University of Wisconsin
Clinical Sciences Center

Center Focus

Winter, 2016

Newsletter of the
Cystic Fibrosis Center

Mental Health Screening

As you know, our Center's mission is to provide the best possible medical care to people with cystic fibrosis to live longer, better quality lives. In that effort, we strive to adhere to guidelines to treat CF, some of which includes regular clinic visits and a variety of tests such as x-rays, sputum cultures and tests done annually or every other year like bone density or oral glucose tolerance tests.

We are writing to inform you of important new recommendations from the Guidelines Committee on Mental Health (GCMH), jointly formed by the CF Foundation and the European CF Society. The Committee was established in response to a large study that found people with CF and their caregivers are at higher risk for symptoms of anxiety and depression. Research in other illness groups has found higher rates of depressive and anxious symptoms compared to the general population and that when left untreated, physical health is negatively affected. A key recommendation is to screen all people with CF, 12 years of age and older, for symptoms of depression and anxiety. In addition, screening will be offered to the parents or caregivers of all children with CF as higher rates of these symptoms can then impact children with CF.

At an upcoming clinic visit, we will invite you to complete two screening tools, the PHQ-9 (Patient Health Questionnaire) and the GAD-7 (Generalized Anxiety Disorder). They are both simple and quick to fill out and are highly reliable tools. The screeners do not diagnose depression and anxiety, but will help us not overlook something we might be able to help with. A qualified member of the CF team will explain the tools when you arrive answer any questions and, if you choose to complete the screeners, will then score the tools during your clinic visit and review the results with you. The completed screeners will be part of your medical record and are confidential and private, as is all of your personal health information.

We look forward to continuing to work with you in supporting your overall health, and please let us know if you have any questions or want more information.

Wrap-up of Cystic Fibrosis Family Education Day on November 7, 2015

Our thanks to all of the speakers and family members who came to the Fluno Center on November 7, 2015 for CF Family Education Day. The day started with an outstanding presentation by Dr. Michael Boyle, the Vice President of Therepeutics Development for the CF Foundation. Dr. Boyle highlighted the development of Orkambi® and provided a look into the future of all of the other medications in development in the therapeutic pipeline.

There were speakers from all of Wisconsin's Affiliate and Core Centers:

- Genetic counselors Kevin Josephson from La Crosse and Sumedha Ghate from Green Bay gave an update on the cftr2.org website.
- Dr. Laura McCauley from Marshfield gave an update about vitamin D in CF.
- Dr. Nick Antos from Milwaukee gave an update on their road map for improving the hospital experience.
- Darci Pfeil, Craig Becker, Cindy Wallace and Jen Harmelink discussed transitions and moderated a panel discussion.
- Alek Trebek (aka Dr. Michael Rock) hosted a spirited round of Infection Control Jeopardy.

We hope that by the time that you are reading this newsletter, that the videos from our CF Family Education Day will be posted at our website: *www.uwcfcenter.org*

We are in the process of planning the 2016 CF Family Education Day. We will send out a notice of the date and location in late spring/early summer.

