

INFORMED CONSENT DOCUMENT

Project Title: **An Open Label Trial of Aripiprazole in the Treatment of Conduct Disorder in Adolescents**

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- If you are the parent/guardian of a child under 18 years old who is being invited to be in this study, the word “you” in this document refers to your child. You will be asked to read and sign this document to give permission for your child to participate.
- If you are a teenager reading this document because you are being invited to be in this study, the word “you” in this document refers to you. You will be asked to read and sign this document to indicate your willingness to participate.

This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not sign this form unless the study research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you are a male between the ages of 13 and 17 and have been diagnosed with Conduct Disorder.

The purpose of this research study is to evaluate the safety and effectiveness of a drug called aripiprazole as a treatment for conduct disorder. Aripiprazole was recently approved by the US Food and Drug Administration (FDA) for use in adults as a treatment for psychotic disorders. However, it has not been approved for use in people under the age of 18 or as a treatment for conduct disorder. Therefore it is considered investigational.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 20 people will take part in this study at the University of Iowa

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for to 7 weeks. If you complete the study there will be a total of 6 visits. Each of the first 5 visits will last about one hour. The last visit will last about 2 hours. The second, third and fourth visits will be weekly. The fifth visit will be 2 weeks after the fourth visit. The final visit will be 2 weeks after the fifth visit.

WHAT WILL HAPPEN DURING THIS STUDY?

The first thing that will happen in this study is the study doctor will perform a physical examination and discuss your medical and psychiatric history with you. Your vital signs (blood pressure and pulse) will be recorded. Measurements of your height, weight, and the distance around your waist, hips and arms will be recorded in order to calculate your body mass index (BMI). A blood sample will be taken for routine tests and you will be required to provide a urine sample for drugs of abuse testing. You will also have an electro-cardiogram (ECG), which is a routine heart test. All of these tests are to make sure you don't have a physical problem that would prevent you from taking part in the rest of the study.

If you are eligible to continue in the study you will be invited back for a second visit. This is called the "baseline" visit. Your vital signs and BMI will again be recorded. The study doctor and one of the other investigators will interview you about your symptoms of Conduct Disorder. Medication side effect ratings will be also be done. One of your parents or guardians will also be asked to fill out 3 questionnaires about your symptoms. All of the information at the baseline visit is to determine your level of functioning before your first dose of aripiprazole. At the end of this visit aripiprazole will be dispensed to you. The study doctor will explain how and when to take the medication.

One week later you will return for the third visit. Your vital signs and BMI will again be recorded. The study doctor and one of the other investigators will interview you about your symptoms of Conduct Disorder. Medication side effect ratings will be also be done. One of your parents or guardians will again be asked to fill out 3 questionnaires about your symptoms. The aripiprazole dose may be increased at this visit, depending on whether you report any side effects from the medication.

One week later you will return for a fourth visit. Your vital signs and BMI will again be recorded. The study doctor and one of the other investigators will interview you about your symptoms of Conduct Disorder. Medication side effect ratings will be again be done. One of your parents or guardians will again be asked to fill out 3 questionnaires about your symptoms. The aripiprazole dose may again be increased at this visit, or decreased depending on whether you report any side effects from the medication.

Two weeks later you will return for a fifth visit. All of the things that were done at the fourth visit will be repeated. The aripiprazole dose may again be increased at this visit, or decreased depending on whether you report any side effects from the medication.

Two weeks later you will return for the sixth and final visit. The study doctor will repeat the physical examination that was performed at the first visit. An ECG will be repeated. Blood will be collected for routine laboratory tests. Urine will be collected for drugs of abuse testing. Your vital signs and BMI will again be recorded. The study doctor and one of the other investigators will interview you about your symptoms of conduct disorder. Medication side effect ratings will be also be done. One of your parents or guardians will again be asked to fill out 3 questionnaires about your symptoms. The study doctor will discuss with you and at least one of your parents or guardians whether you should continue to take aripiprazole. He will also discuss alternative treatments, if applicable. The schedule of events for the study is summarized in the following table:

Procedure	Screening visit	baseline	week 1	week 2	week 4	week 6
Time until next visit	<u>2-7 days</u>	7 days	7days	14 days	14 days	
Physical Exam	X					X
ECG	X					X
Vitals, Height, Weight, BMI	X	X	X	X	X	X
Urine Collection	X					X
Blood collection	X					X
Interview with study doctor	X	X	X	X	X	X
Interview with study team		X	X	X	X	X
Parent/Guardian questionnaires		X	X	X	X	X

WHAT ARE THE RISKS OF THIS STUDY?

There may be some risks from being in this study. The most common side effects seen with aripiprazole in adults were headache, feeling slowed down, fever, upset stomach, vomiting, constipation, anxiety, trouble sleeping, lightheadedness, sleepiness, restlessness, tremor, cold symptoms, coughing, rash and blurred vision.

Blood collection involves a needle stick that may cause pain, bleeding, bruising, fainting and in rare cases an infection.

The interviews and questionnaires may cause emotional discomfort. You are free not to answer questions that cause discomfort.

Are there any Unforeseen Risks?

