

Medications

Liver transplant patients will need to take some combination of medications for life after their transplant. The types and amounts of medications may change over time, but all patients will need an ongoing medication regimen. This section will provide an overview of medications and what transplant patients may expect. You will have an individualized medication plan. If you have any questions about your medications, please discuss them with your transplant team.

The medicines can be put into three different classes:

- **Anti-rejection** – Anti-rejection medications are also called immunosuppressive medications. These drugs weaken your immune system, but they do not eliminate the immune system. Immediately following transplant, you will take three anti-rejection medications in high dosages. Over time, different combinations of medications and smaller dosages are used to develop a balance between reducing your immune system to avoid rejection and minimizing side effects. **While you will always be on at least one immunosuppressive medication for the life of the liver transplant**, the target levels and dosages may be changed over time.
- **Anti-infective** – You will be at a high risk of infection because of decreased immune system from anti-rejection medications. Anti-infective medications help protect you against certain bacterial, fungal, and viral infections, but not all infections. **Anti-infective medications are usually only taken for the first one to six months after transplant.**
- **Miscellaneous** – The medications that help treat the side effects of anti-rejection medications or used to treat other medical conditions. **Your transplant team will tell you which pre-transplant medications can be safely started after transplant.**



What You Need to Know About Your Medications

- The success of the transplanted organ is dependent on the proper use of anti-rejection medications. You **MUST** learn and know all of your medicines. While you are in the hospital for your transplant, your transplant team will teach you and your caregiver about your transplant medications.

- Before discharge from the hospital, you and your caregiver will be expected to pass a quiz on the medications. You will not be discharged from the hospital until you can show that you know the following about medications:
 - Name of each medication
 - When to take each medication
 - How to take each medication
 - Why each medication is needed
 - What are the major side effects of each medication
 - What foods or drugs to avoid while taking each medication
 - What actions to take if a dose is missed
 - How and when to refill medications
- Setting up your medications in a pillbox will help you learn your medications.
- You **MUST** carry a current list of your medications with you at all times. Please bring this list with you to **ALL** clinic appointments and anytime you are admitted to the hospital.
- **Never stop taking any medications, change the way you take them, or change the dosage without the approval or at the direction of the transplant team. Always call the transplant team to get approval to take a medication given to you by another doctor or that is over-the-counter.**

When to Call the Transplant Office About Your Medications

- Call your outpatient transplant nurse one to two weeks in advance when you need a refill. Do not wait until your prescription runs out. Sometimes, you can time your refills with a return office visit. When you have an appointment, make a note of the medications that you need to be renewed.
- If you cannot take your medications by mouth for any reason
- If you have an illness, especially if you have a fever, vomiting, nausea or diarrhea
- When you think the directions on the label are different from what you were taught
- If you are not sure what dose to take. Doses change frequently and may not be the same as the directions printed on the bottle.
- If a doctor (other than your transplant doctor) prescribes or changes any medications
- When you think you need to take pain relievers, cold medicines or any other over-the-counter medications, call to get approval for any new medication you are thinking of taking. Do not take aspirin or non-steroidal anti-inflammatory drugs (ibuprofen, Advil[®], Motrin[®], naproxen, Naprosyn[®], Aleve[®], etc.) unless directed to do so by the transplant team.

- If you think you are having a reaction to your medication
- If your health or eating habits change
- If you have any unusual symptoms, since they might be a side effect
- If the medication that you get from the pharmacy looks different than the medication you had before
- If at any time you cannot afford your medications, please call the transplant team and a social worker will contact you.
- If you have any doubts, questions or concerns

Medications Used to Prevent Rejection (Anti-rejection Medications)

Immediately after transplant, you will start taking a combination of anti-rejection medications. **Tacrolimus, mycophenolate and prednisone are most commonly used** and each medication works differently in the body to prevent rejection of the liver.

Tacrolimus (Prograf[®], generic available; Envarsus XR[®])

Available Formulations:

- Tacrolimus Immediate Release (Prograf[®], generic available)
Frequency: Twice a day, 12 hours apart. Take consistently in relation to meals.
Strengths: 0.5 mg capsule, 1 mg capsule, 5 mg capsule
- Tacrolimus Extended Release (Envarsus XR[®])
Frequency: Once a day. Take consistently in relation to meals.
Strengths: 0.75 mg tablet, 1 mg tablet, 4 mg tablet

Note: These formulations are not interchangeable.