Orkambi®

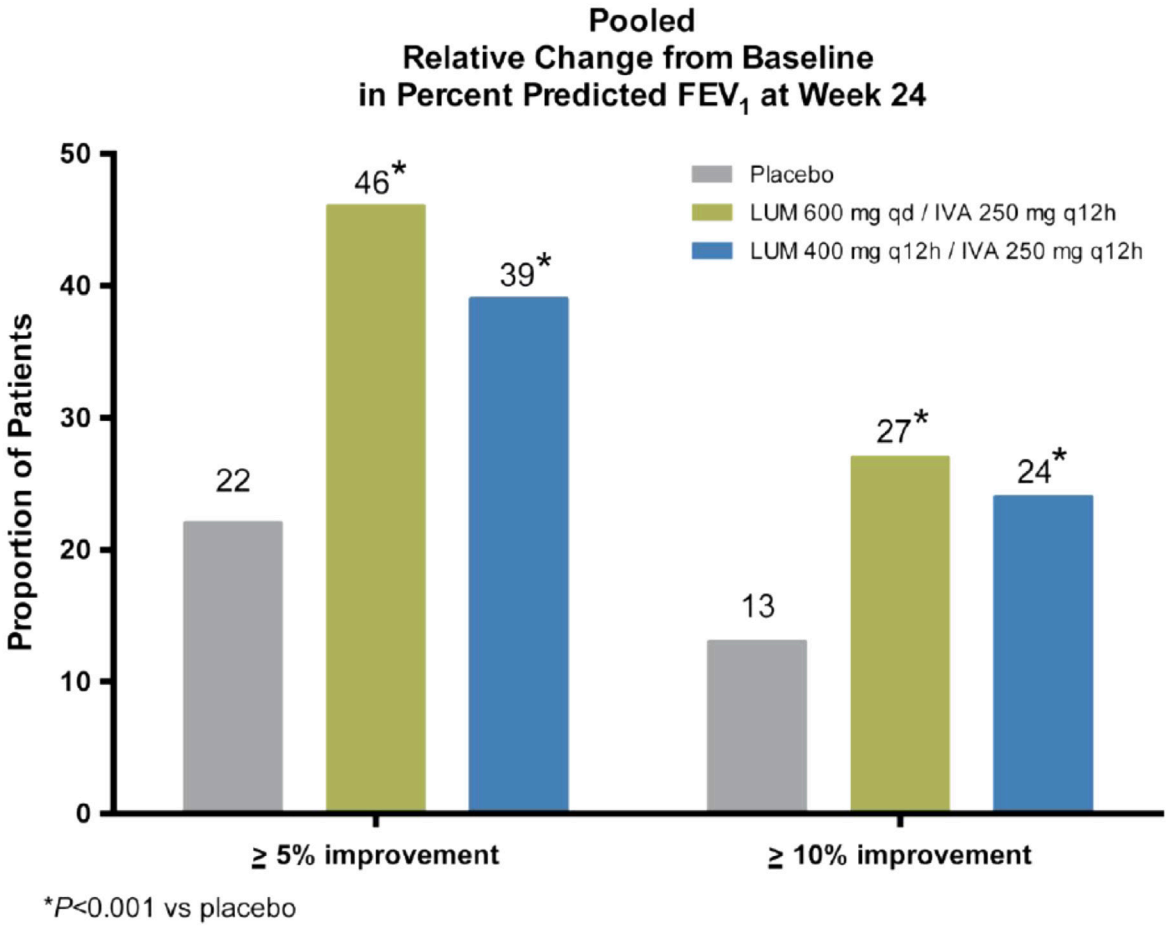
On July 2, 2016, the Food and Drug Administration approved Orkambi® (lumacaftor/ivacaftor) for patients with cystic fibrosis who have two copies of the F508 mutation and who at or above 12 years of age. This oral drug is taken twice a day and partially corrects the chloride channel defect. The FDA approval of this drug was based on a study of almost 1000 patients with CF. There were three groups of patients in the study: a group that received a placebo, a group that received 600 mg of lumacaftor plus 250 mg of ivacaftor, and another group who received 400 mg of lumacaftor plus 250 mg of ivacaftor. There was an overall improvement of FEV_1 percent predicted by approximately 2-3%. Although this was statistically significant, the improvement in FEV_1 is small. However, the following table shows the proportion of patients who had a greater than 5% improvement in FEV_1 and the proportion of patients who had a greater than 10% improvement in FEV_1:

The patients who received either dose of combination drug had a statistically significantly increased proportion of patients who had both a >10% and >5% improvement in FEV_1.

Additionally, the patients who received active drug had a statistically significantly decreased number of pulmonary exacerbations.

We believe that any patient with CF who has two copies of the F508 mutation and who are at or above 12 years of age should be receiving Orkambi®. There have been some challenges with Medical Assistance and some HMO's in placing restrictions on this medication (for example, requiring the FEV_1 percent predicted to be between 40 and 90%.) We are working as hard as possible to educate these third party payors that there should be no restrictions on Orkambi®.

For those of you who have children under the age of 12 years, we are participating in a multi-center study of Orkambi® in children who are 6 to 11 years of age. If this study shows efficacy, then we look forward to a day in the future when the FDA will allow Vertex to change the package label to down to 6 years of age.



