파브리병 치료제 급여기준 관련 질의 및 응답

질문 1 | **파브리병 치료제 관련 급여기준 개정 의미 및 질의·응답 제공의 배경은 무엇인가요?**

<답변>

○ '파브리병의 특징적인 임상 증상' 문구 명확화 요청에 대한 검토과정에서, 다양한 임상진료지침 및 보험재정에 미치는 영향까지 고려하여 설정된 제외국 보험기준을 주요하게 참고하는 것이 현 상황에 비교적 적절한 것으로 논의되었습니다.

○ 이에, 호주 'Life Saving Drugs Program (LSDP) guidelines for initial application and annual reapplication for subsidised treatment for Fabry disease(2018)'를 기본으로 하되, 명확한 수치 등 보완이 필요한 부분은 캐나다 'Canadian Fabry Disease Treatment Guidelines(2018)' 및 관련 가이드라인※과 전문가 의견 등을 종합적으로 고려하는 방식으로 급여기준을 개정하게 되었습니다.

○ 또한, 검토과정에서 심장관련 요건 중 급여기준 ⑦항 관련 '임상적으로 유의한'에 대한 추가적인 설명이 필요한 것으로 논의되어 해당 항목에 대한 질의·응답을 제공하게 되었습니다.

※ · Fabry disease revisited: Management and treatment recommendations for adult patients. Alberto Ortiz et al. Molecular Genetics and Metabolism 123(2018)
· Recommendations for initiation and cessation of enzyme replacement therapy in patients with Fabry disease: the European Fabry Working Group consensus document. 2015
· Fabry nephropathy: indications for screening and guidance for diagnosis and treatment by the European Renal Best Practice. 2012
· 대한 유전성 대사질환 학회. 리소좀 축적 질환의 진단과 치료지침. 2013.
· Adult Fabry Disease Standard Operating Procedures (January 2013)

질문 2 | **급여기준 중 ⑦항의 의미는 무엇인가요?**

<답변>

○ 심장 관련 요건 중 '부정맥 및 전도장애' 등에 대해 LSDP(2018)에서는 'Significant life threatening(생명을 위협할 만큼 유의한)' 경우로 제한하고 있으나, 이러한 환자군에만 특정하여 약제를 투여하기 어렵다는 전문가 의견을 반영하여 급여기준 ⑦항의 '임상적으로 유의한'을 신설하게 되었습니다.

○ 다만, '임상적으로 유의한 부정맥 및 전도장애'의 구체적 해석은 Canadian Fabry Disease Treatment Guidelines(2018), Adult Fabry Disease Standard Operating Procedures(2013) 등의 '부정맥 및 전도장애' 관련 항목을 참고하는 것이 적절한 것으로 논의되었습니다. 따라서 해당 참고문헌의 심장 관련 사항 전문을 첨부하오니 참고하시기 바랍니다.

[첨부]

○ **Canadian Fabry Disease Treatment Guidelines 2018.**

Cardiac Disease Evidence level II-2 - Grade B
2 criteria required

Criteria:

- LV wall thickness >12 mm in males and >11 mm in females
- LV hypertrophy (LVH) by Estes ECG score must be greater than 5
- LV mass index by 2D echo 20% above normal for age
- Increase of LV mass of at least 5 g/m2/year, with three measurements over a minimum of 12 months
- Diastolic filling abnormalities by 2D echocardiogram, Grade 2 or Grade 3 diastolic dysfunction as outlined by ASE and/or the presence of speckle tracking abnormalities
- Abnormal base to apex circumferential strain gradient
- Increased LA size on 2D echo. In parasternal long axis view (PLAX) >40 mm; Left atrial volume index > 34 ml/m2
- Cardiac conduction and rhythm abnormalities: AV block, short PR interval, left bundle branch block (LBBB), ventricular or atrial tachyarrhythmias, sinus bradycardia (in the absence of drugs with negative chronotropic activity or other causes)
- Moderate to severe mitral or aortic insufficiency
- Late enhancement of left ventricular wall on cardiac MRI

- T1 values using a 1.5 Tesla magnet in males below 901 ms and females below 916ms
- Increase of either N-terminal pro-natriuretic brain peptide (NT-proBNP) above the upper limit of normal for age and gender OR an increase of high sensitivity troponin (a surrogate marker of fibrosis) more than 2 times the upper limit of the normal range

○ **Adult Fabry Disease Standard Operating Procedures (January 2013)**

Evidence of cardiac disease

A. ECG
   a. presence of left ventricular hypertrophy (Romhilt-Estes or Cornell criteria)
   b. Isolated repolarisation abnormalities (in absence of other causes such as hypertension, aortic stenosis)
   c. Conduction abnormalities: (Short PR interval, 1, 2 or 3 degree heart block, bundle branch block)

B. Echocardiogram
   a. Increased left ventricular mass (in patients with concentric remodelling or hypertrophy) Criteria (Devereux et al 1977,1986)
      Normal LVMI defined as < 134 gm/m2 for men and < 110 gm/m2 in females.
      Relative wall thickness (RWT) calculated as ((IVS + PW)/LVed) at the mitral valve level.
      LV remodelling or LVH defined as a RWT > 0.4514.
      LV geometry defined as normal (normal LV mass and normal RWT), concentric remodelling (normal LV mass and increased RWT), eccentric LVH (increased LV mass and normal RWT), and concentric LVH (increased LV mass and increased RWT).
   b. Increased left ventricular wall thickness (13 mm in any segment).
   c. Left atrial enlargement
   d. Valvular thickening/insufficiency
   e. Systolic impairment (regional wall motion abnormality or reduction in left ventricular ejection fraction (< 50%)
   f. Diastolic dysfunction (using age corrected Doppler assessment)

C. Arrhythmia
   a. 24 hour ECG (or other documented ECG evidence) showing bradyarrhythmia, atrial arrhythmia, ventricular tachycardia.