Individual Dosing:

- Tacrolimus dose is adjusted frequently during the first several months by taking the following into consideration:
 - Actual trough level (see page 4 of this section for more information)
 - Presence of any side effects
 - How recently the transplant was done
 - Whether the patient is on any other anti-rejection medications
 - Any previous episodes of rejection
 - Presence of active infections

Blood Levels

- It is important to maintain therapeutic blood levels of tacrolimus. (Your transplant doctor will determine what tacrolimus level to target.)
- Tacrolimus blood levels are measured at their lowest level before your morning dose, which is referred to as a “trough level.”
 - For example, if tacrolimus IR (Prograf®) is taken at 9 p.m. on Monday night, you need to go to your lab on Tuesday at 9 a.m. to have your blood drawn before taking your morning dose of tacrolimus.
 - For example, if tacrolimus XR (Envarsus XR®) is taken at 9 a.m. on Monday, you need to go to your lab on Tuesday at 9 a.m. to have your blood drawn before taking your morning dose of tacrolimus.

Possible Side Effects:

- Kidney toxicity
- High blood pressure
- Neurotoxicity (tremor, headache, tingling)
- Diabetes (high blood sugar)
- Diarrhea and nausea
- Hair loss
- High potassium
- Low magnesium



Important Notes about Tacrolimus:

- On blood drawing days, do not take your morning dose of tacrolimus until after blood is drawn.
- Other medications can raise or lower tacrolimus levels. Do not take any prescription medications, over-the-counter medications, or herbal/dietary supplements without the transplant team’s approval.
- **Avoid grapefruit, grapefruit juice and pomelo** as they increase tacrolimus levels. For other fruits, very limited information is available. Some studies suggest that papaya, pomegranate and star fruit may also cause fluctuations in tacrolimus levels.

Important Notes about Tacrolimus IR (Prograf®):

- If you miss a dose of tacrolimus and it is within four hours of your normally scheduled dose, go ahead and take the dose. If more than four hours have passed since the scheduled dose, call the transplant team. Do not double the dose.

Important Notes About Tacrolimus XR (Envarsus XR®)

- Do not confuse tacrolimus IR (Prograf®) capsules with tacrolimus XR (Envarsus XR®) tablets.
- If you miss a dose of Envarsus XR® and it is within fifteen hours of your normally scheduled dose, go ahead and take the dose. If more than fifteen hours have passed since the scheduled dose, call the transplant team. Do not double the dose.

Mycophenolate (CellCept®, generic available; Myfortic®)

Frequency:

- Twice a day, 12 hours apart. Take consistently in relation to meals.

Strengths:

- 250 mg capsule and 500 mg tablet for CellCept® (mycophenolate mofetil)
- 180 mg tablet and 360 mg tablet for Myfortic® (mycophenolate sodium)

Individual Dosing:

- Initial dose is usually 1,000 mg twice a day for CellCept® (mycophenolate, mofetil) or 720 mg twice a day for Myfortic® (mycophenolate sodium).
- Lowering the dose should be done under the care of a transplant doctor.

Possible Side Effects:

- Diarrhea, abdominal cramping, nausea, vomiting
- Low white blood cell, red blood cell and platelet counts
- Pregnancy warning (see pregnancy after transplant for more information)

Prednisone (a steroid anti-inflammatory drug)

Frequency:

- Once a day in the morning; sometimes every other day. Take with food.

Strength:

- Various tablet sizes are available between 1 mg and 50 mg. You will be discharged with either 5 mg or 10 mg tablets.

Individual Dosing:

- Instructions for dose tapering are given by your transplant team and must be followed carefully. Prednisone taper should only be done under the care of a transplant doctor. Do not stop abruptly.

