Parent Booklet

EXCOR® Pediatric Ventricular Assist Device

Table of Contents

BACKGROUND

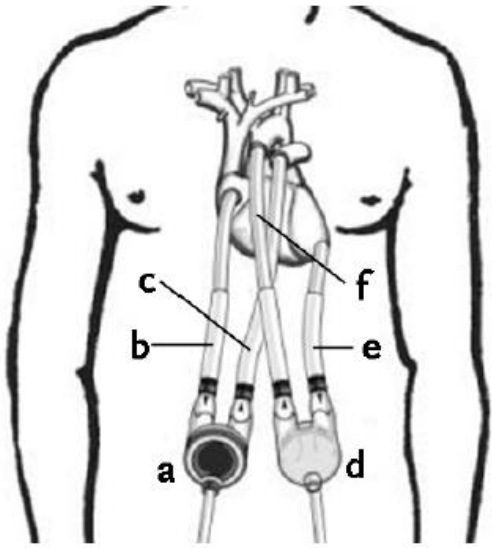
Your child's doctor has given you this booklet because the doctor has determined that your child's heart is having trouble pumping blood to the rest of his/her body. Your child's doctor will provide details specific to what caused your child's heart to have trouble pumping. This heart trouble is dangerous and your child's heart needs medical treatment to prevent damage to organs like the kidneys or to prevent your child from dying. Your child is a candidate for a heart transplant and since no organ is available right now, your child's doctor thinks a ventricular assist device might help your child's heart have the best chance for surviving until a donor heart becomes available. Your child's doctor has tried to help your child's heart pumping with the usual medical care. Unfortunately, this care has not been able to fix the pumping problems your child's heart has, something else is needed to help improve his/her heart's pumping. If your child is not able to take blood thinners or has a leaking Aortic valve, they may not be able to receive the EXCOR® system.

DEVICE DESCRIPTION

Devices are made that can possibly help a person whose heart function is not pumping enough blood to their body. One device is the Berlin Heart EXCOR® Pediatric Ventricular Assist Device (or simply "EXCOR® device"). The EXCOR® device has been approved by the Food and Drug Administration (FDA) with a Pre-Market Approval (PMA). The

FDA and a team of doctors reviewed the information from a clinical study that included 48 children that used the EXCOR® device and decided it was safe for use in children in the United States. The FDA asked that additional information on use of the device after this clinical study to be collected. More information is included in the back of this booklet about the Clinical Study reviewed by FDA and the additional information collected after the study.

The EXCOR® device has small pumps that can be used to support the left or right or both sides of your child's heart. The pump or pumps is/are connected to tubes (cannulas) that are sewn onto your child's heart. A machine outside of your child's body is used to make the pumps move the blood through your child's heart. This may help improve the blood flow to your child's body. A picture of the pumps attached to both sides of the heart is shown below.



a - Right pump *(pumps blood to the lungs)*

b - Right inflow cannula *(puts blood in the pump from the right side of the heart)*

c - Right outflow cannula *(sends blood to the lungs)*

d - Left pump *(pumps blood to the body)*

e - Left inflow cannula *(puts blood in the pump from the left side of the heart)*

f - Left outflow cannula *(sends blood to the body)*

Figure 1. EXCOR® Pump and Cannulas - Right and Left Heart Support

Blood Pump and Cannula Warnings

- Do not kink the tubes (cannula) to the heart needlessly. A kink could cause the blood to stop pumping through your child's body or cause the tubes (cannulas) to break that could lead to a leak in the tube.
- Do not pull, kink or do any activity that could put stress on the tubes to the heart. It is important to protect the cannula and blood pump. Do not allow your child to belly flop, pull or stretch the cannula, as this may damage the cannula resulting in injury or death.
- Do not use pointed or sharp-edged objects near the EXCOR® device. The blood pump or tubes (cannulas) could be damaged causing a leak that could cause your child to not get enough blood.

IKUS Driver
(makes the pumps work by pushing the air into them)

Figure 2. The EXCOR® "IKUS" driver

Figure 2 shows the IKUS driver that is used to pump the blood through the blood pumps. The IKUS driver has three different sections that can provide air to the blood pump. The air is pumped through the tubes (drivelines) that connect to the machine and the blood pump shown in Figure 3. The IKUS is a heavy machine that may be rolled around on the wheels. It has a battery that will allow a short walk and outing from the hospital room when the doctors decide it is safe to let your child go out of the room. The IKUS has a backup system that will provide air and also has a manual air pump if needed. The IKUS must be plugged in; unless your child's clinical care team is with you and has a reason to unplug it. The care team is trained on the special programming and settings required for your child.

