

## Coping with Accutane

Your child's Accutane treatment will likely require some "coping," possibly with the actual administration of the drug in addition to its side effects. Knowing what has worked for others will give you a good start on getting your child through the treatment.

The tips and insights below are based on the experiences of parents who have participated on the ACOR Neuroblastoma listserv over several years. Also, Dr. Patrick Reynolds, a neuroblastoma specialist, has occasionally shared information about Accutane on the listserv. Dr. Reynolds was one of the principal investigators into the effectiveness of Accutane in neuroblastoma treatment, and much of his advice to the listserv is summarized below. (He reviewed this document in June 2007.)

Although we hope the information below will be helpful, it is of course crucial that you discuss the details about Accutane administration and side effects with your oncologist, because new information may be available since this writing. Moreover, like everything else in NB treatment, each child's response to Accutane is very individual and needs to be carefully monitored by your oncologist.

Please note that Accutane is a trade name, as are Amnesteem, Claravis, and Roaccutane. The generic name of the drug is isotretinoin, and it is often called by its chemical name, 13-*cis*-retinoic acid. Also, please note that this section does not deal with the medical purposes of Accutane. See section on "Accutane" in "Understanding the Basics of Frontline Treatments: Overview of Treatment for High Risk NB."

### Helping your child take Accutane

Accutane is available only in capsule form and is given in two daily dosages for two weeks on and two weeks off, generally for about six months. Administering Accutane is really easy – IF your child can swallow capsules! Some parents have started training their child to swallow pills well in advance of Accutane treatment, and have had success using tiny candies such as M&Ms. If your child does not like to swallow pills, start by making sure you are getting a prescription for the minimum number of capsules required. For example, if your child is taking 60mg twice a day, you can get a prescription for one 40 and one 20 mg capsule, as opposed to three 20 mg capsules – and your child will have two fewer pills a day to swallow. Also, determine if you have the smallest size capsule available, and if not, using a smaller capsule may be helpful.

**How to administer Accutane if your child cannot swallow pills and why it matters how you do it.** Since so many neuroblastoma patients are very young and cannot swallow pills, parents are often uncertain how to get their child to take Accutane in the best way. The main concern is that Accutane is extremely sensitive to light and oxygen, and will degrade very shortly into other chemical forms after being exposed to oxygen and light. Also, the drug must be administered in a way to ensure that the child gets the prescribed dose. (See also warning below about danger of Accutane to pregnant women.)

Some parents have put the capsules into a food the child loves, such as pudding, or inside melted chocolate, and the child has simply eaten the capsules whole. This naturally achieves the same effect as swallowing the capsules, if the child will tolerate it. Dr. Reynolds points out that, to facilitate chewing and swallowing the capsules, carefully poking a hole in the capsule as it is being embedded into the food is known to help. Some children have enjoyed "popping" the capsules they find embedded in the food, but the latter can't be done easily without the capsule first being pierced. Care should be taken to avoid loss of drug when doing this.

During early studies in children with Accutane, investigators recommended that the capsule can be pierced with a clean, large needle, and the contents of the capsule (a gel) can be squeezed out into a spoonful of food that the child likes. Other suggestions by parents are to pierce the capsule with a sharp toothpick or nail clippers. One parent found that a clean pair of pliers did the trick and squeezed out all of the liquid very quickly, with no mess and little contact with the product. One must be very careful to squeeze out the entire amount in the capsule so that the child will get the full dosage.

The original recommendation in clinical studies of Accutane for neuroblastoma was that the drug must be taken immediately after being squeezed out of the capsule, and also must be squeezed into the middle of the food and immediately covered over, so as not to be exposed to light and oxygen. Cottage cheese, ice cream, pudding or oatmeal with butter are foods recommended by investigators for the clinical trials, and they have been used successfully by many. Parents have also used yogurt, cool whip, peanut butter, applesauce, and others. In addition, protocols for the clinical trials have pointed out (and several NB experts have agreed) that oral absorption of Accutane is increased when taken with food or milk (or other liquid which contains fats).

Many parents have agonized about whether they were following the recommended procedures correctly. For example, some children have taken the Accutane when squeezed onto a spoon without other food, and washed it down with milk or another beverage. This raised the question of whether the brief exposure of the Accutane to light and oxygen meant the drug would not be effective.

On the one hand, Dr. Reynolds has warned on the listserv that there is serious risk of degrading the drug if you remove it from the capsule hours or days before use. However, Dr. Reynolds has also reiterated that the conversion of Accutane into another chemical is not an immediate event upon opening the capsule and exposing its contents to light or oxygen. He has written that there is clinical evidence that children did get sufficient amounts of the Accutane when their parents carefully squeezed out the contents and gave it to the child shortly thereafter, or if the child actually ate the capsule itself, in both cases in food or with milk. "I do not feel parents should feel it is essential for their child to swallow the capsules 'whole'," Dr. Reynolds has said. "Certainly if you can get whole capsules into the child that is the optimal way to administer the drug, but it should not be considered 'the only safe way'."

