***PTEN* HAMARTOMA TUMOUR SYNDROME** **CLINICAL PATHWAY**
*The **Patient Clinical Pathway** is "the whole care pathway from identification, diagnostics, and multidisciplinary case discussions to surveillance and preventive surgery", so indeed a pathway in time, focusing on **HOW***
Review Recommended
PHTS is a multi-system disorder associated with benign tumours such as skin and connective tissue tumours, including vascular malformations as well as neurodevelopmental disorders, including autism spectrum disorders. The syndrome also predisposes to a high hereditary risk of breast, thyroid, endometrial and a moderate risk of kidney, colorectal and skin cancer.
At time of diagnosis, or if PHTS is suspected, ALL patients should be evaluated by a clinical genetics specialist, to genetically confirm the diagnosis and discuss the consequences for patients and close relatives. Those with significant complications will be followed up as appropriate through the nationally recognized PHTS reference centre if available. GPs, paediatricians and other specialists can contact their local genetics service for PHTS-related concerns and if available have access to the national PHTS reference centre.
***PTEN* HAMARTOMA TUMOUR SYNDROME** **Review Checklist**

	WHAT TO LOOK FOR	**WHEN TO REFER AND WHERE TO**
SKIN	Check for symptomatic lesions, facial trichilemmomas, lipomas, acral keratosis, papillomatous papules of the gum and/or the tongue, penile freckling, vascular anomalies (arteriovenous malformation, venous malformation, superficial cutaneous haemangioma) and melanoma.	Rapidly growing or changing pigmented lesion: **REFER** to national PHTS reference centre, or specialist dermatology or vascular team. Lesions being removed for other reasons need referral to plastic surgeon or dermatologist.
NEUROLOGICAL	Adult Lhermitte-Duclos disease (LDD) (cerebellar tumours), autism spectrum disorders (ASD), developmental delay; Intellectual disability, anxiety disorder.	**REFER** to National PHTS Reference Centre or neurologist for evaluation of neuropsychiatric problems or if increase in frequency and/or severity of headaches or onset of other symptoms.
ENDOCRINE	Multinodular goiter, thyroid tumours/cancer, hypothyroidism, hyperthyroidism.	**REFER** to endocrinologist if symptoms of thyroid dysfunction exist. **REFER** to endocrine surgeon if suspicion of thyroid cancer or mechanical symptoms from multinodular goiter exist.
PREGNANCY	Depending on the country there might be options for prenatal and preimplantation genetic testing.	Individuals who are planning pregnancy should be offered **REFERRAL** to clinical genetics services

ANY OTHER NEW SYMPTOMS	Consider other possible complications. For instance: vaginal bleeding outside menstrual periods; new lump or pain in the breast; skin changes; blood in the urine or flank pain; black faeces or changes in bowel habits.	**REFER** to appropriate specialist

UNSURE? Treating physicians can contact the PHTS team/local clinical genetics.

The most serious consequences of PHTS in adulthood relate to the increased risk of cancers including those of the breast, thyroid, endometrium, and with a less increased risk of cancers including those of the kidney, colon and skin (melanoma).

The most important aspect of management of any individual with a germline *PTEN* pathogenic variant is **increased cancer surveillance** to detect any tumours at the earliest, most treatable stages. Additionally, women over 25, can be offered risk reducing breast surgery.

Cancer Surveillance for individuals with PHTS

According to ERN GENTURIS cancer surveillance guideline for individuals with *PTEN* hamartoma tumour syndrome (PHTS) *Authors: Nicoline Hoogerbrugge, Ana Blatnik, Charlotte Kvist Lautrup, Robert Hüneburg, Daniela Turchetti, Anne van Altena, Frédéric Caux, Sophie Da Mota Gomes, Kelly Kearley, Chella (RS) van der Post, Alex Teulé, Jolanda Schieving, Inga-Lena Nilsson, Ritse Mann, Per-Olof Lundgren, Thera Links, Emma Tham, Sjaak Pouwels, Marc Tischkowitz.*

- Update published online on 16 July 2026 in the European Journal of Human Genetics: 10.1038/s41431-026-02181-z
- Complete guidelines on www.genturis.eu

	SURVEILLANCE METHOD	INTERVAL	FROM AGE
Breast cancer	MRI	As for *BRCA1**	25
	Mammography	As for *BRCA1**	40 *
	Risk reducing surgery offered	Yes	25
Thyroid cancer	Ultrasound	Yearly, frequency decreases to every 2-3 years after 2 USs with no suspicious findings	10-18
Endometrial cancer	Ultrasound (endometrial biopsy can be considered)	Yearly	35-40
Renal cancer	Baseline imaging	No further surveillance unless required by baseline outcome	35-40
Colorectal cancer (CRC)	Baseline colonoscopy preferably in expert centre	No further surveillance unless required by baseline outcome or CRC family history	35-40
Skin melanoma	Baseline skin examination by dermatologist or expert	No further surveillance unless required by baseline outcome	30

* Most national guidelines for *BRCA1* surveillance recommend yearly surveillance with MRI and mammography every 1-2 years.