Driveline Warnings

- Do not kink the tubes (drivelines) to the IKUS. A kink could cause the blood to stop pumping through your child's body.

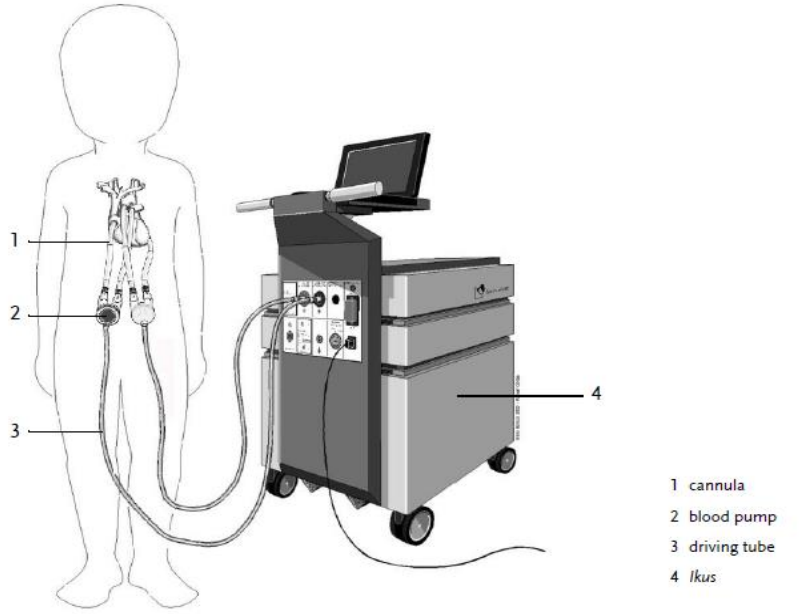


Figure 3. The whole system as it looks when on a patient that needs right and left pumps.

IKUS Driver Warnings

- Do not use water or fluids near IKUS. There is a risk of a short circuit or a malfunction of the device if it gets wet.
- Protect the IKUS from exposure to moisture and wetness. Never store or use the IKUS in a damp environment (e.g. bathroom, etc.). There is a risk of malfunction of the device in damp environments.
- Never unplug the IKUS, a hospital person trained on the EXCOR® will do that. If the IKUS has trouble or runs low on battery it could stop pumping, causing your child to not get enough pump output.
- Do not cover the air vents, they must not be covered or obstructed during operation. The IKUS could overheat if the vents are blocked and may have a malfunction in device operation that would cause your child to not get enough support from the EXCOR®.
- Place the IKUS driving unit on a firm and even surface. The IKUS is heavy and could roll away if not a firm, even surface. This could cause harm to your child or other people in the room.
- Never place other objects on top of an IKUS driving unit. The objects could fall causing damage to the IKUS that could lead to a problem with the IKUS.
- Avoid exposure to strong electromagnetic radiation (from items like a mobile/cell phones and cordless phones when switched on, electromagnetic security systems etc.). When using a cell phone in the immediate environment of an IKUS in operation

please make sure to keep a distance of at least 3 feet. The radiation from the devices could cause a problem with the IKUS.

- Protect the IKUS against extreme temperature changes and overheating (e.g. direct sunlight or from heaters). There is a risk that it could cause a problem with the IKUS that could lead to your child not having enough support from the EXCOR®.

WHAT ARE THE STEPS FOR GETTING AN EXCOR®?

If you allow your child to receive the EXCOR® device, your child's doctor will review the whole procedure with you and maybe with your child. A basic description of what will happen is listed here.

Before the Procedure:

Your child will have a physical exam and other tests before the EXCOR® device implant. Tests will include measuring your child's heart rate and blood pressure, urine output, blood tests, and possibly other tests for your child's heart. These tests will help the doctor know if your child is sick enough to receive the EXCOR® device or too sick to have the EXCOR® device. The doctors will also check if your child is able to take blood thinning medications that need to be used while on the EXCOR® device.

If the tests show that he/she can receive the EXCOR® device, the device will be implanted in the operating room like regular heart surgery.

