

MEDICINES

What to Know About Medicines Before and After Transplant

To help prevent problems and keep your child's heart healthy, you need to know your child's current medicines. The transplant team (including the physicians, nurses, pharmacists and nurse practitioner) will work with you to improve your understanding of your child's medicines and the importance of giving them as directed. The team will help you to decide on the best times to give your child his/her medicines. To ensure that the medications are given correctly, we need your help in supervising administration of **ALL** medicines. Many pre-teen and adolescents will say that they are taking their medicines, but they are not. We will work with you and your child beginning at age 10 to develop strategies to help him/her develop independence, but until the team and you agree together that he/she is able to take medicines without supervision, we ask for your help in making sure all doses of medicines are taken. Even though they may feel that they are at an age to understand the importance of the medicines and are responsible, it is critical to your child's health and wellbeing that you, as a parent/caregiver, still supervise.

You are encouraged to keep a list with you of all current medicines (this can be either a hand-written list or a printed list such as the one we hand out in clinic) that your child is taking. This list should also include any over-the-counter, herbal medicines or supplements. Since medicines are frequently adjusted or changed to meet the medical changes of your child, it is important that you update your list of medicines after each change (especially when these are done between clinic visits). Changes will be necessary before you finish all the medicines in a bottle. There will be times that the medicine instructions you have been given over the phone or in clinic are not the same as what is written on the prescription bottle. Your medicine list should include the following:

- Name of the medicine
- Concentration of the medicine if it is a liquid or compounded medicine (Examples: 1 mg /ml; 15 mg /5 ml)
- Dose of the medicine (Example: give 10 mg. Don't just list 1 ml)
- How often the medicine should be taken (Example: 10 mg daily [or 1 time per day] or 10 mg twice a day or every 12 hours)



Important Information to Know About the Medicines:

- The brand name and generic name of the medicine
- When to give each medicine
- How to give them
- Reason for giving that medicine to your child
- Major side effects from the medicine
- What food or other medicines should be avoided when giving the medicine
- What to do if you miss a dose
- When and how to order refills
- What the medicine looks like
- Always wash your hands before and after giving your child medicines

You Should Know the Following About Storing Medicines:

- Keep the medicines tightly capped
- Store them in a cool, dry place away from direct sunlight
- Do not store in an area that has too much moisture such as the bathroom
- Keep all medicines out of the reach of children
- For liquid medicines, do not draw up doses more than 48 hours in advance
- Do not let the liquid medicines freeze if they require refrigeration
- Do not store the medicine in the refrigerator unless instructed by the pharmacist
- Do not crush or cut the tablet, capsules or caplets unless instructed to do so

You Should Call the Transplant Team About the Medicines if:

- Your child cannot take his/her medicines for any reason
- Your child develops a rash, fever, nausea, vomiting, diarrhea or any unusual symptoms
- You are not sure what dose to give your child
- The medicine looks different when you picked it up from the pharmacy than it did other times you picked it up (received it) from the pharmacy
- You believe your child needs an over-the-counter medicine – pain relievers, cold medicines, etc.
- Another physician prescribes or changes any of your child's medicines
- You have any doubts or questions about your child's medicines
- You need a refill of any of your child's medicines

You Should be Aware of the Following Related to Refills of Your Child's Medicines:

- Refills should be discussed at your child's clinic visit.
- Do not run out of medicines! Plan ahead by always checking prescription bottles for the number of remaining refills. If in doubt, ask the pharmacist.
- Call the pharmacy to request refills at least one week before the medicines are gone. Most mail order pharmacies require at least two weeks to process your child's medicine refill.
- Prescriptions can be written for either a one-month or a three-month supply. The choice is determined by the patient's insurance coverage.
- Most non-liquid medicines are good for one year. Many **liquids** are only good for one to four weeks after compounding. The pharmacist will inform you how long a liquid medicine is effective. **ALL medicines should be taken as directed by the transplant team.**
- If your child is planning to be away from home during medicine time, you should bring his/her dose(s) of medicine with you. This is to ensure you stay on time with your medicine.
- You should always bring your child's medicines with you when traveling, whether it is a short or a long trip. When traveling by plane, **ALWAYS** carry the medicines in your carry-on bag instead of packing them in your checked bag. For liquid medicines, put all original bottles in a zip-lock bag for inspection.
- If you need a refill of medicine before your child's next clinic visit, you should call the Pediatric Heart Transplant office at **734-764-5176**. You will need to leave the following information:
 - Your child's name
 - Your child's date of birth
 - The name and dosage of the medicine that is needed for refill
 - How much of the medicine you have left
 - The pharmacy's name and phone number so we can call in the prescription for you
 - A telephone number where you can be reached between 8 a.m. and 4:30 p.m.