CF Clinical Trials

We are participating in the following clinical trials:

- VX809-109: A Phase 3, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Lumacaftor in Combination With Ivacaftor in Subjects Aged 6 Through 11 Years With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation

- OPTIMIZing Treatment for Early Pseudomonas aeruginosa Infection in Cystic Fibrosis: The OPTIMIZE Multicenter, Placebo-Controlled, Double-Blind, Randomized Trial (OPTIMIZE-IP-12)

- The EPIC Observational Study: Longitudinal Assessment of Risk Factors For and Impact of Pseudomonas aeruginosa Acquisition and Early Anti-Pseudomonal Treatment in Children with CF

- A Long-Term Prospective Observational Safety Study of the Incidence of and Risk Factors for Fibrosing Colonopathy in US Patients with Cystic Fibrosis Treated with Pancreatic Enzyme Replacement Therapy: A Harmonized Protocol Across Sponsors

- Nivalis SNO6: A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of N91115 to Evaluate Efficacy and Safety in Subjects with Cystic Fibrosis who are Homozygous for the F508del-CFTR Mutation

- Nivalis SNO-7 "A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of N91115 to Evaluate Efficacy and Safety in Patients with Cystic Fibrosis who are Heterozygous for F508del-CFTR and a Gating Mutation Approved for Use and Being Treated with Ivacaftor (KalydecoTM)". Enrollment should begin early May 2016 and go through Nov. 2016

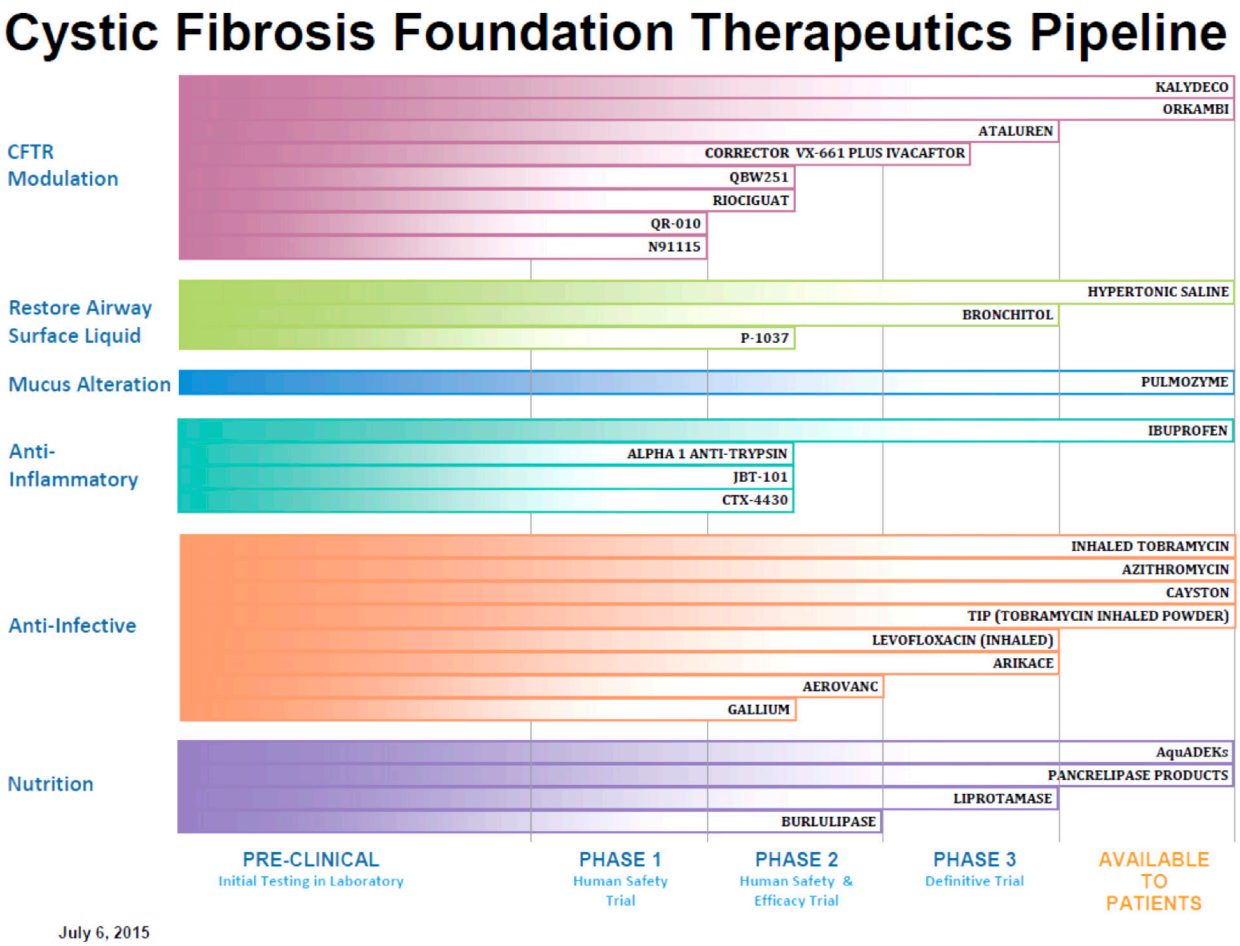
- Vertex VX15-371-101: A Phase 2a, Randomized, Double-blind, Placebo-controlled, Incomplete Block, Crossover Study to Evaluate the Safety and Efficacy of VX-371 in Subjects Aged 12 Years or Older With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation, and Being Treated With Orkambi. Screening to begin Mar 2016, end Q1 2017.