During the Implant Procedure:

For the surgery, your child will receive medication to help him/her relax, and anesthesia medications to prevent discomfort and pain by keeping your child asleep during the operation. A breathing tube will be placed in your child's throat to help your child's lungs receive oxygen from a machine called a ventilator. This tube will remain in place until your child's doctor determines your child is able to breathe on his/her own without the help of a ventilator. During the surgery, the tubes (cannulas) that connect to the EXCOR® blood pump(s) will be secured to your child's heart and blood vessels with stitches. Once the tubes (cannulas) are sewn to the heart, they will be connected to the EXCOR® blood pump(s). The pumps will stay outside your child's body. Your child's doctor will start the pump(s) and after the pump(s) is/are started, your child's doctor will finish the surgery. After the surgery your child will be moved to the Pediatric Intensive Care Unit until he/she wakes up from the surgery.

After the Implant Procedure:

After the device is implanted, your child will be treated at the Pediatric Intensive Care Unit. He/she may be supported with a breathing machine and will have medications that will keep him/her comfortable and likely sleepy. Your child may have many wires attached to their body to monitor your child's heart, blood pressure and breathing; the hospital staff will explain each of those to you. The nurses and doctors will also be drawing blood to do lab tests to be sure your child is recovering as expected. One reason they need to draw blood is to be sure that your child has enough blood thinning medications to avoid blood clots. Your child should not have an MRI test done while on the device.

The doctors and nurses will also have to check the sites where the tubes (cannulas) for the EXCOR® pumps come through the skin. These sites will be cleaned on a regular schedule to keep your child from getting an infection.

As your child recovers, the hospital staff may start several types of therapy, light school work, art projects, etc. as they do for other children in the hospital. Your child may get well enough to go for walks around the hospital to visit areas such as the playrooms, the cafeteria, etc. Each time your child is transported, you must have a hospital employee that is trained on the EXCOR® device to help care for the device. The device should never be unplugged to go out of the hospital room without a trained hospital employee there to help. Your child will not be able to leave the hospital while on the EXCOR® device. The system is not approved for use outside of a hospital setting.

WHAT TESTING IS PERFORMED WHILE ON THE EXCOR®?

Your child will have a physical exam and tests before the EXCOR® device is implanted and will be repeated during the time your child is on the EXCOR® device, after the device has been implanted. These tests include: heart rate and blood pressure measurements, urine output, and blood tests. Your child may also have an x-ray done of their heart called an echocardiogram. This x-ray will help your child's doctor determine when it is time to adjust the EXCOR® and help them see how the device is functioning to help your child's heart.

HOW LONG WILL MY CHILD BE ON THE EXCOR®?

The situation for every child is different and that makes it difficult to predict how long your child will need the EXCOR® device. Some children are on the device for only a few weeks while others are on the device for many months. Unfortunately, there is no way to tell how long your child will need the EXCOR. The longest time a child has been on the EXCOR® device in the United States is 435 days. The average time children were on the device in the United States was 78 days.

HOW IS THE DEVICE REMOVED?

The removal of the EXCOR® device must take place in the operating room. This procedure will

require medications and other steps your child had when the pump was inserted. Your child will go back to the operating room and the pump will be stopped and removed. Typically, your child will receive a heart transplant at this time. In some cases, when the heart has regained enough strength so that a child doesn't still need a heart transplant, the pump will be removed. Prior to deciding whether to remove the pump, your child's doctors will make changes to the pump settings and your child's medications. More x-rays (echocardiogram) of the heart will be completed to ensure that the heart has regained strength and that a transplant is not needed.

WHAT ARE THE POSSIBLE RISKS?

The EXCOR® device is FDA-approved under a Pre-Market Approval (PMA). This approval was based on a clinical study that showed that the device was safe compared to the other options. There are risks associated with this type of device that are similar to those risks identified with other heart assist devices and with heart surgery. It is possible that these risks could result in serious or permanent injury or disability.

In the back of this booklet are some tables that explain the likelihood of the risks for the EXCOR® and how these risks led to problems reported in the children in the Clinical Studies reviewed by FDA.

Your child is at risk of having some of the same events, including:

- Death
- Major infection
- Major bleeding
- Hypertension
- Neurological dysfunction
- Respiratory failure
- Renal dysfunction
- Pericardial fluid collection
- Right heart failure
- Cardiac arrhythmia
- Psychiatric episode
- Hemolysis
- Hepatic dysfunction
- Arterial Non-Central Nervous System Thromboembolism
- Venous Thromboembolism
- Device Malfunction
- Wound dehiscence

The back of this booklet will help explain how these risks led to problems reported in the children in the Clinical Studies reviewed by FDA. It will also explain more of the information from the studies such as how many children were transplanted or that died while on support.

