

Oncogenetic testing for persons with Multiple Endocrine Neoplasia type 2 (MEN2)

Multiple Endocrine Neoplasia type 2 (MEN2) is a group of disorders associated with endocrine tumours (typically of the thyroid, parathyroids and adrenals). MEN2 is typically associated with mutations of the proto-oncogene RET. Epidemiological data are not available for Belgium, but the prevalence is estimated to be 2.5 per 100 000 in the general population.

Nearly all patients develop a medullary thyroid carcinoma (MTC). In general, three major phenotypes are distinguished:

- **MEN2A** (60% of all MEN2 cases) combines MTC with pheochromocytoma (10-50% of MEN2A cases) and/or primary hyperparathyroidism (5-20% of MEN2A cases).

Criteria for clinical diagnosis

MEN2A: individual with (1) MTC and at least one family member with primary hyperparathyroidism and/or pheochromocytoma, or (2) with at least two of the three major manifestations (MTC, pheochromocytoma, primary hyperparathyroidism)

- **MEN2B** (5% of all MEN2 cases) combines MTC with pheochromocytoma (50% of MEN2B cases) and typical phenotypic features such as a Marfan-type dysmorphism, ganglioneuromatosis and/or skeletal abnormalities.

Criteria for clinical diagnosis

MEN2B: individual with MTC, pheochromocytoma and other characteristic features (i.e. mucosal ganglioneuromas, gastrointestinal ganglioneuromas, eye abnormalities including corneal nerve thickening, and/or skeletal abnormalities including marfanoid body habitus)

- **Familial MTC** (35% of all MEN2 cases), in which the other components of the disease are absent.

Criteria for clinical diagnosis

Familial MTC: family with at least 4 members diagnosed with MTC (in the absence of pheochromocytoma or parathyroid adenoma/hyperplasia)



Clinical Recommendations

- Pre- and post-test genetic counselling should be offered to all patients with a clinical diagnosis of MEN2 or a sporadic MTC (strong recommendation)
- All patients with a clinical diagnosis of MEN2 or a sporadic MTC, and selected patients with a pheochromocytoma should be offered germline RET testing (strong recommendation)
- Once a germline RET mutation has been identified in a proband, RET mutation analysis should be offered to all first-degree relatives#, preferably before the age of 5 years (strong recommendation)

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