- STOP2-IP-15 "Standardized Treatment of Pulmonary Exacerbations II (STOP 2)."

- FIRST study: Feeding Infants Right from the Start

Below is the Cystic Fibrosis Foundation Therapeutic Pipeline.

Besides the medications listed on this pipeline, there are many other drugs that are in development. We hope to participate in other studies and if you are asked about being in a study, we hope that you will say yes. Kalydeco® and Orkambi® were developed due to patients with CF participating in clinical trials.



ANTIBIOTICS - EVERY DAY AS ORDERED!

by Karen Hickel, RRT/NPS Respiratory Therapist

Recently in the news, there have been reports of 'super-germs' which are becoming resistant to antibiotics. This means, antibiotic medicine becomes less able to kill the bacteria germs causing lung, and other types of infections.

There are many reasons why these 'super-germs' are becoming more resistant to treatment. One way bacteria change and become resistant is when antibiotics are not taken exactly as ordered. For example, if antibiotic pills or nebulizer treatments are taken occasionally or taken for a few days, stopped, then started again days later.

Taking your antibiotic pills or nebulizer treatments, exactly as ordered, and not missing doses, is the best way you can help avoid developing 'super-germs' in you or your child's lungs. If you would like suggestions about how to fit in all of your prescribed treatments - airway clearance, breathing medicines and antibiotic pills or nebulizers, please talk to your Doctor, Pulmonary Nurse or Respiratory Therapist. We are here to support and encourage you, to take all of your prescribed treatments and therapies, as ordered.

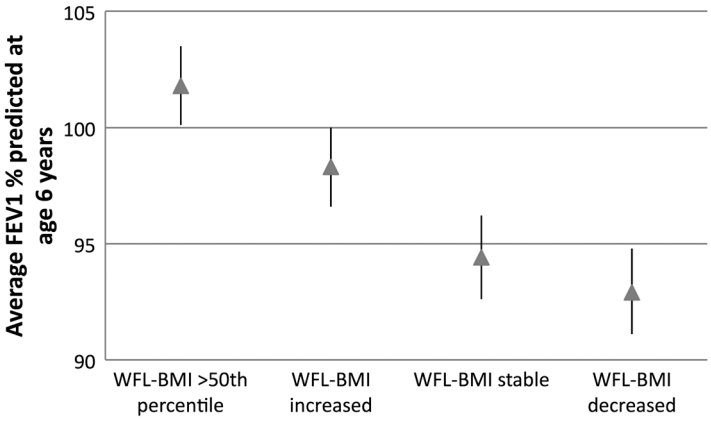
Recent Research on the Relationship Between Weight and the Lungs

The importance of having good nutrition has been known in the CF community for a long time: people with CF who weigh more, are taller, or have higher BMIs have better lung function and live longer. It is not exactly clear why this is, but because of this relationship the CF Foundation recommends that all children with CF who are less than 2 years of age have a weight-for-length >50th percentile for age, and all children with CF who are 2 years or older have a BMI >50th percentile for age.

