Endocrine cancer and tumours – referring to genetics

ID: 1145 v.7 **Under review**

Guideline

Referral to a clinical genetics service or familial cancer centre for assessment should be considered for all people meeting the categories below:

Endocrine cancer or tumour
UNTESTED blood relative of a person with an identified pathogenic variant in an endocrine cancer/tumour predisposition gene (e.g. MEN1, VHL, SDHx, RET)
UNTESTED blood relative of a person with a clinical diagnosis of a familial cancer syndrome that predisposes to endocrine cancer (e.g. MEN1, VHL)

Phaeochromocytoma/paraganglioma*[1, 2]
Unilateral phaeochromocytoma diagnosed under the age of 50 years
Bilateral phaeochromocytoma (regardless of age)
Unilateral phaeochromocytoma with a high risk factor (regardless of age): • abnormal SDHB and/or SDHA immunohistochemistry **OR** • malignant tumours **OR** • multifocal tumours **OR** • family history of phaeochromocytoma or paraganglioma
Unilateral phaeochromocytoma with other features (regardless of age): • also has one or more paraganglioma **OR** • also has renal cancer **OR** • another feature of VHL disease (see VHL clinical criteria) **OR** • features of neurofibromatosis type 1 (see NF1 clinical criteria)
Paraganglioma* (regardless of age)

**In this document "phaeochromocytoma" refers to a paraganglioma of the adrenal gland; "paraganglioma" refers to a paraganglioma at any site other than the adrenal gland.*

Other adrenal tumours
Adrenocortical adenocarcinoma[3]
Primary pigmented nodular adrenocortical disease (PPNAD), primary macronodular adrenal hyperplasia (PMAH)[4, 5]
Functional adrenal adenoma associated with other features of McCune Albright syndrome

Parathyroid tumour
Parathyroid adenoma/hyperplasia diagnosed under the age of 40 years
Atypical parathyroid adenoma
Parathyroid adenoma/hyperplasia with a high risk factor (regardless of age): • multi-gland adenoma or hyperplasia (in the absence of chronic renal failure or lithium therapy) **OR** • abnormal parafibromin immunohistochemistry **OR** • family history of multi-gland parathyroid adenoma/hyperplasia, or GDP-NET, or pituitary adenoma (excluding microprolactinoma in an adult)
Parathyroid adenoma/hyperplasia with other features (regardless of age): • another feature of MEN1 disease (see MEN1 clinical criteria) **OR**

Parathyroid tumour
• jaw tumours (ossifying fibromas of the mandible or maxilla) (see CDC73 genetic testing)
Parathyroid carcinoma

GDP-NET (Gastroduodenalpancreatic neuroendocrine tumour)^
Gastrinoma (gastrin secreting GDP-NET) (regardless of age)[6]
GDP-NET with clear cell histology (regardless of age)
GDP-NET with a high risk factor: • diagnosed under the age of 40 years[6] **OR** • multifocal **OR** • family history of GDP-NET, or multi-gland parathyroid adenoma/hyperplasia or pituitary adenoma (excluding microprolactinoma in an adult)
GDP-NET with other features (regardless of age): • another feature of MEN1 disease (see MEN1 clinical criteria)

^Other terms used to refer to GDP-NET include pancreatic islet tumour, gastropancreatic NET, pancreatic NET (pNET), gastric-NET, gastric enterochromaffin-like NET, type II gastric enterochromaffin-like carcinoids, and gastric carcinoid; this tumour group includes gastrinomas, insulinomas, glucagonomas, vasoactive intestinal polypeptidomas (VIPomas) and non-functional GDP-NET.

Pituitary tumour
Pituitary adenoma diagnosed under the age of 18 years regardless of adenoma size[7]
Pituitary macro-adenoma diagnosed under the age of 30 years (over 10mm)[7]
Growth hormone secreting pituitary adenoma with the phenotype of gigantism[7]
Family history of pituitary adenoma, or GDP-NET or multi-gland parathyroid adenoma/hyperplasia

Thyroid tumour
Medullary thyroid cancer (regardless of age)
Cribriform-morula form of thyroid cancer (regardless of age)
Epithelial thyroid cancer (follicular or papillary) and other features of PTEN hamartoma tumour syndrome (Cowden syndrome) (see PHTS clinical diagnostic criteria)
Multinodular thyroid disease in childhood OR differentiated thyroid cancer and other features associated with DICER1 syndrome (see DICER1 genetic testing)

Multiple endocrine tumours
Characteristics that warrant **referral** irrespective of other factors
Two or more endocrine tumours in a single individual at any age (excluding non-medullary thyroid cancer and microprolactinoma in an adult)
Two first degree relatives with rare endocrine tumours or family history of multiple endocrine tumours

References

1 Lenders, J. W., Q. Y. Duh, G. Eisenhofer, et al. 2014. "Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline." J Clin Endocrinol Metab 99(6):1915-1942.

