DFMO Information for Patients and Caregivers

What are the different names for this medication?
The chemical name is difluoromethylornithine (or DFMO for short), and the generic drug name is eflornithine. The brand name is IWILFIN. In this chapter, we'll be using DFMO for simplicity. When we discuss the prescription process, we will call it IWILFIN.

How does DFMO target neuroblastoma cells?
DFMO blocks an enzyme called ornithine decarboxylase (ODC), which is made by the ornithine decarboxylase 1 gene. ODC is important for the growth of neuroblastoma cells. When ODC is blocked by DFMO, neuroblastoma cells have a harder time growing and dividing. DFMO may also help immune cells to become more active in attacking the neuroblastoma cells.

How does DFMO affect neuroblastoma in patients?
Neuroblastoma cells usually behave aggressively because they have very high levels of MYCN or MYC. These are known cancer genes that turn on the ODC1 gene. ODC1 tells the cancer cells to make polyamines, which are essential chemicals that help cells grow and divide. When cells have very high levels of polyamines, they can grow and divide too much. Neuroblastomas that have high levels of polyamines are more aggressive, respond less well to therapy, and relapse more often. In fact, the extent to which a tumor has turned up the polyamine making system correlates very highly with how aggressively it behaves.

Scientists did many experiments in the lab to test their theory that blocking ODC would decrease the polyamines in neuroblastoma cells and slow their growth or maybe kill them. They found that they were right: blocking ODC with DFMO reduced the amount of polyamines in neuroblastoma cells. These cells had a harder time growing and surviving. Because of these results, doctors began studying the effects of DFMO in patients with neuroblastoma, both in patients with relapsed (came back after treatment) disease and in patients with refractory (never responded well to treatment) disease. They also studied DFMO in patients who had completed their upfront high risk neuroblastoma treatment.

How long has DFMO been studied?
DFMO was first FDA-approved to treat an infectious disease called *Trypanosomiasis*, also known as African Sleeping Sickness, in 1990. It is given at very high doses for that purpose. Adult oncologists also studied high dose DFMO (>4 gm/m^2/day) in the 1980s and 1990s for a range of aggressive cancers. Not all of those cancers had high MYC or ODC levels, so many results were disappointing. DFMO has also been studied as a cancer prevention therapy at low doses (<2 gm/m^2/d) to try to prevent cancer from occurring in cancer-prone adults.

Laboratory scientists began studying DFMO as a possible neuroblastoma treatment in the early 2000s. The first clinical trial to study DFMO in patients with high-risk neuroblastoma began in 2010 using low dose DFMO, while later clinical trials have also studied high dose DFMO.

When during the treatment process can DFMO be given?
Currently, DFMO is only FDA-approved as a "maintenance therapy" for patients who have completed upfront therapy for high-risk neuroblastoma, including immunotherapy, and have responded to their upfront therapy. The aim is to prevent neuroblastoma from coming back (relapsing) or worsening (progressing). Low dose DFMO is used in this maintenance therapy. Maintenance therapy means low dose DFMO is given for a long period of time after upfront therapy to decrease the chance that the neuroblastoma will relapse or progress.

DFMO's ability to treat actively growing disease (at diagnosis, relapse, or if the tumor does not respond) is not known. The role of high dose DFMO in patients with relapsed or refractory neuroblastoma is still being studied in clinical trials.

How long does a patient take DFMO?
At this time, DFMO is approved for use for a maximum of 24 months. It is taken two times a day by mouth. Patients may need to stop taking the medicine if they have significant toxicities or their cancer relapses.

How does a patient take DFMO?
DFMO is only available in tablet form. The tablet can be swallowed whole, chewed, or crushed. If crushed, the tablet should be mixed with a small amount of liquid or soft food. DFMO can be taken by mouth or through an NG or G tube.

What are the major side effects of DFMO?
DFMO has important side effects to watch out for. Like many medicines, the side effects of low dose DFMO are typically less significant than the side effects of high dose DFMO. Sometimes, your doctor may need to pause your DFMO or reduce your dose due to side effects. If the side effects are very severe, you may have to stop DFMO entirely.

DFMO can cause *low blood counts*, including red blood cells, platelets, and white blood cells. DFMO can also cause *liver injury*. Patients on DFMO will need routine lab monitoring to make sure that their blood counts and liver function values remain in a safe range. DFMO can cause *hearing loss*. Patients on DFMO will need to have their hearing checked regularly. Hearing loss from DFMO usually improves once the medication is paused. DFMO can cause *nausea, diarrhea, and stomach upset*. Patients need to tell their doctor if they are having these side effects. Patients taking DFMO may also be more prone to *ear infections* and *pneumonia*. Patients should contact their doctor with any concerning symptoms.

Pregnant women should not take DFMO. Any patient of reproductive age, male or female, should use effective contraception while taking DFMO and for one week after their last dose. Women should not breastfeed while taking DFMO and for one week after their last dose.

How long do the treatment effects and side effects of DFMO last?
We don't know how long the effects of DFMO treatment last against neuroblastoma. DFMO remains active in the body for only a short time, which is why it is taken twice a day. Once DFMO treatment is completed, the medication is fully eliminated from the body in a matter of days.

Sometimes side effects from DFMO will require your doctor to pause your medication. Your doctor will usually recheck your labs in one week to see if you can restart your medication at the same dose or a lower dose. Hearing loss from DFMO often improves, but it may take several weeks after discontinuing the medicine.

Is there an age limitation for DFMO?
There is no age limitation for taking DFMO.

Are there any interactions between DFMO and other drugs or therapies?
There are no known interactions between DFMO and other medications.

Should a patient stop taking DFMO if they relapse?
Yes, if you relapse while taking DFMO, this means that your tumor is not benefiting from DFMO anymore. You should discuss other possible treatment options with your doctor.

Can a patient restart DFMO if they return to NED status?
We don't have any data about this. You should discuss restarting DFMO with your primary oncologist.

Is DFMO part of any standard Children's Oncology Group (COG) protocols? Will it be included in the future?
DFMO is currently being studied at high doses for patients with relapsed high-risk neuroblastoma through the COG. It will likely be part of future upfront COG protocols at low dose following maintenance therapy as approved by the FDA.

Can a parent ask for DFMO to be prescribed or given to their child?
Yes, a parent can request DFMO at the end of standard-of-care upfront therapy, which includes immunotherapy with anti-GD2 therapy. You should discuss all of the risks and benefits with your child's oncologist to make the best decision for your child.

Do you know if DFMO is covered by insurance?
All insurance plans are different. Please work with your insurance company to find out if DFMO ("IWILFIN") is covered under your plan.

Is there patient assistance to help pay for DFMO?
Yes, there is a patient assistance program through US WorldMeds, the producer of IWILFIN.

Is DFMO readily available from the manufacturer?
IWILFIN is only available through a single, central, mail-order pharmacy. This may change in the future.

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CNCF would like to thank Dr. Alison Celello, Dr. Meg Macy and Dr. Mike Hogarty for writing and reviewing this chapter.

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