ARIZONA PEDIATRIC PULMONARY CENTER

NEWSLETTER

PHAN-TASTIC PHARMACY UPDATES: SYMDEKO™

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What is It and Who Can Use It?

Tezacaftor - Ivacaftor (Symdeko™) is the newest cystic fibrosis transmembrane regulator protein (CFTR) modulator approved by the FDA on February 12, 2018 for treatment of persons with cystic fibrosis 12 years of age or older with F508del homozygous or have one of 28 other mutations shown to produce CFTR and are responsive to Symdeko™ (see table below).

CF Gene Mutations Responsive to Symdeko™

Table 1. CF Gene Mutations Responsive to Symdeko™

E56K	*E193K*	*711+3A→G*	*A1067T*	*3272-26A→G*
P67L	*L206W*	*E831X*	*R1070W*	*3849+10kbC→T*
R74W	*R347H*	*S945L*	*F1074L*	F508del*
D110E	*R352Q*	*S977F*	*D1152H*	
D110H	*A455E*	*F1052V*	*D1270N*	
R117C	*D579G*	*K1060T*	*2789+5G→A*	

*Must have 2 CF mutations (i.e., F508del/F508del)

Dosing and How to Take It

- The usual dosing of Symdeko is one yellow pill (which contains tezacaftor 100 mg and ivacaftor 150 mg) in the morning and one blue pill (which contains ivacaftor 150 mg) in the evening, with doses taken 12 hours apart.
- Similar to the other CFTR modulating agents, such as Kalydeco™ and Orkambi™, this medication has to be administered with a fat-containing meal for absorption of the medication.

Important Considerations (Drug Interactions, Possible Side Effects, Monitoring)

- Drug interactions with CFTR modulators may require medication dose adjustments, so it is important to update your CF care team on your current medications and any herbal or alternative supplements you are taking.
- Monitoring liver function is also similar between the different CFTR modulators. Liver function tests (by lab draw of blood) must be done every 3 months for the first year of therapy, then annually thereafter if tests are within normal limits.
- Baseline eye exams must be completed prior to starting the medication in children ages less than 18 years, due to the rare, but potential risk of cataract development.
- Even if you have been on another CFTR modulator, such as Kalydeco™ and Orkambi™, these items (i.e., labs for all ages and eye exam for children), must be repeated when switching to Symdeko™ to make sure use of this new medication is safe for you/your child.

What are the Possible Benefits?

Currently, there are no head to head studies or clinical trials directly comparing Symdeko™ to Orkambi™. Symdeko™ showed more of an increase of FEV1 when compared with Kalydeco™ in patients with a single Phe508del plus a residual function mutation. One noteworthy difference between Symdeko™ and Orkambi™ is that there were fewer reports of chest pain or tightness with use of Symdeko™. The most common adverse reactions reported with Symdeko™ included headache, nausea, sinus congestion, and dizziness. Similar to other CFTR modulators, such as Kalydeco™ and Orkambi™, there is potential for drug interactions; however, there are fewer of them with Symdeko™ compared to Orkambi™. It is important to talk with your pharmacist about any new or current medications, herbal supplements, vitamins, etc. if you are taking Symdeko™, Kalydeco™, or Orkambi™.

Can and/or Should I Change from Kalydeco™ or Orkambi™ to Symdeko™?

Your/your child's genotypes are reviewed by the CF care team prior to each clinic visit to see if they are eligible for Symdeko™, Kalydeco™, or Orkambi™ as part of their medication regimen. CF mutation/genotype alone is not the only thing considered when determining if any of these medications are right for you/your child. Other considerations such as liver function, potential drug interactions, potential clinical outcomes are evaluated in this process. Another important aspect of this decision is discussion between you and the CF care team. This discussion will include risks versus benefits of changing to or starting Symdeko™ and steps to transition medications, if that is the case.

Patients who were previously unable to tolerate Orkambi™ due to chest tightness may benefit from trialing Symdeko™. Additionally, patients who have potential drug interactions with Orkambi™ may benefit from changing to Symdeko™.

If a patient decides to transition from Kalydeco™, or Orkambi™ to Symdeko™, the CF Clinical Pharmacist will review the correct way to transition medications and what will need to be monitiored in your/your child's first year of therapy (see above, Important Considerations). Additionally, prior authorizations will likely need to be processed before starting the medication, which can be taken care of by our CF Pharmacy Technician (Meredith Reams).

This is an exciting time in the development of future care in CF! If you have any additional questions or concerns, please feel free to contact the CF Care Team to discuss any additional information.

References:

Symdeko [package insert]. Boston, MA : Vertex; 2018.

Taylor-Cousar J, Munck A, McKone E, et al. Tezacaftor-Ivacaftor in Patients with Cystic Fibrosis Homozygoiys for Phe508del. The New England Journal of Medicine. 2017; 377(21): 2013-2023.

Rowe S, Daines C, Ringshausen F, et al. Tezacaftor-Ivacaftor in Residual-Function Heterozygotes with Cystic Fibrosis. 2017; 377(21):2024-2035.

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A FAREWELL FROM MARY MCGUIRE

Dear patients and families,

I wanted to let you know of an upcoming change this summer as I transition out of the University of Arizona Pediatric Pulmonary Center Social Work Faculty and CF clinic social work position end of June/mid July. It's not a decision I took lightly because of the amazing teams I work with and all of you. It has truly been such an incredible blessing and privilege to work with you all over the past six years. Thank you for sharing your lives and your children's lives. We are in the process of hiring an individual who will be a good fit for this position. I know that whomever comes to fill this position will work alongside you all to help take things to the next level of care for you and you family. I am available for any questions. Please feel free to contact me at mmcguire@peds.arizona.edu or 520-626-1569.

With much gratitude,
Mary McGuire, LMSW

RECAP FROM CF LEARNING NETWORK SPRING CONFERENCE

Several members from our quality improvement team attended the CF Learning Network (CFLN) Spring Conference. Here are couple team members' thoughts from the conference.

Glenda Drake, RRT says: The CF Learning Network conference brings together people from different educational levels, backgrounds, institutions and regions for one purpose, to make life better and easier for our patients and families. Either by giving a presentation which sparks a conversation on how to improve a process, or by watching a family member participate in a skit on communication, the highlight is always sitting at a table, clinicians and family members together, making a difference in each others' lives.

Katrina Stogner, Parent says: As a parent partner on the Family Patient Advisory Committee, I was invited to participate in the CFLN Spring Conference. I was fortunate to be there with CF professionals from around the country, witnessing the dedication these teams have to this terrible disease. They choose to continue to learn from each other and tackle hard challenges that people with CF must deal with in their life. What makes this conference so unique is that they ask for MY input on any given issues, large or small. I feel they have learned from me small and large details that they have overseen or didn't realize. I'm now not only improving the life of my son, but for the first time, I'm also able to impact other people with CF as well. I look forward to this continued partnership and thank everyone involved to make this unique co-production of care possible.

PARENT CAREGIVER RETREAT: TELL US WHAT YOU THINK

We are looking to host a retreat for parents and caregivers of children with cystic fibrosis. We would like your feedback in order to create an event that would be beneficial for you. Visit this link to take the survey: www.surveymonkey.com/r/ParentCaregiverRetreat. Please provide any feedback in the survey by 6/30/18, so we can begin planning. Thank you!

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