Possible Side Effects:

- Swelling of face (“moon face”), hands or feet
- Increased appetite and weight gain
- Stomach irritation that may cause nausea, ulcers and /or heartburn
- Acne
- Mood swings (anger, crying, guilt, irritability, short temper, etc.)
- Sodium and water retention
- Muscle weakness, bone loss and bone pain
- Diabetes mellitus (high blood sugar)
- High blood pressure
- High cholesterol
- Visual changes, cataracts
- Poor wound healing
- Insomnia

Common Side Effects of Anti-Rejection Medications

Tacrolimus	Mycophenolate	Prednisone
Kidney toxicity High blood pressure High blood sugar Tremor, headache Diarrhea	Diarrhea Upset stomach Decreased blood counts	Weight gain High blood sugar High blood pressure Increased cholesterol levels Mood changes Insomnia Bone loss (osteoporosis) Poor wound healing

Alternative Anti-rejection Medications

Over time your transplant team will work with you to find the right balance of medications and dosages to prevent rejection and minimize side effects. Sometimes, changing tacrolimus or mycophenolate to the following medications may be necessary.

Cyclosporine (Neoral[®], generic available; Gengraf[®])

Frequency:

- Twice a day, 12 hours apart. Take consistently in relation to meals.

Strength:

- 25 mg capsule
- 50 mg capsule
- 100 mg capsule

Individual Dosing:

- Cyclosporine dose is adjusted frequently during the first several months by taking the following into consideration:
 - Actual 12-hour trough level (see below for more information)
 - Presence of any side effects
 - How recently the transplant was done
 - Whether the patient is on any other anti-rejection medications
 - Any previous episodes of rejection
 - Presence of active infections

It is important to maintain therapeutic blood levels of cyclosporine. Your transplant doctor will determine what cyclosporine level to target. Cyclosporine blood levels are measured at their lowest level before your morning dose, which is referred to as a “trough level.” For example, if cyclosporine is taken at 9 a.m. on Monday night, you will need to go to your lab on Tuesday at 9 a.m. to have your blood drawn before taking your morning dose of cyclosporine.

Possible Side Effects:

- Kidney toxicity
- High blood pressure
- Neurotoxicity (tremor, headache, tingling)
- High cholesterol
- Overgrowth of gums in mouth
- Increased hair growth
- High uric acid or gout
- High potassium
- Low magnesium

Important Notes About Cyclosporine:

- Can be used in place of tacrolimus
- Do not remove Neoral[®] capsules from the foil pack until you are ready to take them.
- On blood drawing days, do not take your morning dose of cyclosporine until after blood is drawn.
- Other medications can raise or lower cyclosporine levels. Do not take any prescription medications, over-the-counter medications, or herbal/dietary supplements without the transplant team's approval.
- **Avoid grapefruit, grapefruit juice and pomelo** as they increase cyclosporine levels. For other fruits, very limited information is available. Some studies suggest that the following fruits may also cause fluctuations in drug levels: papaya, pomegranate and star fruit.
- If you miss a dose of cyclosporine and it is within four hours of your normally scheduled dose, go ahead and take the dose. If more than four hours have passed since the scheduled dose, call the transplant team. Do not double the dose.

Everolimus (Zortress®)

Frequency:

- Twice a day, 12 hours apart

Strengths:

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

Individual Dosing:

- Dose adjustment is made based on everolimus blood levels.

Possible Side Effects:

- High cholesterol and triglyceride levels
- Low white blood cell, red blood cell and platelet counts
- Delayed wound healing
- Mouth ulcer
- Protein in urine

Important Notes About Everolimus

- Can be used in place of tacrolimus or mycophenolate
- Do not remove everolimus tablets from the blister pack until you are ready to take them.
- On blood drawing days, do not take your morning dose of everolimus until after blood is drawn.
- Other medications can raise or lower everolimus levels. Do not take any prescription medications, over-the-counter medications, or herbal/dietary supplements without transplant team's approval.
- **Avoid grapefruit, grapefruit juice and pomelo** as they increase everolimus levels. For other fruits, very limited information is available. Some studies suggest that the following fruits may also cause fluctuations in drug levels: papaya, pomegranate and star fruit.

Sirolimus (Rapamune®)

Frequency:

- Once a day in the morning

Strengths:

- 0.5 mg tablet
- 1 mg tablet
- 2 mg tablet

Individual dosing, possible side effects and important notes are the same as everolimus.