We often discuss this goal during clinic visits. One question that we have not been able to answer is which comes first – the healthy lungs? Or the good nutrition? Children with CF who have healthy lungs will have a much easier time gaining weight. To address this question, we used data from the national CF Foundation Patient Registry to study changes in weight-for-length and BMI in the first 6 years of life and pulmonary function test results at age 6 years (when most children are first able to perform them). Our study included over 6,800 children with CF born since 1994. Our results were published in the *Journal of Pediatrics* in November 2015.

Our main results were that lung function (FEV_1 % predicted) was the highest for children who always met the CF Foundation's goals (see the Figure below). Children who had increases in weight-for-length and BMI had the next highest lung function results. Children whose nutrition remained stable (but below the CF Foundation's goals) or decreased over the first 6 years of life had the lowest lung function at age 6 years.

Figure. The triangles represent the average lung function (FEV_1 % predicted) at age 6 years; the vertical bars represent the 95thpercent confidence intervals. Children with weight-for-length (WFL) and BMI always >50th percentile for age had the highest lung function, followed by children who had increases in their nutrition. Children who had stable or decreasing WFL and BMI that fell below the 50th percentile had the lowest lung function.



Fundamentals Learning and Leadership Collaborative (LLC)

At your next clinic visit, you may see some information about an effort to improve the nutritional outcomes for our youngest CF patients. So, what's going on?

First, the history. Earlier this year, 36 CF centers around the country applied to be part of a nationwide initiative to improve care for CF patients. Our center at the American Family Children's Hospital was one of 15 centers ultimately selected to participate. It's a wonderful opportunity for CF centers to learn from each other and to improve the outcomes for our kids.

What makes this initiative different? For one thing, it's more than just a group of well-intentioned docs making changes in isolation. Each team has members from multiple disciplines. Our team at AFCH includes pulmonology, nutrition, nursing, and social work, as well as a CF patient and the parent of a CF patient. (I am the parent representative.) Candidly, I was a little skeptical that each voice on the team would be equally valued. I was wrong. I've been impressed by the willingness of our team to consider all viewpoints respectfully, and to make adjustments to reflect those viewpoints. Additionally, each team works closely with a coach who has expertise in improving health care. And, finally, each of CF centers participating in this initiative shares information on its improvement efforts, so that we can learn from each other and better evaluate what works and what doesn't.

What do we hope to accomplish? After looking critically at how our patients fare relative to other CF patients across the country, our team realized that the nutritional outcomes of our younger CF patients could stand improvement. We believe this particular metric is important, because there is a correlation between the body mass index (BMI) in younger CF patients and lung function later in life. If you want to see data that has been compiled by the LLC team, go to the CF Center website at *www.uwcfcenter.org*

How do we intend to accomplish our goal? Our improvement team has been evaluating our procedures and making changes to help us track and improve BMI. In fact, if you have a young child being seen at the AFCH, you have probably noticed greater attention to checking your child's height and weight at the start of your clinic visit. But looking more broadly at the issue, we have identified seven categories that impact BMI. In no particular order, they are:

- Financial (such as the cost of food and formula, or issues with insurance coverage)
- Societal (for example, our culture's sometimes unhealthy preoccupation with being thin)
- Co-Morbidities (such as meconium ileus or prematurity)
- Materials (including the need for properly calibrated scales at the clinic, or the availability of high quality educational materials for families)
- Patients and Families (which may include lengthy travel times required for some families to get to clinic, or trust issues with the health care providers seeing your child)
- Processes (such as inaccurate height or weight measurements, or insufficient follow up visits)
- Clinic Staff (including turnover or inadequate coordination between CF specialists and primary care physicians)

Why are you telling me all this? For two reasons:

- To keep you up to date on what's going on behind the scenes at the CF team, and
- To solicit your input.

No one knows your child like you do. Your thinking on how we can improve the nutritional status of kids at our center is invaluable. We would love to hear what you have to say.

