INTRODUCTION
The PTEN gene is a tumour suppressor gene which is somatically mutated in a large number of tumours. Germline mutations of the PTEN gene are associated with several syndromes;
- PTEN hamartoma tumour syndromes including Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome and Proteus–like syndrome
- Lhermitte-Duclos disease (LDD)
- Autism spectrum disorder / developmental disorder
Cowden syndrome is characterised by multiple hamartomas and a high risk of tumours of the breast, thyroid and endometrium. Patients usually have macrocephaly. Mucocutaneous lesions, thyroid abnormalities, fibrocystic disease and multiple leiomyoma may also be seen. The lifetime risk of developing cancer is up to 33% for female breast cancer and 9% for endometrial cancer. The lifetime risk for thyroid symptoms is 35%, (Tan et al 2011, The American Journal of Human Genetics, 88, 42-56).
Lhermitte-Duclos is a rare cerebellar tumour associated with Cowden syndrome. Autism spectrum disorder and macrocephaly are seen in some patients with PTEN mutations (McBride et al, Autism Research, 2010, Jun3(3)). These patients are at risk of developing further PTEN related symptoms.

TESTING AND REFERRALS
Diagnostic:
- Clinically affected patients
- From Clinical Genetics*

Carrier/Presymptomatic/Test for Familial Mutation:
- Individuals at risk of inheriting a pathogenic mutation in PTEN
- From Clinical Genetics only
- Requests for presymptomatic testing should either be accompanied by details of the known pathogenic mutation in the family or discussed with the laboratory in advance.

Prenatal:
- Prenatal testing is not usually requested.
- Prenatal requests would only be accepted from Clinical Genetics and must be discussed with the laboratory and arranged in advance.

STRATEGY AND TECHNICAL INFORMATION
Molecular analysis is undertaken by Sanger sequencing of exons 1-9 including the exon/intron boundaries. Multiplex Ligation-dependent Probe Analysis (MLPA) is also undertaken to detect whole exon deletions.

CLINICAL SENSITIVITY
Tan et al 2011, Identified a pathogenic mutation in PTEN in 9.5% of patients who met relaxed International Cowden Consortium operational criteria for Cowden syndrome.

TARGET REPORTING TIMES
Diagnostic: 40 days
Presymptomatic/Familial Mutation test: 10 days

*Diagnostic referrals from patients with autistic spectrum disorder or developmental delay only may be accepted via Consultant Paediatricians. If a pathogenic change is identified the report will be copied to a Consultant Clinical Geneticist.

N.B Details are correct for the date of printing only – last updated 02/07/2015