Generic Medications

Several anti-rejection medications are available in generic products. A generic medication is identical to a brand name medication in dosage form, strength, route of administration, intended use and blood levels in healthy individuals. They may look different in color, size and shape, so you need to check your medication bottle to ensure correct name and strength of the medication. Generic medications are approved by the U.S. Food and Drug Administration (FDA) and considered to have similar performance characteristics to that of brand name medications; however, their effectiveness and safety have not been studied extensively in transplant patients. Generic medications are often available at a much lower cost than brand name medications.

The decision to change from a brand name medication to a generic medication should always be made by a transplant doctor on a patient by patient basis. In order to provide consistent and safe blood levels, it will be necessary that you stay on a product from the same manufacturer, either brand or generic medication. If your pharmacy fills your prescriptions with a medication that looks different than before, please call your transplant team right away so we can closely monitor your blood levels as a safety measure.

Medications Use to Prevent Infection (Anti-infective Medications)

Since you take anti-rejection medications that lower the resistance to infection, several medications are given to help prevent infections. These infections can come from bacteria, fungus or viruses that are normally found in the environment or the body.

Sulfamethoxazole/Trimethoprim (Bactrim[®], Septra[®], Cotrimoxazole[®] or generic)

Purpose:

- Prevents Pneumocystis infection (a type of pneumonia)

Dose:

- Single strength (80 mg trimethoprim), one tablet once a day for one month

Possible Side Effects:

- Do not take if you are allergic to sulfa. You will be given an alternative medication.
- Increased sensitivity to sun. Limit sun exposure.
- May cause rash.

Nystatin (Mycostatin[®] or generic) or Fluconazole (Diflucan[®])

Purpose:

- Prevents fungal infection

Dose:

- Nystatin swish and swallow (500,000 units/5 ml) four times a day for one month or Fluconazole 100 mg once a day for one month or as dictated

Do not eat, drink or brush teeth for 15 minutes after taking nystatin.

Valganciclovir (Valcyte[®]) or Acyclovir (Zovirax[®])

Purpose:

- Prevents viral infection caused by cytomegalovirus and/or herpes virus. Cytomegalovirus (CMV) is a common herpes virus most people have had as a child. Patients have often been exposed to CMV and have developed antibodies to it. Before transplant, patients have a blood test to identify the presence of the antibody. The result of this test and a similar test given to the organ donor determine which anti-viral medications are used.

Dose:

- Valganciclovir 450 mg to 900 mg once a day for three to six months, or Acyclovir 400 mg twice a day for one month (depending on the CMV status of the donor and the recipient).
- Doses may be adjusted based on your kidney function

Possible Side Effects:

- Nausea or vomiting
- Diarrhea
- Low white blood cell counts

Entecavir (Baraclude®)

Purpose:

- Prevents hepatitis B infection if you receive an organ from a donor who was exposed to hepatitis B

Dose:

- 0.5 mg once a day; dose may be adjusted depending on your kidney function.

Possible Side Effects:

- Nausea
- Dizziness
- Headache
- Fatigue



Mavyret (Glecaprevir/Pibrentsavir)

Purpose:

- Prevents hepatitis C infection if you receive an organ from a donor who was exposed to hepatitis C.

Strength:

- Glecaprevir 100 mg/Pibrentsavir 40 mg tablet

Dose:

- 3 tablets once a day with a meal for 12 weeks

Possible Side Effects

- Headache
- Fatigue
- Nausea

Miscellaneous Medications

Most pre-existing medical conditions will continue after transplantation. Medications for pre-existing conditions, such as diabetes or high blood pressure, will be prescribed at the time of discharge. The medications prescribed may be different than those taken previously. You will be instructed to return to your primary care physician who will evaluate your response to the new medications and to have them continued or changed. All patients are asked to return to their primary care physician as soon as possible following discharge for medical care for all conditions other than transplant-related issues.