In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study. Aripiprazole is not approved by the FDA for use in people under the age of 18 or for people with Conduct Disorder. Information about the use of aripiprazole in people under the age of 18 is limited.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study. However, we hope that, in the future, other people might benefit from this study because of knowledge gained by the investigators about the use of aripiprazole in people age 13 to 17 with Conduct Disorder.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could receive counseling; take other medications, or both.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study. You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will be paid \$50 for each completed visit. Payment will be by a check issued by the University of Iowa in the name of the minor participant (the person who actually receives the study drug), not the parent or guardian. It usually takes 1 to 2 weeks after a visit before you receive payment. If you complete all 6 visits the total payment will be \$300. You will need to provide your social security number (SSN) in order for us to pay you. You may also need to provide your address if a check will be mailed to you.

WHO IS FUNDING THIS STUDY?

Bristol-Myers Squibb Co. is funding this research study. Bristol-Myers Squibb Co. is the drug company that makes aripiprazole. This means that the University of Iowa is receiving payments from Bristol-Myers Squibb Co. to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or an increase in salary from for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- No compensation for treatment of research-related illness or injury is available from the University of Iowa unless it is proven to be the direct result of negligence by a University employee.
- If you experience a research-related illness or injury, sustained from the administration of the study drugs in accordance with the protocol, sponsor, BMS will pay for the all hospital and medical costs required for diagnosis and treatment provided that such costs are not covered by any third party or governmental programs providing such coverage.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people may become aware of your participation in this study. For example, federal government regulatory agencies, the U.S. Food and Drug Administration, Bristol-Myers, Squibb Co. auditing departments of the University of Iowa and the University of Iowa Institutional Review Board (a committee that reviews and approves research studies) may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

In the future, Bristol-Myers Squibb Co. may continue to use your health information that is collected as part of this study. For example, Bristol-Myers Squibb Co. may combine information from this study with the results of other studies to re-analyze the safety and effectiveness of the study medication, to evaluate other products or therapies, to develop a better understanding of a disease, or to improve the design of future research studies. Bristol-Myers Squibb Co. may also share information from the study with regulatory agencies in foreign countries.

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To help protect your confidentiality, we will include replacing your name on the interview forms with a 5-digit number, storing records in a locked file cabinet in a locked room in a building with access limited to members of the study team, and storing electronic records on computers that are protected with passwords. Laboratory reports, ECG reports and doctor's notes will be placed in your hospital chart. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

We are taking some special steps to protect your confidentiality. The University of Iowa Hospitals and Clinics generally requires that we put a copy of this Informed Consent Document in your medical record chart. Instead of doing that, we'll ask you to sign another form, called a Record of Consent, which gives no specific information about this study. The Record of Consent will be placed in your medical record chart. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). This Certificate means that the researchers cannot be forced (for example by court subpoena) to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding. However, a Certificate of Confidentiality does not prohibit the researcher from disclosing information about you or your involvement in this research that you have agreed to disclose or make available. For example, if you or your legally authorized representative request in writing that information about you or your participation in the research be released to an insurance company, the researcher may not use the Certificate of Confidentiality to withhold this information. This means that you and your family should actively protect your own privacy. Finally, the researcher is not prevented from taking steps, including reporting to appropriate authorities, to prevent serious harm to yourself or others. You may receive a copy of the Certificate of Confidentiality upon request.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires your health care provider to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once your health care provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff, and Bristol-Myers Squibb Co.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes your health care provider to give us permission to use or create health information about you.

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Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to Samuel Kuperman, M.D., 1873 JPP, University of Iowa, Iowa City, Iowa 52242. However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

If you decide to leave the study early, we will ask you to return for a close out visit in which we will conduct all the safety testing and interviews that are scheduled at the final visit. If you choose not to have the safety testing it won't be possible for the study team to know whether you had any bad effects from taking part in the study. You also would be expected to return all un-used study drug at the end of the study or if you choose to stop the study early.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers or the study sponsor might decide to end your participation in this research study earlier than planned. This might happen because the sponsor stops funding the study. This might also happen because the study doctor feels it would not be safe for you to continue or because you experience side effects.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Samuel Kuperman, M.D. at 319-356-1482, Anne Kolar, M.D. at 319-356-1182 or Chadi Calarge, M.D. at 319-335-8771. If you have a problem during evening or weekend hours that you feel needs immediate medical attention and neither Dr. Kuperman nor Dr. Kolar nor Dr. Calarge are available, you should go to the nearest emergency room. The University of Iowa Healthcare general number is 319-356-1616. You can ask to speak with the psychiatric resident (who is a medical doctor) on call.

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If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 340 College of Medicine Administration Building, The University of Iowa, Iowa City, Iowa, 52242, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, <http://research.uiowa.edu/hso>.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

(Signature of Subject)

(Date)

Parent/Guardian or Legally Authorized Representative's Name and Relationship to Subject:

(Name - printed)

(Relationship to Subject - printed)

(Signature of Parent/Guardian or Legally Authorized Representative)

(Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

(Signature of Person who Obtained Consent)

(Date)