Open Letter, From One CF Parent to Another

If you are reading this, you are probably in the midst of discussions regarding your child's weight. I feel for you. I've been there. Supplements are an excellent start, and sometimes supplements are all your child needs to keep his or her weight up. In any event, we, as parents, need to embrace this: there is a direct correlation between body mass index in young children with CF and lung function in later life.

So, with that data firmly in mind, what should you do if supplements are not enough? I can't answer that for you, and neither can your pulmonologist. But I can share my experiences with you.

First, I'd like to tell you about our oldest child with CF. We lived on the west coast when she was little. The doctors treating our daughter at the time did not initially offer us the option of a feeding tube. Instead, we tried supplement after supplement with limited success. We also tried every form of bribery, cajoling, and manipulation we could think of to get our daughter to eat. Every meal became a battle, and every CF visit a failure. Finally, when she was about six, the doctors suggested a feeding tube. It was the first time we had heard of that option, and we were not on board. Ultimately, we decided not to have a g-tube placed. Was it a good decision? I really don't know. She's a young adult now and heading off to college next fall. Her lung function is decent, but not stellar. She had trouble growing during her formative years, and finally topped out at 4'10". Overall, she is happy and doing well, but there are some days when I wonder if we made the best decision on her behalf.

My son is a different story. When he was three months old, his doctors told us he needed a feeding tube. We agreed. That was a hard decision, but it was the right decision. The surgery went off without a hitch, and the feeding tube allowed us to get my son the extra nutrition he needed without the drama that often accompanies meal times. Today, nearly a dozen years later, he is a happy, healthy boy. We removed his feeding tube when he was about 2½ - he just didn't need it anymore. He has some scars along his abdomen, and he loves telling a story about how that's where the shark bit him while he was surfing off the California coast.

If I could go back in time, I would give myself this piece of advice: be open to considering options that are best for your child long term. Because that's what we want for our kids: a long term. I have three children with CF, and I want to support their dreams. I want to applaud my son as he walks across the stage to pick up his diploma. And I want to help my daughters on their wedding days. And the hard truth is, if I want them to have the best shot at those dreams, I need to make wise choices today. Some of those choices are obvious. Make sure junior takes his medicine. Be diligent about keeping the neb equipment clean. Some choices are not so obvious.

We're a tough breed. We've weathered a hard diagnosis. We battle with insurance companies. We manage well-meaning but often ill-informed friends and family members. We are experts on getting medicines into uncooperative little ones. We multi-task like nobody's business. And we spend many, many sleepless nights worrying about our children. But we need to be more than tough. We need to be wise.

I wish you and your child the very best.

Patient and Family Experiences Survey

Patients and families are truly partners in the care that is provided. The CF Foundation has realized that we need input from our patients and families in order to improve care. To this end, the CF Foundation has contracted with a company called Quality and Data Management (QDM) to perform a patient and family experiences survey. We have a business associate agreement with the CF Foundation that allows them (the CFF) to contract with QDM to contact families twice per year after clinic visits in order to complete the survey. This arrangement meets all of the requirements of HIPAA and protected health information and has been approved by our hospital attorney.

What does this all mean for you? Sometime after a clinic visit, but no more than twice per year, you will receive a call from QDM. They are located in Cleveland, Ohio. What appears on your caller ID depends on your local phone company and their directory. The Cleveland area code is 440. You will initially speak to a live person about the survey. Then, you will be listening to a voice activated system that will go through the survey questions. We hope that everyone will participate in the survey and help us to improve our care and patient satisfaction.

Farewell to Dr. D.B. Sanders

Our best of wishes go to Dr. Sanders and his family who are relocating to Indianapolis, where he will be joining the pediatric pulmonology division at the Riley Children's Hospital.

CF Enzyme, Vitamin, and Supplement Assistance Programs

CF is a costly disease. Prescriptions, equipment, vitamins, supplements, and even extra food all add up. However, there are many resources you may not be aware of that can help offset some of these costs. Below is a chart outlining benefits that may be available to you based on the enzyme you use. For example, if you use Creon® enzymes, you can get free vitamins and nutritional supplements each month (including high calorie sports bars) as well as up to $50 per month back on your copay. If you use Zenpep® or Ultresa® enzymes, you can get free enzymes until the age of 2 years, never pay more than $40 for a copay, get free nutritional supplements and vitamins, and earn points to redeem for gifts like an iPod touch. By using Pertzye® enzymes, you can get $75 per month to use towards groceries.