Frequently, patients find they are taking medications that are new to them. Anti-rejection medications and the surgery itself can cause a patient to have high blood pressure, high blood sugars and stomach problems. These conditions can be temporary or permanent. The following are examples of medications that may become necessary:

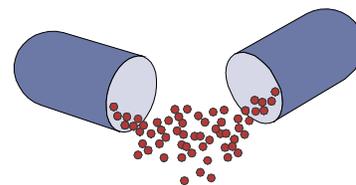
- **Gastric Acid-reducing Medications:** These medications protect the digestive system and will be prescribed as long as you need them. Once some of the medications (prednisone or mycophenolate) are tapered, you may not need gastric acid-reducing ulcer medications and will be asked to stop using them. Examples of these medications include Pepcid® (famotidine), Protonix® (pantoprazole), Prilosec® (omeprazole), Prevacid® (lansoprazole) and Nexium® (esomeprazole).
- **Bowel Regimen:** Colace® (docusate), Senokot® (senna), Miralax® (polyethylene glycol), Dulcolax® (bisacodyl) suppository and other medications may be given to help prevent and relieve constipation. Eating a diet high in fiber (bran, fresh fruits and vegetables), drinking more water and physical activity like walking will help prevent constipation.
- **Anti-Hypertensive:** High blood pressure may be a result of the surgery and the anti-rejection medications. The high blood pressure may be a short-term or a long-term problem. Long-term high blood pressure will be managed through your primary care physician.
- **Diuretics:** You may need to go home on a water pill, such as Lasix® (furosemide). This drug will be decreased and stopped as swelling decreases. It can take several weeks to several months for the swelling to resolve. If you have other causes for swelling, such as kidney or heart problems, your primary care physician or specialist who cares for that problem will need to monitor the condition and order the medications for it.
- **Insulin:** Tacrolimus and prednisone can cause blood sugar to increase. Elevated blood sugars will be managed using insulin or oral medications.

As prednisone and tacrolimus are decreased, blood sugars may come down. Therefore, it is important for you to closely monitor your blood glucose levels. Monitoring blood sugar levels at home requires a machine (glucometer) which is prescribed at the time of discharge. You will be instructed on the proper use of the glucometer and how to record your sugar levels. Elevated blood sugars may be a short-term or a long-term problem. Long-term management of high blood sugar will be managed through your primary care physician.

- **Surgical Pain:** Surgical pain may last up to a month, depending on the presence of certain complications. The transplant team will prescribe oral pain medications at discharge; these medications will only be refilled at follow-up clinic appointments.
- **Chronic Pain:** Chronic pain issues, such as migraine headaches or chronic back pain, need to be addressed by your primary care physician. The transplant team will not prescribe pain medications used for chronic pain conditions.
- **Actigall® (ursodiol):** This medication is used after transplant to help increase bile flow. It may be stopped if liver numbers improve. It is routinely given twice a day with meals. Common side effects include dizziness, nausea and diarrhea.

Over-the-counter (OTC) Medications

There are many medications that do not require a prescription and can be purchased over the counter. These drugs are used to treat minor ailments and are generally safe to use. However, there are some OTC medications that may cause problems in a post-transplant patient.



Acetaminophen

Acetaminophen (Tylenol®) can be taken safely after liver transplant if the daily dose does not exceed 2 grams (2,000 mg) in a 24-hour period. You may take acetaminophen without contacting the transplant team for minor aches and pains and fever. Acetaminophen is often found in combination with other medications, for example, prescription pain relievers like hydrocodone or oxycodone or over-the-counter cold medications. **It is important to read the labels on medications to know the content and dosage of acetaminophen before taking the medication.**

Non-steroidal anti-inflammatory drugs (NSAIDs): Do not take NSAIDs after transplant. NSAIDs can interact with anti-rejection medications and cause kidney failure. Examples of NSAIDs include ibuprofen (Advil®, Motrin®) and naproxen (Naprosyn®, Aleve®).

Aspirin: Do NOT take aspirin-based drugs UNLESS prescribed by a doctor. Many times low-dose aspirin is prescribed to prevent heart attacks and is usually safe.

Other OTC Medications: For all other OTC medications, you **MUST** get approval from the transplant team before taking. Examples are cough and cold medications and anti-diarrhea medications.

Herbal Supplements

Do NOT use herbal or dietary supplements without consulting the transplant team first. There are many supplements available to the public – often promoted as cures for many illnesses. Herbal and dietary supplements are not regulated by the Federal Drug Administration (FDA) which means there are no standards for the ingredients used in each bottle. There can be a wide variation in the contents from one bottle to another – even with the same brand. Some supplements are harmless, but others can be a serious health risk or interact with anti-rejection medications. For example, St. John's Wort decreases tacrolimus, cyclosporine, everolimus and sirolimus levels and should be avoided.