PTEN hamartoma tumour syndrome Clinical Pathway

Faculty: .....

Family name:

Given name(s)

Address:

Date of Birth: Sex: ☐ M ☐ F ☐ I

Review Recommended

PHTS is a multi-system disorder associated with benign tumours such as skin and connective tissue tumours, including vascular malformations as well as neurodevelopmental disorders, including autism spectrum disorders. The syndrome also predisposes to a high hereditary risk of breast, thyroid, endometrial and a moderate risk of kidney, colorectal and skin cancer.

WHEN	WHOM	REVIEWS CARRIED OUT BY
At time of diagnosis, or if PHTS is suspected	All patients	Clinical genetics department to confirm diagnosis and discuss consequences for patients and close relatives.
	Those with significant complications	The nationally recognized PHTS reference centre, if available. GPs, paediatricians and other specialists can contact their local genetics service for PHTS-related concerns and if available have access to the national PHTS reference centre.

Review Checklist

Clinical Presentation:

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Other symptoms:

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Genetic counselling completed ☐

Date Completed:

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Clinical diagnosis

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Genetic Test '+'ve ☐

Diagnosis Date:

.....

General Health Check:

Please record:

Height

.....

Weight

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Head Circumference

.....

Blood Pressure

.....

WHAT TO LOOK FOR	WHEN TO REFER AND WHERE TO
SKIN: Check for symptomatic lesions, facial trichilemmomas, lipomas, acral keratosis, papillomatous papules of the gum and/or the tongue, penile freckling, vascular anomalies (arteriovenous malformation, venous malformation, superficial cutaneous haemangioma) and melanoma.	Rapidly growing or changing pigmented lesion: REFER to national PHTS reference centre, or specialist dermatology or vascular team. Lesions being removed for other reasons need referral to plastic surgeon or dermatologist. ☐ **Date Referred**: .....
NEUROLOGICAL: Adult Lhermitte-Duclos disease (LDD) (cerebellar tumours), autism spectrum disorders (ASD), developmental delay; Intellectual disability, anxiety disorder.	REFER to National PHTS Reference Centre or neurologist for evaluation of neuropsychiatric problems or if increase in frequency and/or severity of headaches or onset of other symptoms. ☐ **Date Referred**: .....
ENDOCRINE: Multinodular goiter, thyroid tumours/cancer, hypothyroidism, hyperthyroidism.	REFER to endocrinologist if symptoms of thyroid dysfunction exist. REFER to endocrine surgeon if suspicion of thyroid cancer or mechanical symptoms from multinodular goiter exist. ☐ **Date Referred**: .....
PREGNANCY: Depending on the country there might be options for prenatal and preimplantation genetic testing.	Individuals who are planning pregnancy should be offered REFERRAL to clinical genetics services ☐ **Date Referred**: .....
ANY OTHER NEW SYMPTOMS: Consider other possible complications.For instance: vaginal bleeding outside menstrual periods; new lump or pain in the breast; skin changes; blood in the urine or flank pain; black faeces or changes in bowel habits.	Refer to appropriate specialist ☐ **Date Referred**: .....
UNSURE? Treating physicians can contact the PHTS team/local clinical genetics.	

Notes:

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Doctor:

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Review date:

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CANCER	SURVEILLANCE METHOD	INTERVAL	FROM AGE
BREAST	MRI	As for *BRCA1**	25 years
	Mammography	As for *BRCA1**	40 years
	Risk reducing surgery offered	yes	25 years
THYROID	Ultrasound	Yearly**	10-18 years
ENDOMETRIAL	Ultrasound (endometrial biopsy can be considered)	Yearly	35-40 years
RENAL	Baseline imaging	No further surveillance unless required by baseline outcome	35-40 years
COLORECTAL (CRC)	Baseline colonoscopy preferably in expert centre	No further surveillance unless required by baseline outcome or CRC in family history	35-40 years
SKIN MELANOMA	Baseline skin examination by dermatologist or expert	No further surveillance unless required by baseline outcome	30 years

* most national guidelines for *BRCA1* surveillance recommend yearly surveillance with MRI and mammography every 1-2 years.
** Frequency can decrease to every 2-3 years after 2 ultrasounds with no suspicious findings

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