The implant procedure may involve more risks that are unknown at this time. Precautions will be taken to avoid harmful side effects including close monitoring of your child during and after pump placement by the medical staff trained in procedures like these. In addition, this procedure may involve unforeseeable risks to your child's fetus if she is pregnant. Therefore, pregnant women should not receive the EXCOR® device. Should your child become pregnant after receiving the device, you or your child should notify your child's doctor right away.

WHAT ARE THE POTENTIAL BENEFITS OF THE EXCOR® SUPPORT?

Possible benefits from this device may include:

- providing enough support to your child's heart to allow your child to have a heart transplant operation;
- protection from further heart and organ damage due to lack of blood flow;
- reduced work load on your child's heart;
- increased blood flow and oxygen delivery and supply to other parts of your child's body;
- providing enough support to your child's heart to allow your child's heart to regain strength to allow removal of the device without a need for a heart transplant.

In the back of this booklet are some tables that explain how these benefits led to outcomes or success reported in the children in the Clinical Data reviewed by FDA.

ARE THERE ANY ALTERNATIVE PROCEDURES AND TREATMENTS?

You may choose for your child to have no treatment performed. If your child does not receive this device your child will still have the same medical treatment options your child had before. Options that are available to your child may include: placement of another device such as a ventricular assist device (VAD) which requires placement and removal with an operation, and/or extracorporeal membrane oxygenation (ECMO); heart transplant surgery if your child is a candidate, and medications. There may be other options specific to your child's case; you, and if appropriate your child, should discuss these options with your child's doctor.

WHO DO I CONTACT FOR QUESTIONS?

For more information concerning risk or injuries you or your child may contact your child's primary doctor. You or your child may also want to discuss items such as rehabilitation, play time or social issues with team members listed here:

AREA OF SUPPORT	NAME	PHONE NUMBER
Primary Doctor		

GLOSSARY

Ventricular Assist Device – a pump that connects to the ventricles of the heart to help the heart pump.

Humanitarian Device Exemption – an FDA approval for a device that is intended for use in less than 4000 people.

FDA (Food and Drug Administration) – the US government agency that helps decide if certain foods, medications, or devices are safe for use.

Blood pump – the main part of the pump that keeps the blood moving through the heart and the body.

Cannula – the tube that connects the pump to the heart.

Right side of the heart – the side of the heart that pumps blood through the lungs and into the left side of the heart.

Left side of the heart – the side of the heart that pumps blood to all of the body including the brain.

IKUS Driver – the machine that pushes air in and out of the blood pumps to get the blood through the heart and to the body.

Driving Tube – the air line from the blood pump to the IKUS driver that carries air to the blood pump.

Anesthesia – drug used by doctors to keep a person asleep, free of pain and not moving during surgery.

Infection – when someone gets sick or when a certain virus or bacteria starts growing in a certain area of the body.

Ultrasound or ECHO – a video of the heart for doctors to see how well it is working.

CT Scan – a video of the brain for doctors to decide if the brain is normal.

Inflammatory reaction – a reaction that causes swelling or a lab value to be out of range.

ECMO (Extracorporeal membrane oxygenation) – a device that supports the heart and lungs that is like the heart-lung machine used in surgery.
Intra-aortic balloon pump – a balloon on a long wire that is put into the body close to the heart to help the heart pump.

CLINICAL STUDY SUMMARY and COMMERCIAL USE

Pre-Market IDE Study

Approval for the primary clinical study was granted in 2007. This study included 48 children. An additional 46 children were enrolled in a study called continued access which allowed children to receive the device after enrollment in the primary study was finished. More children who were not included in the study received the device with special permission from the FDA called Compassionate/Emergency Use. 167 children received the device with this special permission. Information on these patients were included in the study report to the FDA to help support the approval of the EXCOR device.
FDA granted approval on December 16, 2011 at which time the primary study was closed. A total of 281 children received EXCOR Pediatric implants during the study time period.

Post Approval Study

A condition of the FDA approval was another study called a post approval study. 39 children were included in this study. The last child was enrolled into the post approval study on March 10, 2014.

Post Approval Commercial Use

The FDA requested that Berlin Heart gather information for children implanted with the EXCOR Pediatric in the United States following the approval who were not included in the post approval study.

A total of 245 children have been implanted with the EXCOR Pediatric through December 31, 2015 in the post approval period who were not included in the post approval study.