Pregnancy After Transplant

Pregnancy after transplant is considered high risk.

- Pregnancy may increase the risk of rejection to your transplanted organ.
- There are higher rates of fetal complication such as premature delivery and low birth weight in transplant patients.
- There are increased risks for maternal complications, including preeclampsia (a medical condition that may occur during pregnancy characterized by high blood pressure and significant amounts of protein in the urine) in transplant patients.

Although successful pregnancies have occurred after transplantation, **it is important that pregnancies in transplant patients be planned and managed preferably by both transplant doctor and high-risk obstetricians.** Please discuss your plans of becoming pregnant with your transplant doctor. If you are pregnant, you should let your transplant doctor and obstetrician know as soon as possible.

Some anti-rejection medications may cause fetal harm.

- The use of mycophenolate (CellCept® or Myfortic®) during pregnancy has been associated with a higher risk of miscarriage in the first three months and birth defects. Therefore, the FDA has developed a program to educate patients of possible risks while taking a medication that contains mycophenolate:
 - Mycophenolate mofetil
 - Mycophenolate sodium
 - CellCept®
 - Myfortic®

ACCEPTABLE CONTRACEPTION METHODS — Choose One Option

Option 1

- Methods to Use Alone
- Intrauterine devices (IUDs)
 - Tubular sterilization
 - Patient's partner had a vasectomy

Option 2

Choose One Hormone Method **AND** One Barrier Method

Hormone Methods (choose 1)

Estrogen and Progesterone

- Oral contraceptive pills
- Transdermal patch
- Vaginal ring

Progesterone only

- Injection
- Implant

AND

Barrier Methods (choose 1)

- Diaphragm with spermicide
- Cervical cap with spermicide
- Contraceptive sponge
- Male condom
- Female condom

Option 3

Choose One Barrier Method from EACH column (must chose **TWO** methods)

Barrier Methods (choose 1)

- Diaphragm with spermicide
- Cervical cap with spermicide
- Contraceptive sponge

AND

Barrier Methods (choose 1)

- Male condom
- Female condom

- Commonly used birth control methods may be less effective in combinations with anti-rejection medications. **Female transplant recipients MUST use the recommended effective contraception (see table) during the entire treatment with mycophenolate and for six weeks after stopping mycophenolate** unless abstinence is the chosen method.
- A member of the transplant team will discuss the potential risks with you and acceptable birth control options while you are taking mycophenolate.
- If you discover that you are pregnant, **do NOT discontinue any anti-rejection medications without talking to your transplant doctor.** Discontinuing anti-rejection medications can result in rejection or loss of the transplanted organ.

How Medications Should Be Stored

- Keep them away from children and pets/animals.
- Store them in the original container. Keep them tightly capped.
- If you use a special container to store them, keep it tightly closed.
- Store them in a cool, dry place away from direct sunlight.
- Do not store them in an area that has a lot of moisture, such as the bathroom. Moisture can make them lose their strength.
- Do not store them in the refrigerator unless instructed by your pharmacist.
- Do not freeze liquid medications.
- Do not crush or cut tablets, capsules or caplets unless instructed to do so.
- Do not remove cyclosporine capsules (Neoral®) from the foil pack until you are ready to take them.
- Do not remove everolimus or sirolimus tablets from the blister pack until you are ready to take them.

Medication Refills

The long-term success of your transplant requires you to maintain appropriate and constant levels of your medications in your system. For this reason, it is crucial you plan ahead and do not run out of your medications. The following guidelines will help you be prepared and stay healthy.

- Call the pharmacy to request refills when you still have at least a one-week supply on hand.
- Allow more time if you use a mail order pharmacy.
- Allow more time when reordering medications near a holiday.
- Call **(800) 333-9013** and follow the prompts to request our transplant office process a refill. These requests are recovered daily. Be sure to tell us if you are out of a medication so we can prioritize your request.
- Allow three business days when contacting our transplant office for a refill. Mail order prescriptions can take longer for delivery, so plan accordingly.
- If you are using Michigan Medicine Transplant Specialty Pharmacy, call **(866) 946-7695** and follow the prompts.
- Contact Michigan Medicine Transplant Specialty Pharmacy with questions regarding billing for your transplant medications.