**Accutane should not be administered in a liquid form.** Although it is possible to have Accutane converted into an "extemporaneous" liquid formulation, Dr. Reynolds and other NB experts have strongly urged that this should not be attempted because the drug will likely degrade in the process and not be effective. Although it is possible an individual pharmacist may have developed a liquid formulation, there is too much of a risk that a liquid formulation will not deliver the drug effectively, or that such a liquid formulation could result in conversion of Accutane to a form that increases toxicity to the child.

Women of child-bearing age should carefully avoid contact with Accutane. It is important to be aware that Accutane has caused serious birth defects when taken by pregnant women. Any woman administering the drug who is of child-bearing age must take care not to accidentally swallow the drug (e.g., by getting some on your hands and inadvertently licking fingers, etc.). Dr. Reynolds has advised that any woman of child-bearing age who opens any of the capsules should wear gloves and carefully avoid contact with the Accutane inside of the capsules.

**Standard daily doses of most vitamins are believed safe, but supplemental vitamin A should be avoided during Accutane treatment.** Dr. Reynolds and other experts have advised against taking vitamin A during Accutane treatment, although the consensus is that a normal daily multi-vitamin should be safe. The data on this topic is based on the doses of Accutane for acne, which is very different from the dose for neuroblastoma, but nonetheless Dr. Reynolds doesn't feel comfortable with a patient taking supplemental vitamin A during Accutane treatment. There has been no evidence that other vitamins such as vitamin E could interfere with the anti-neuroblastoma effect of the Accutane. Dr. Reynolds has said,

*We did not find any evidence for vitamin E antagonizing the anti-neuroblastoma effects of Accutane. However, to truly determine this would require a clinical trial and I don't see that happening anytime soon. Our laboratory data make me very comfortable in recommending liberal topical use of vitamin E (such as vitamin E cream, especially on lips). As to other vitamins, I would think that giving standard 'recommended daily dose' supplemental vitamins (all except vitamin A) should be quite safe. There are no data to address this, but based on what we know about Accutane, there are no reasons to suspect any interactions with low doses of vitamins.*

**What is the timing of the doses?** Accutane doses are generally given 12 hours apart (e.g., 8 am and 8 pm). Some parents have asked what to do if they are traveling or otherwise unable to administer the Accutane at the optimal time. Dr. Reynolds has said that a parent should not worry about adjusting the time between doses, especially if done only occasionally, but that it would be best to avoid more than 16 or fewer than 8 hours between the doses.

**Can Accutane be given through a G-tube?** Some parents have administered Accutane through their child's G-tube. The concern here is to make certain the Accutane gets through the tube without sticking to the sides, and to use a carrier which does not prevent the Accutane's absorption by the GI track. Some parents have suggested that fatty meals or vegetable oil is a good carrier, and that mineral oil is not a good carrier. The fear was that since mineral oil is not being absorbed by the intestine and the Accutane is dissolved well in it, the mineral oil may serve as a carrier that will take the Accutane out of the body and prevent the Accutane's absorption by the GI track.

One parent "primed" the tube with half a ml of oil, then pushed the Accutane and finally flushed with 5-10 ml of slightly warmed milk (suggested by the parent's hospital pharmacist, since it helps with absorption). Another parent mixed the Accutane with about 5 cc's of flax seed oil.

There does not appear to be any "official" advice on the best way to administer Accutane through a G-tube. The above is what some parents have done, and their children got the standard side effects, suggesting the child was getting a sufficient dosage. However, you should discuss this with your oncologist.

### **Dealing with your child's side effects**

The majority of children will have some sort of side effect from taking Accutane, although adverse reactions almost always disappear when the treatment is completed.

**Skin.** The most common side effect is severely dry skin and related issues. Almost all children taking Accutane develop extremely dry skin, especially on the face, lips and hands, but also on the ears, feet, arms, legs and sometimes the trunk. The child will likely experience itching, severe chapping, peeling skin, possibly dry eczema-like patches or rashes, and sometimes even cracking and bleeding of the affected area.

These symptoms are usually mitigated if the parent slathers some sort of ointment on the child – especially at night, since many children do not like having it applied during the day. You will have to experiment and determine which ointment or cream your child prefers and which is most effective. Some that parents have recommended are Vaseline, Aquaphor, Eucerin cream, Aveeno Oatmeal lotion, Cetaphil lotion, Cabot cream, Neutrogena Norwegian Formula Hand Cream, and vitamin E (squeeze it from the gelcaps onto the affected area). Some parents have found it helpful to apply the ointment liberally at bedtime and then put socks or gloves on the child's hands. Most parents apply the ointment even when the child is not on the Accutane to keep ahead of the dryness.

