

## Genomic Testing (Secondary Findings) ACT Sheet **APC Pathogenic Variants (Familial Adenomatous Polyposis [FAP])**

Pathogenic or likely pathogenic variants (mutations) in the *APC* gene may result in familial adenomatous polyposis (FAP), a condition of numerous polyps in the large intestine that leads to colon cancer. Other *APC*-associated polyposis conditions include: attenuated FAP, and gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS).

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### **YOU SHOULD TAKE THE FOLLOWING ACTIONS:**

- Inform the individual (or parent/guardian) of the genomic screening result and that there is a high lifetime risk of developing disease
  - Review family and medical history
  - Refer to gastroenterologist for evaluation and treatment or surveillance based on risk as described in clinical considerations
  - Refer for genetic consultation and counseling.
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**Clinical Considerations:** Individuals affected with FAP develop hundreds to thousands of polyps with development of colorectal carcinoma is nearly 100%, sometimes as early as adolescence. Attenuated FAP is characterized by multiple more proximally located colonic polyps (average of 30) and a diagnosis of colon cancer at a later age than in FAP. GAPPS is characterized by gastric fundic gland polyposis, increased risk of gastric cancer, and limited colonic involvement in most individuals reported. Individuals with pathogenic/likely pathogenic *APC* gene variants have increased risk for cancer outside the gastrointestinal tract, including papillary thyroid cancer, hepatoblastoma (typically at very young ages) and medulloblastoma. Response to a report of an *APC* pathogenic variant must include colonoscopy (screening begins at age 10-15 years). Management includes frequent colonoscopy with polypectomy. Prophylactic colectomy is indicated if there are more than 100 polyps, severe dysplastic polyps, or multiple polyps larger than 1 cm. Reported molecular variants also convey increased risk for other malignancies.

**Mode of Inheritance:** FAP has an autosomal dominant pattern of inheritance. As FAP may develop early in life, it is imperative that immediate and extended family members be offered genetic testing for FAP.

### **Additional Information:**

[GeneReviews](#)

[Medline Plus](#)

[NCCN](#)

### **Referral (local, state, regional and national):**

[Testing](#)

[Find Genetic Services](#)

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.

**LOCAL RESOURCES:** Insert local website links

State Resource site *(insert website information)*

Name

URL

Comments

Local Resource Site *(insert local and regional website information)*

Name

URL

Comments

**APPENDIX: Resources with Full URL Addresses**

*Additional Information:*

Gene Reviews

<http://www.ncbi.nlm.nih.gov/books/NBK1345/>

Medline Plus

<https://medlineplus.gov/genetics/condition/familial-adenomatous-polyposis/>

NCCN

[https://www.nccn.org/professionals/physician\\_gls/pdf/genetics\\_colon.pdf](https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf)

*Referral (local, state, regional and national):*

Testing

<https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=APC>

Find Genetic Services

<https://clinics.acmg.net/>

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