You Should Know

Do not run out of medicines!

Please allow a minimum of three days for refill requests to be processed. While a sincere effort will be made to process requests in less than three days, it cannot be guaranteed. If your child's medicines are a compounded liquid, your pharmacy will need **at least a TWO day notice and often more.**

Never stop giving medicine, skip doses or decrease the dosage of the prescribed medicines on your own. Doing so can risk your child's health. If your child has missed any of the doses of his/her medicines, contact your transplant coordinator immediately for instructions. Do not try to catch up by taking two doses of the medicine. When in doubt as to what to do, give the transplant office a call.

You Should Know

Never stop giving medicine, skip doses or decrease the dosage of the prescribed medicines on your own.

The reality is that every child may vomit after taking their medicines. Here are guidelines to follow if this should occur:

- If your child vomits within 15 minutes after the dose, the entire dose must be given again.
- If your child vomits more than 15 minutes after the dose, there is no need to give the dosage again.
- If your child **cannot** keep any medicines, food or fluids down, **you must** contact the transplant office immediately.
- If you have any questions about whether or not you should give your child a supplemental dose of medicine after he/she vomits, call the transplant team.

Types of Transplant Medications

- Anti-rejection medications
- Anti-infection medications
- Other medications

ANTI-REJECTION MEDICINES

Your child will take at least one anti-rejection medicine for the rest of his/her life. Anti-rejection medicines are also called immunosuppressive drugs. These drugs decrease the body's ability to fight off what it sees as foreign. They help to prevent the body from attacking the newly transplanted heart. The medical team attempts to minimize the amount of immunosuppression while preventing rejection. This allows an appropriate balance for your body to fight infection without rejecting the transplanted organ.

Since the chance of rejection is highest immediately following the transplant surgery, patients receive the greatest number of drugs and in higher dosages shortly after surgery. As the time after surgery increases, it is likely a patient will take fewer drugs and in smaller doses.

You Should Know

The key to maintaining a successful heart transplant is following medication instructions correctly for the rest of your child's life. Skipping medications will lead to rejection of the heart or decreased life of the heart.

There are four types of anti-rejection medicines that are commonly used. Each type works differently in the body to prevent rejection, but all affect T-cell (lymphocytes) function.

Patients often take a combination of the following:

- Tacrolimus (Prograf)
- Mycophenolate Mofetil (CellCept)
- Prednisone
- Sirolimus
- Everolimus

You Should Know

Do not take morning dose on day of labs, but **DO** bring dose to clinic to take after labs are drawn.

Tacrolimus (Prograf®, various generics)

Tacrolimus (Prograf®) is taken twice a day, 12 hours apart. Tacrolimus XR (Envarsus XR®) is taken once a day, 24 hours apart. Some infants and children may require three doses per day of the medicine because of their higher rate of metabolism. As the time from transplant increases, they can eventually move to twice a day dosing. It may be taken with or without food, but try to be consistent in how taken with regard to meals. When taking tacrolimus, your child should not eat or drink grapefruit (juice) since it increases the amount of the medicine absorbed into the blood stream. There are several tropical fruits that should not be consumed including star fruit, pomegranate, pomelo, and papaya. Juices and fruits that are OK to use include grape, orange, apple, cranberry, tangerine and pineapple.

It is important to maintain therapeutic blood levels as this is the only way to tell if your child is on enough medicine. Blood concentrations are measured at their lowest level, which is referred to as a “trough level.” For example, if the Tacrolimus is taken at 8 p.m. on Monday night, you need to have your child in the lab on Tuesday at 8 a.m. to have the blood drawn. Once the blood has been drawn, you should give your child his/her morning dose of Tacrolimus. Measuring trough levels reflects whether adequate blood levels are being maintained. Based on this trough level, the transplant team will adjust the medicine.

