

Zurich, April 12, 2016

Clinical application of High throughput sequencing (HTS) analysis

Dear SGMG members, As you probably know, since 1st of January 2015, the BAG/OFSP has officially introduced high throughput sequencing (HTS) to the List of Analysis, together with a HTS good practice document (Bonnes Pratiques) of the Swiss Society of Medical Genetics (SSGM). Please find the links to the new version of the List of Analysis (in German and in French) as well as the “Bonnes Pratiques” (for the moment only available in French) at the end of this letter. With this following letter we would like to inform you about some practical aspects and the most important requirements for reimbursement.

1) Positions in the List of Analysis for HTS analysis

The HTS analysis was implemented in the List of Analysis as an additional position (position number 28XX.XX) in the section Molecular and Genetic Analyses (chapter 2, section 2.2.2.). Our initial purpose was to introduce HTS in the List of Analysis as a method, but unfortunately this was not possible. As a consequence a HTS position was added to almost all existing disorders in this section of the List of Analysis. This explains why some disorders like Friedreich's Ataxia (caused by triplet repeats) or Cri-du-Chat syndrome already have a HTS position although at the moment these disorders are more efficiently detected by traditional methods due to technical limitations or high costs of HTS. As long as no changes occur regarding these issues, you will continue to use for these disorders the traditional positions, which are still valid (see in this context also point 3 below).

2) Positions in the List of Analysis and prices

The positions and prices for HTS analysis are based on a combination of three steps which can be added together: the high throughput sequencing, the bioinformatic analysis (the price depends on the number of analyzed genes) and the Sanger sequencing confirmation.

- High throughput sequencing:
 - 2300 points (independent of the number of genes analysed)
- Bioinformatic analysis:
 - 1-10 genes: 600 points (total: 2900 points)
 - 11-100 genes: 1000 points (total: 3300 points)
 - Over 100 genes: 1500 points (total: 3800 points)
- Confirmation of variants using the Sanger sequencing (215 points per variant):
- Maximum 2 Sanger reactions after HTS analysis of 1-10 genes (total: 3'330 points)
- Maximum 4 Sanger reactions after HTS analysis of 11-100 genes (total: 4'160 points)
- Maximum 6 Sanger reactions after HTS analysis of more than 100 genes (total: 5090 points)

It is furthermore allowed to add an MLPA analysis in case no mutation has been found after HTS.

3) Main restrictions related to the prescription of HTS analysis

- The reimbursement of HTS analysis is only acknowledged if the HTS analysis of the corresponding gene/genes is cheaper than with classical method like Sanger sequencing. Thus, for small genes (< 13 exons) or individual mutation search, Sanger sequencing will stay the method of choice. HTS can be applied only if you have to charge more than 13 Sanger reactions (> 2795 TP).
- As for the orphan diseases, the prescription of an HTS analysis of 1-10 genes can be performed by physicians with an FMH in "Medical Genetics" or with an FMH of a specialty closely related to the investigated illness (following the federal law of 23 June 2006 concerning the university medical professions – RS/SR 811.11).
- The prescription of an HTS analysis of more than 10 genes can only be performed by physicians with an FMH in "Medical Genetics" (following the federal law of 23 June 2006 concerning the university medical professions – RS/SR 811.11).

4) Laboratories entitled to perform the HTS analysis

The laboratory performing HTS analyses must be in conformity with the standards of the Swiss federal law on health insurance (KVG, SR 832.10 or LAMAL, RS 832.10) and the head of the laboratory must have an FAMH in medical genetics. Furthermore, all steps of the HTS procedure (sequencing, bioinformatic analysis and Sanger confirmation) have to be performed in Switzerland. It is however not necessary that all steps are performed in the same institution. In addition, the laboratory should be accredited for the HTS analysis by the Swiss Accreditation Service (SAS) following the ISO 15189 and/or ISO/IEC 17025 before 31st of December 2017.

5) Useful links

Analysenliste (AL)	http://www.bag.admin.ch/themen/krankenversicherung/00263/00264/04185/index.html?lang=de&lan_g=de
Liste des analyses (LA)	http://www.bag.admin.ch/themen/krankenversicherung/00263/00264/04185/index.html?lang=fr&lan_g=fr
Bonnes Pratiques	http://sgmg.ch/wordpress/wp-content/uploads/2015/12/Bonnes_Pratiques_BAG.pdf