To register, you simply go to the website listed by each enzyme and fill out the form. You can also get a brochure and benefits card in clinic. If you have medical assistance, you cannot participate in these programs. However, a new program is now available through the Healthwell Foundation.

The Healthwell Foundation provides financial assistance grants to eligible individuals to provide reimbursement coverage for medication co-pays, CF vitamins, supplements, and hypertonic saline. If approved, you will receive a grant of up to $15,000 per year. Even if you have medical assistance, you may qualify. The income guidelines are as follows:

Household Size	Income Limit
1	$58,850
2	$79,650
3	$100,450
4	$121,250
5	$142,050
6	$162,850

To find out more, call Healthwell at 1-800-675-8416 between 8 am and 4 pm (CST) or visit their website at *http://healthwellfoundation.org*. Applying typically takes less than 10 minutes. You will need to be ready to provide your date of birth, insurance information, number of people in your household, annual income, and provider's name and fax number. Once approve, you will receive a number and card to use when placing your orders. If you have any questions, please give Healthwell a call or talk to your dietitian or social worker in clinic.

Any Wisconsin resident, regardless of income or type of insurance, may also get free MVW multivitamins and vitamin D as well as supplements like Ensure, Ensure Plus, EnsureClear, Pediasure, Pediasure 1.5, and Scandishake. Simply ask your CF dietitian for more information.

Enzyme Brand	Program Name	What's Available	How to sign up
Creon® (Abbvie)	CF Care Forward	**Vitamins(choose one):** • MVW Complete Chewable • MVW Complete Softgel • MVW Complete Softgel D3000 • MVW Complete Pediatric Drops • Libertas Chewable • Libertas Pediatric Drops **Nutritionals** • Supplements: Ensure®, Ensure Clear®, Ensure Plus®, Pediasure®, Pediasure 1.5®, Pediasure Peptide 1.5®, Similac Advance Powder®, Myoplex Shakes® • Bars: ZonePerfect® Bars, Myoplex® Bars	Online: https://www.creon.com/CFPatients/EnrollInCFCareForward
Creon® (Abbvie)	Deductible & Co-Pay Assistance	Enzymes completely covered until deductible is met. After deductible is met, enzymes completely covered when prescription cost is $50 or less. Co-pay applies when enzyme prescription cost is over $50.	Ask at CF clinic for a co-pay card
Zenpep or Ultresa® (Aptalis)	Live2Thrive	**Vitamins (receive both):** • AquADEK: liquid, chewable, and softgel • Carlson Vitamin D softgels: 2000 IU **or** Super Daily D for Kids drops: 400 IU with added Vitamin E **Nutritionals** • Supplements: Scandishake®, Scandical®, Boost® VHC, Boost Plus®, Boost® Kid Essentials 1.5 • Bars: Clif Bar®, Clif Kid Zbar™ **Deductible/Co-pay Assistance** • Enzymes completely covered from Jan-March 2016 (no monthly limit), to help with deductibles. • After March 31, enzymes completely covered if co-pay is $40 or under • Co-pay applies, up to $40, for co-pays over $40, up to a co-pay yearly savings limit of $1500 a month. **Rewards Program** • Earn points by taking nutrition-related quizzes, watching educational videos, filling enzyme prescriptions • Points can be redeemed on the website for a variety of items	Sign up to receive the benefits and a card at: www.Live2Thrive.org
Pertzye® (Chiesi)	Chiesi Care Direct	**Co-Pay Assistance** • $0 out-of-pocket cost for enzymes up to a co-pay yearly savings limit of $1440 a month. **Nutritional Rebate Program℠** • Provides up to $75 rebate on vitamin supplements, high-calorie drinks, or other nutritional food sources for each 30-day prescription filled, or up to $225 for each 90-day prescription filled.	Download assistance form from: http://www.pertzyecf.com/patient/free-support-and-savings/ The form needs to be completed by both the patient and the physician. Call 1-888-865-1222 or ask at office for the nutritional rebate form (must be sent in with receipts for nutritional products that were purchased).

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