If cost is an issue and you or your insurance state that your child must change to a **generic** brand, the following actions need to be taken:

- Notify the transplant office before the change
- Obtain drug levels within two weeks of beginning the new drug
- Do not interchange different generic brands

Dose Strengths:

- Compounded liquid 0.5 mg/ml
- 0.5 mg capsule (yellow in color)
- 1 mg capsule (white in color)
- 5 mg capsule (pink or salmon color)

Frequency:

- Tacrolimus (Prograf®) is taken twice a day, 12 hours apart. Tacrolimus XR (Envarsus XR®) is taken once a day, 24 hours apart. Some infants and children may require three doses of the medicine per day because of their higher rate of metabolism. As the time from transplant increases, they can eventually move to twice a day dosing.
- **The medicine must be given on time**

Individual Dosing:

- Dose varies based on drug levels.
- Higher doses are usually required shortly after transplant or after an episode of rejection.

Effects You May Notice:

- Tremor, tingling, shaking hands
- Headache
- Nausea, vomiting, diarrhea
- Hair loss
- Infection
- Trouble sleeping

Effects We Will Monitor In Clinic:

- Kidney function
- High blood pressure
- High blood glucose/diabetes
- High potassium, low magnesium levels
- Post-transplant lymphoproliferative disorders (PTLD)

The side effects of tacrolimus are usually dose-related. They generally get better or disappear as the dose is lowered over time. When your child comes to the clinic or has local lab studies drawn, we will continue to monitor the level of tacrolimus in the blood and make adjustments in the dosage based on these levels.

Mycophenolate (CellCept®, Myfortic®, MMF)

This drug works by inhibiting production of white blood cells (WBC). Many patients are weaned off mycophenolate by the end of the first year after a transplant. This drug is taken twice a day, 12 hours apart. It may be taken with or without food, but try to be consistent in how taken with regard to meals. Use of this drug during pregnancy may cause birth defects or death of the unborn baby. If you are able to become pregnant, you must use birth control that you can trust to prevent pregnancy while taking this drug. Caregivers of childbearing potential should wear gloves during handling and administration of this medicine.

Mycophenolate Mofetil (CellCept)

Dose Strengths:

- Liquid 200 mg/ml
- 250 mg capsule
- 500 mg tablet
- If your child takes the capsules, he/she must take them whole
- **Do not cut, crush or chew them**

Frequency:

- Taken twice a day, 12 hours apart
- **The medicine must be given on time**

Individual Dosing:

- Dosing is according to weight and WBC/platelet counts.
- Dose may be adjusted for infections or low WBC/platelet counts.

Effects You May Notice:

- Nausea, vomiting, diarrhea
- Bloating, cramping, abdominal pain
- Heartburn
- Infection

Effects We Will Monitor In Clinic:

- Low white blood cell and platelets
- Post-transplant lymphoproliferative disorders (PTLD)

Prednisone, Prednisolone

Prednisone is a generic name for a corticosteroid used as an anti-inflammatory drug. We use this medicine to help prevent rejection from occurring in the first few months after transplant. Prednisone is usually weaned off within the first year after transplant and is typically done via a taper individualized for your child. It is used again with episodes of rejection. It is usually given once a day and **must be taken with food** to prevent stomach upset or ulceration. If desired can be crushed or mixed with liquid or food.

Dose Strengths:

- Liquid: 5 mg/5 ml or 15 mg/5 ml
- 1 mg tablet
- 2.5 mg tablet
- 5 mg tablet
- 10 mg tablet
- 20 mg tablet
- 50 mg tablet

Frequency:

- Usually only once a day in the outpatient setting; sometimes every other day

Individual Dosing:

- Dosing will be higher immediately post-transplant. The transplant team will then start to taper the dose. **Decreasing the dose should only be done under the care of the transplant team.**

Effects You May Notice:

- Mood swings
- Trouble sleeping
- Swelling of face (moon shape), hands and feet
- Increased appetite and weight gain
- Thin arms and legs
- Muscle weakness
- Sweating
- Poor wound healing
- Increased susceptibility to infections

Effects We Will Monitor In Clinic:

- Diabetes, increased blood sugar
- High blood pressure
- Sodium, water retention and edema
- Increased cholesterol
- Bone loss, brittle bones
- Vision changes, cataracts

These side effects may be more noticeable during the tapering process.

Sirolimus (Rapamune®)

Sirolimus is classified as an mTOR inhibitor. We use this type of medicine because it helps us protect against transplant coronary artery vasculopathy (CAV). It is not started early in post-transplant as it can affect wound healing. It is usually started at approximately one year post-transplant to replace mycophenolate. Sirolimus is given once a day and should be administered at the same time every day. It may be taken without regard to meals.

