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RE: Cystinosis patients in Canada

We as the Canadian Association of Paediatric Nephrologists (CAPN), representing all pediatric nephrologists and the Canadian Society of Nephrologists (CSN) representing all adult nephrologists practising in Canada are writing to raise ours concerns over recent drug approval policies that affect our patients suffering from cystinosis.

Cystinosis is a rare genetic disease affecting 1 in every 100,000 to 200,000 children. If not treated, cystinosis will lead to kidney failure, severe growth restriction, impaired vision, diabetes and severe muscle disease.

Cysteamine is the only therapy shown to be effective at slowing the progression of this disease in children (Markello NEJM 2013; Brodin-Sartorius KI 2012). Importantly, none of these data were obtained in the context of randomized clinical trial. Because of strong mechanistic data, it was indeed unethical to include a placebo arm. Immediate-release cysteamine (CYSTAGON) has been used for years to treat patients with cystinosis.

Recently Health Canada approved the long-acting form of cysteamine, PROCYSBI, which was shown to be non-inferior to CYSTAGON to treat cystinosis (Langman CJASN 2012). A prospective non-randomized study also suggests that a switch from CYSTAGON to PROCYSBI may result in improvements in quality of life indicators (Langman J Peds 2014). The current standard of therapy (CYSTAGON) is approximately 100-fold less expensive than the predicted yearly costs of $1 million for each patient treated with PROCYSBI.

Patients and physicians are happy about the recent approval to begin marketing PROCYSBI in Canada. We were however alarmed to learn that we will no longer be able to prescribe CYSTAGON as of January, 2018 because it is not officially approved for marketing in Canada. We believe that this will create undue financial

hardships for our private insurance companies, provincial medicine formularies, and most importantly, for our patients, including those who are currently well-controlled on CYSTAGON.

Indeed, since learning of the changes a number of our patients and their families have expressed strong concerns about the lack of availability of CYSTAGON going forward. PROCYSBI is very expensive, we anticipate that provincial drug plans will take time to conduct independent research on the medication before deciding whether to cover the costs or not. We expect many provincial formularies will have difficulty justifying such a costly treatment since there is no outcome-based evidence suggesting that PROCYSBI is better than CYSTAGON. While it is approved for use in the European Union, the Scottish Medicines Consortium[1], Ireland's Centre for Pharmacoeconomics[2] and France's Hautes Autorité de Santé[3] all recently ruled against approving PROCYSBI for this reason. CYSTAGON is approved, available and affordable in these countries.

It is therefore unclear if any of the provincial jurisdictions will have a financially viable solution in place by January 1st, 2018. As such, it is likely that many of our patients will be left without any treatment for an extended period of time if nothing changes. We strongly feel that it would be negligent and irresponsible to allow for a regulatory quirk to trigger therapeutic gaps of any duration for patients that have been stable and compliant on CYSTAGON for years. This is a life-sustaining therapy: treatment interruption will allow the disease to progress, causing kidney failure, problems with motor and nerve function, and ultimately death. At the very least, there needs to be a discussion between the various stakeholders to clarify which stopgap measures will be in place to be certain to avoid the disastrous scenario described above.

The simplest temporary solution would be for Health Canada to allow for CYSTAGON to be prescribed everywhere in Canada until patients with cystinosis from all provinces have equitable and affordable access to PROCYSBI. We ask that both formulations remain available to Canadians, as many patients have no personal or medical reasons to change therapy.

We are deeply concerned that if patients cannot find a way to pay for PROCYSBI, they will be forced to live with progressively worsening symptoms of a terminal disease that were kept at bay by CYSTAGON. Cysteamine in any formulation is the only proven therapy to treat cystinosis. It is essential that any therapy be reimbursed by provincial drug plans equitably across the country. .

We hope that you will consider our request. Our membership and executive remain available to discuss this further.

Véronique Phan MD MSc FRPCP
CAPN President

Amit Garg, MD PhD FRCPC
CSN President

[1] http://www.scottishmedicines.org.uk/SMC_Advice/Advice/1272_17_mercaptamine_Procysbi

[2] http://www.ncpe.ie/drugs/cysteamine-bitartrate-procysbi/

[3] https://www.has-sante.fr/portail/jcms/c_2561313/en/procysbi-cysteamine-metabolism-product