Most parents also apply chapstick, Blistex cream, or vitamin E to the child's lips frequently during the day. One parent discovered that the only thing to relieve the burning sensation on her son's severely chapped lips was "Bag Balm" – the antiseptic ointment used to protect cow udders.

Many parents have observed that it helped their child's comfort level when they increased the child's fluid intake substantially. Some parents have also found it helpful to use a cool mist vaporizer at night (which should be wiped down daily with an antibacterial and antifungal wipe or solution).

**Sun Exposure.** Most children are very susceptible to sunburn during Accutane, even during winter. Dr. Reynolds has warned that sun exposure should be very limited for any patient on Accutane. It is advisable to make the child wear a good sun hat, long sleeves and pants, and to apply sunscreen liberally (although a sunscreen may actually irritate the dry skin issues in some children). These measures are advisable even in winter and regardless of geographical area. Dr. Reynolds said that there isn't enough data to be certain of how many days after completing a course of Accutane you could be more relaxed about sun exposure. His recommendation was to avoid the sun until the 2nd week of the 2 weeks off drug and even then one should still use plenty of sunscreen.

**Moodiness and other side effects.** Individual children will likely experience additional side effects, which may be severe in some cases. Other side effects have included dry eyes, pink eye, dry nasal passages, headaches (some severe), neck, back, leg or knee pain or stiffness, leg cramps, muscle jerks, nausea, vomiting, constipation, diarrhea, lethargy, nosebleeds, and sensitivity to light. Crankiness, mood swings, flying off the handle, tantrums, and other "horrid" behavior are not uncommon. (One grandmother described her granddaughter's personality on Accutane as "satantic"!)

Moodiness may be more severe for teenagers and adults. Warnings provided by the manufacturer of Accutane state that the prescribing doc should ask about family history of mental disorders and emotional stability of the patient, and that the patient's ongoing emotional status should be discussed at each check-up. It is important to note that although studies have reported rare but serious depression, suicidal behavior, and psychotic events in teens and adults, those studies refer to use of much lower dose used for acne.

**Treating side effects.** Each child's reaction to Accutane is unique to him or her, and you will have to respond accordingly. Most side effects are manageable with a little trial and error. For example, constipation can be alleviated by having the child drink more juice and by using stool softeners. Several parents have recommended that either oral or IV Zofran enabled their vomiting child keep down Accutane. One child was so sensitive to light that the parent had to keep shades pulled in the house and cover the child's eyes during car rides. Saline nose sprays and artificial teardrops have been used for dry nasal passages and eyes. One parent's dermatologist recommended Bactroban nasal during the days of Accutane, for preventing infections in the nose due to dryness. In addition to Tylenol or other pain medicines, a hot tub bath may ease leg or back pain.

However, some children on Accutane treatment have had even more serious health concerns. Some children have had such severe pain (such as headaches or leg pain) that morphine, oxycodone or other heavy painkillers were required. Some have experienced high blood pressure. One of the most serious side effects experienced by some children during Accutane is very elevated calcium levels, in some cases high enough to require hospitalization. It is therefore very important to have physical exams and blood tests while your child is on Accutane to see how his or her system is handling it. Any symptoms that concern you should be reported immediately to your child's oncologist.

High triglycerides can also be induced by retinoid use and fibrates can be used to lower triglycerides so Accutane treatment can be continued.

**Early or cumulative side effects.** The timing of Accutane side effects varies from child to child. Some children may experience a side effect that increases in severity with each dose; others experience the side effect only with the first couple of dosages or during the first few days of each dose. Most symptoms disappear during the time in between doses. The persistence of adverse reactions after Accutane treatment is completed is believed to be very rare.

The dose may need to be cut back if the adverse reaction becomes too severe. Dr. Reynolds has said that the recommended approach is to begin at the standard dose and then decrease it if necessary due to side effects. The oncologists of some children have added an additional round when the dose

was lowered. Many children have been able to return successfully to the higher dose after the adverse reaction subsided.

### **Summary**

As explained above, Accutane can be difficult to administer to some children, but most parents have been able to get their children to take Accutane successfully. Accutane is an easily degradable drug, and it is important to administer it as recommended by neuroblastoma experts. Accutane can cause a wide spectrum of side effects, with dry skin problems the most common. Although we have summarized above many tips for administering Accutane and coping with side effects, each child is different; parents will have to determine what works best for their child and monitor individual reactions. Some side effects of Accutane can be very serious, and it is important that the child be carefully monitored by parents and his or her oncologist. Keep in mind that, as with any medical treatment, it is crucial to discuss all issues with your oncologist and get the most up-to-date advice.

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