It is important to maintain therapeutic blood levels as this is the only way to tell if your child is on enough medicine. Blood concentrations are measured at their lowest level, which is referred to as a “trough level.” For example, if the Sirolimus is taken at 8 p.m. on Monday night, you need to have your child in the lab on Tuesday at 8 p.m. to have the blood drawn. Once the blood has been drawn, you should give your child his/her dose of Sirolimus. Measuring trough levels reflects whether adequate blood levels are being maintained. Based on this trough level, the transplant team will adjust the medicine.

Dose Strengths:

- 1 mg/ml solution
- 0.5 mg tablet
- 1 mg tablet
- 2 mg tablet

Frequency:

- Taken once a day at the same time every day

Individual Dosing:

- Dosing is initially based on body surface area and further adjustment is based on drug levels.

Effects You May Notice:

- Mouth sores
- Dizziness (especially when changing positions)
- Lethargy
- Light-headedness

Effects We Will Monitor In Clinic:

- Low red blood cell count
- Low platelet count
- Low white blood cell count
- High cholesterol and triglyceride levels
- Infection
- Renal function



Everolimus (Zortress®, Afnitor®)

Everolimus is very similar to sirolimus and is also classified as an mTOR inhibitor. The transplant team may switch your child from mycophenolate to everolimus after one year post-transplant. Everolimus is given twice a day and should be administered at the same time every day 12 hours apart. It may be taken without regard to meals.

It is important to maintain therapeutic blood levels as this is the only way to tell if your child is on enough medicine. Blood concentrations are measured at their lowest level, which is referred to as a “trough level.” For example, if the Everolimus is taken at 8 p.m. on Monday night, you need to have your child in the lab on Tuesday at 8 a.m. to have the blood drawn. Once the blood has been drawn, you should give your child his/her morning dose of Everolimus. Measuring trough levels reflects whether adequate blood levels are being maintained. Based on this trough level, the transplant team will adjust the medicine.

Dose Strengths (Zortress®):

- 0.25 mg tablet
- 0.5 mg tablet
- 0.75 mg tablet
- 1 mg tablet

Dose Strengths (Afnitor®):

- 2.5 mg tablet
- 5 mg tablet
- 7.5 mg tablet
- 10 mg tablet

Frequency:

- Taken twice a day at the same time every day, 12 hours apart

Individual Dosing:

- Dose is initially based on body surface area and further adjustment is based on drug levels.

Effects You May Notice:

- Mouth sores
- Dizziness (especially when changing positions)
- Lethargy
- Light-headedness

Effects We Will Monitor In Clinic:

- Low platelet count
- Low white blood cell count
- High cholesterol and triglyceride levels
- Infection
- Renal function

ANTI-INFECTION MEDICATIONS

Valganciclovir (Valcyte®)

This is an antiviral medication used to prevent cytomegalovirus infection (CMV). Before the transplant, the blood is checked to see if there has been any exposure to CMV. Most people have been exposed at some time in their lives but never know it because the symptoms are usually no different than common cold symptoms. We also check the CMV status of the donor. Patients are on valganciclovir if they are considered “high risk.”

Dose Strengths:

- 50 mg/ml liquid
- 450 mg tablet

Frequency:

- Used once per day
- Take with food

Individual Dosing:

- Given for a total of 30 to 90 days after transplant. Your transplant team will decide how long to continue valganciclovir.

Effects You May Notice:

- Irregular heartbeat
- Swelling of hands and feet
- Nausea, vomiting
- Diarrhea
- Headache
- Trouble sleeping

Effects We Will Monitor In Clinic:

- Kidney dysfunction
- High blood pressure
- Decreased white blood cell counts

Sulfamethoxazole-trimethoprim (Bactrim®, Septra®, SMX-TMP®)

This is an antibiotic used to prevent certain bacterial infections, such as urinary tract and respiratory infections (specifically pneumocystis jirovecii pneumonia [pjp]). It should be taken with lots of fluids. Avoid heavy or prolonged exposure to sunlight.