2 Brito, J. P., N. Asi, I. Bancos, et al. 2015. "Testing for germline mutations in sporadic pheochromocytoma/paraganglioma: a systematic review." Clin Endocrinol (Oxf) 82(3):338-345.

3 Raymond, V. M., T. Else, J. N. Everett, et al. 2013. "Prevalence of germline TP53 mutations in a prospective series of unselected patients with adrenocortical carcinoma." J Clin Endocrinol Metab 98(1): E119-125.

4 Assie, G., R. Libe, S. Espiard, et al. 2013. "ARMC5 mutations in macronodular adrenal hyperplasia with Cushing's syndrome." N Engl J Med 369(22): 2105-2114.

5 De Venanzi, A., G. A. Alencar, I. Bourdeau, et al. 2014. "Primary bilateral macronodular adrenal hyperplasia." Curr Opin Endocrinol Diabetes Obes 21(3): 177-184.

6 Thakker, R. V., P. J. Newey, G. V. Walls, et al. 2012. "Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1)." J Clin Endocrinol Metab 97(9):2990-3011.

7 Hernandez-Ramirez, L. C., P. Gabrovska, J. Denes, et al. 2015. "Landscape of Familial Isolated and Young-Onset Pituitary Adenomas: Prospective Diagnosis in AIP Mutation Carriers." J Clin Endocrinol Metab 100(9):E1242-1254.

History

Version 7

Date	Summary of changes
23/01/2023	First sentence updated to align with the new eviQ cancer genetics referral guidelines template: • Changed from "All of the people who fall into the categories below warrant a referral to a clinical genetics service or familial cancer centre for assessment." to "Referral to a clinical genetics service or familial cancer centre for assessment should be considered for all people meeting the categories below".

Version 6

Date	Summary of changes
26/10/2021	Document reviewed and discussed at October 2019 cancer genetics reference committee meeting. Discussions continued via email and MS Teams. Approved for publication with the following changes made: • Table 1 - Endocrine cancer or tumour: ◦ Row 2: 'UNTESTED Blood relative of a person with a clinical diagnosis of a familial cancer syndrome that predisposes to endocrine cancer (e.g. MEN1, VHL)' added • Table 3 - Other adrenal tumours: ◦ Row 1: 'diagnosed under the age of 40 years' removed ◦ Row 2: 'Primary macronodular adrenal hyperplasia (PMAH)' added ◦ Row 3: 'Functional adrenal adenoma associated with other features of McCune Albright syndrome' added and link to article with Clinical features of McCune-Albright syndrome • Table 4 - Parathyroid tumour: ◦ Row 2: 'Atypical parathyroid adenoma' added ◦ Row 3 - Bullet 1: '(in the absence of chronic renal failure)' changed to '(in the absence of chronic renal failure or lithium therapy)' ◦ Row 4 - Bullet 2: 'Jaw cysts' changed to 'Jaw tumours' and link to CDC73 genetic testing added • Table 5 - GDP-NET (gastroduodenalpancreatic neuroendocrine tumour): ◦ GEP-NET (Gastroenteropancreatic neuroendocrine tumour) changed to GDP-NET (gastroduodenalpancreatic neuroendocrine tumour) and through out document • Table 7 - Thyroid tumour: ◦ Row 4: 'Multinodular thyroid disease in childhood OR differentiated thyroid cancer and other features associated with DICER1' added and link to DICER1 genetic testing added • Table 8 - Multiple endocrine tumours ◦ Row 2: 'Two first degree relatives with rare endocrine tumours or family history of multiple endocrine tumours' added • 'Mutation' changed to 'pathogenic variant' for consistency among eviQ cancer genetics protocols per agreement among the cancer genetics reference committees' chairs. Definition of 'pathogenic variant' added as a pop-up Version increased to V.6. Review in 2 years.

Version 5

Date	Summary of changes
17/08/2012	Presented and discussed at April 19, 2012 reference committee meeting. Approved for publication.
15/10/2012	Placed in new format.
30/04/2013	Format updated.
04/09/2013	Following discussion at March 6, 2013 reference committee meeting : • It was agreed to add the following point under individual characteristics ◦ multiple bowel carcinoid tumours < 40 yrs - category yellow. • Review second yearly.
08/03/2017	Protocol presented at the October 2016 cancer genetics RCM, content reviewed and format updated.
31/05/2017	Transferred to new eviQ website. Version number changed to V.4.
17/11/2020	Document title changed from "Referral guidelines for endocrine cancer risk assessment and consideration of genetic testing" to "Endocrine cancer and tumours - referring to genetics" in accordance with cancer genetics reference committee chairs consensus. Version increased to V. 5

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https://www.eviq.org.au/p/1145
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