

Risk of acute pancreatitis

There have been post-marketing reports of acute pancreatitis with the use of medicines containing carbimazole. While the mechanism is poorly understood, the presence of cases reporting recurrent acute pancreatitis with a decreased time to onset after re-exposure to carbimazole might suggest an immunological mechanism. Immediate discontinuation of medicines containing carbimazole including Neomercazole® is required in patients who develop acute pancreatitis following exposure. Neomercazole® must not be restarted and affected patients should be switched to an alternative therapy based on the individual benefit/risk assessment. Any future re-exposure to Neomercazole® in patients who have experienced acute pancreatitis with carbimazole in the past must be avoided, since it may result in recurrence of potentially life-threatening acute pancreatitis, with decreased time to onset.[1]

Carbimazole teratogenicity and foetal/neonatal hypothyroidism and/or goitre

A review of available evidence from epidemiological studies and case reports strengthens the evidence that carbimazole is teratogenic, crosses the placenta and is associated with an increased risk of congenital malformations, especially when administered in the first trimester of pregnancy and may cause foetal/neonatal hypothyroidism and/or goitre when administered during pregnancy.

ADVICE TO HEALTHCARE PROFESSIONALS

- Healthcare professionals are advised to ensure that women of child-bearing potential use effective contraceptive measures during treatment with Neomercazole®.
- The use of Neomercazole® during pregnancy should be preserved for situations in which a definitive therapy of the underlying disease (thyroidectomy or radioiodine treatment) is not suitable prior to pregnancy and in case of new occurrence or reoccurrence during pregnancy.
- If Neomercazole® is used during pregnancy, close maternal, foetal and neonatal monitoring is recommended.[1]

The PI and PIL for Neomercazole will be amended to include the new safety information. Healthcare professionals should report all suspected adverse events associated with the use of Neomercazole to:

Company	Contact Details
SAHPRA Pretoria Office	**Tel:** 012 842 7609/10 **Email:** adr@sahpra.org.za
National Adverse Event Monitoring Centre (NADEMC)	**Tel:** 021 447 1618 **Fax:** 021 448 6181

OR

Product to be updated	Company	Application Number	Contact Details
Neomercazole 5 mg Tablets	Pharmacare Limited	G3021 (Act 101/1965)	Tel: 0800 118 088 Fax: 011 239 6306 E-mail: drugsafety@aspenpharma.com

Yours sincerely,

Lorraine Hill

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Lorraine Hill
Group Operating Officer and Responsible Pharmacist
Aspen Pharmacare

References

1. Carbimazole or thiamazole* (synonym: methimazole)-containing products: (1) risk of acute pancreatitis and (2) strengthened advice on contraception. Published January 2019. DHCPL. https://assets.publishing.service.gov.uk/media/5c66c9c740f0b61a1e93a280/Carbimazole_DHPC_Final-_UK.pdf