Dose Strengths:

- 200/40 mg per 5 ml
- 400/80 mg tablet
- 800/160 mg tablet

Frequency:

- Two days per week

Individual Dosing:

- Weight based

Effects You May Notice:

- Nausea, vomiting, diarrhea
- Rash, itching
- Increased sun sensitivity

Effects We Will Monitor In Clinic:

- Liver function/enzymes
- Kidney function
- Low blood cell counts

OTHER MEDICATIONS

The following medications are not immunosuppressants but have an important role in long-term therapy. They are used to treat symptoms a recipient may experience after transplant. These drugs are prescribed as needed.

Antihypertensives

These medications control blood pressure. Most recipients develop elevated blood pressure levels even if levels were normal before surgery. There are many different drugs for controlling blood pressure. The doctor will determine the antihypertensive most suitable. Common antihypertensives used are Captopril, Enalapril, Amlodipine, and Lisinopril.

Electrolyte Replacement

Many patients require supplementation with various electrolytes in order to maintain normal levels as a result of side effects of some of the medications used in heart transplant patients. Patients who are maintained on diuretics such as furosemide may require potassium supplementation. Tacrolimus, an immunosuppressant, can cause the body to waste magnesium. As a result, many patients are also on magnesium supplements to keep their magnesium at a normal level. Other electrolyte may also be added to your child's medication regimen as needed.

Diuretics

The medicines that help prevent rejection of the new heart may cause fluid retention (swelling, edema). Diuretics help the body to get rid of extra fluid or “water weight.” The common diuretics used include furosemide (Lasix), chlorothiazide (Diuril) and spironolactone (Aldactone). Most recipients go home on one or two diuretics. Side effects include dehydration, decreased potassium and decreased blood pressure. These medications will increase urine output. It would be helpful to administer these medicines first thing in the morning and/or several hours before bedtime to prevent the recipient from having to get up and urinate throughout the night.

Antibiotics

Occasionally the recipient will develop a cold, an ear infection or sinus problems that require an antibiotic. Always check with the heart transplant team before giving any medication not prescribed by the team. The most important point to remember about allowing the recipient to take any other medication, including non-prescription drugs, is that some medications interact with immunosuppressants and could cause severe illness or complications.

DO NOT TAKE AN ANTIBIOTIC OR ANY OTHER MEDICATION BEFORE YOU CHECK WITH THE HEART TRANSPLANT TEAM!

Over-the-Counter (OTC) Medications

There are many medications that do not require a prescription and can be purchased over the counter at your local pharmacy. These drugs can be used to relieve minor pain, cough and cold symptoms, and diarrhea. These medications are generally safe, but can cause problems in a heart transplant recipient such as interfering with immunosuppressant trough levels.

Common Symptoms and Recommended Over-the-Counter Medications

CHECK WITH THE TRANSPLANT TEAM PRIOR TO TAKING ANY OTHER MEDICATIONS THAT ARE NOT LISTED BELOW.

Allergy and Cold Medications: Do not take any cold medications without the approval of the transplant team.

Headache, Aches, and Pain: Tylenol (acetaminophen) is okay to take. Do not take any medications that contain ibuprofen, naproxen, or ketoprofen because they can interact with heart transplant medications. Examples that include ibuprofen, naproxen, or ketoprofen include Advil, Motrin, Naprosyn, Aleve or Orudis.

Diarrhea: Imodium and Kaopectate are acceptable medications. Increase fluid intake to prevent dehydration until diarrhea goes away. **NOTIFY THE TRANSPLANT TEAM IF THE DIARRHEA LASTS MORE THAN TWO (2) DAYS.**

IT IS IMPORTANT TO READ THE INGREDIENTS ON THE LABEL FOR ALL OVER-THE-COUNTER MEDICATIONS!

You Should Know

Do not take anything that contains ibuprofen or naproxen including Advil, Motrin, Naprosyn and Aleve.

Nutritional Supplements

It is generally recommended that your child receive a multivitamin supplement after transplant. That is particularly important if your child's nutritional status was poor before transplant, had a difficult recovery with complications following surgery, or if he/she has poor eating habits. If your child requires something more than a multivitamin, the dietitian will recommend this to you. In Michigan, it is also common to require a Vitamin D supplement because of our long winter.

Diet Pills and Herbal Products

It is strongly recommended that transplant recipients avoid taking any type of diet pill or herbal products, remedies or teas. Before giving your child any of these products, it should be approved by the transplant team. Many of these products interfere with the transplant medicine and could lead to problems with the liver. All transplant patients should avoid St. John's Wort because of its serious health risk.