There are now a total of 565 children who were implanted with the EXCOR device from June 21, 2007 to December 31, 2015; 187 under a study protocol, 133 with special permission from the FDA who were not included in a study and 245 post approval commercial use patients.

This table summarizes the implants for each Group.

Implants per Group

Study Group	Implant Period	N
Primary IDE study patients	2007-2011	94
Primary IDE study Compassionate Use	2007-2011	54
Compassionate Use	2007-2011	133
Post Approval Study	2013-2015	39
Post approval Commercial Use	2011-2015	245
TOTAL	**2007-2015**	**565**

Brief Summary of Results

Summary information is presented in three groups. The first group (Study Group) contains information on the primary study patients and the post apporval study patients. The second group (Database Group) contains information on the primary study patients, the post approval patients along with the Compassionate Use information collected from the patients who received the device with special permission from the FDA. The third group (All Implant Group) is a comprehensive group containing information on all pre and post approval patients from the time of the primary study approval in 2007 through 2015.

This table summarizes the basic demographic information that is available for all children. Overall, the children ranged in age from 0 days to 389.3 months, the weight ranged from 2.8 to 112 kilograms.

Basic Demographic Information all Children

Variable	Category	Study Group (IDE + PAS) n=187	Database Group (IDE + Comp Use + PAS) n=320	All Implant Group n=565
Age (mo)	Range	0 – 194.7	0 – 239.3	0.0 – 389.3
Weight (kg)	Range	3.0 – 70.0	2.8 – 71.0	2.8 – 112.0
Device Type	LVAD	63.1%	62.8%	67.6%
	BVAD	36.9%	37.2%	32.4%

This table summarizes the demographic and pre-implant information that is available for the study and database groups.

Demographic information for Study and Database Groups

Variable	Category	Study Group (IDE + PAS) n=187	Database Group (IDE + Comp Use + PAS) n=320
Gender	Male	48.1%	158 (49.4%
	Female	51.9%	162 (50.6%
Diagnosis	Congenital Heart Disease	25.2%	28.4%
	Dilated Cardiomyopathy	52.9%	52.8%
	Myocarditis	12.3%	12.2%
	Other Cardiomyopathy	4.8%	4.1%
	Other	3.7%	2.5%
Pre-implant support: ECMO		35.3%	38.4%
Pre-implant support: Ventilator		71.7%	74.1%
Pre-implant support: Inotropes		90.4%	90.0%
Pre-implant support: VAD		3.7%	3.4%
History of blood transfusions		78.6%	80.0%

Each of the children implanted with an EXCOR® device either went on to get a heart transplant, were taken off the EXCOR® and found that they did not need a heart transplant (weaned) or died before they could receive a heart transplant.

This table shows what happened to all of the children who received the EXCOR® device.

Outcomes and Support Time

Outcome	**Study Group** (IDE + PAS) **n=187**	**Database Group** (IDE + Comp Use + PAS) **n=320**	**All Implant Group** **n=565**
Transplant	74.3%	67.2%	68.7%
Weaned	3.2%	4.1%	3.4%
Wean-Failure*	4.8%	3.8%	4.8%
Death	17.7%	25.0%	21.6%
On Device	0.0%	0.0%	1.6%
Success**	77.5%	71.3%	73.2%
Support Time, Median [Range]	42.0 [0 – 457]	40.5 [0 – 457]	48.0 [0 – 457]

Adverse Events

Children were followed very closely during their stay in the hospital while on the EXCOR® device. Some of the children had minor or major issues due to the device or their own health. The events listed below were reported during the clinical studies. Some children might have had more than one event so that there are less "children with an event" than the total number of events.

Adverse Event Summary

Adverse Event	Study Group (IDE + PAS) n=187		Database Group (IDE+Comp Use+PAS) n=320		All Implant Group n=565	
	431.6 months		747.2 months		1430.8 months	
	# events	Per 100 patient months	# events	Per 100 patient months	# events	Per 100 patient months
Major Infection	181	41.94	281	37.61	294	20.55
Major Bleeding	120	27.80	232	31.05	247	17.26
Hypertension	59	13.67	81	10.84	81	5.66
Neurological Dysfunction	57	13.21	101	13.52	135	9.44
Respiratory Failure	55	12.74	114	15.26	114	7.97
Right Heart Failure	25	5.79	39	5.22	39	2.73
Renal Dysfunction	19	4.40	34	4.55	34	2.38
Pericardial Fluid Collection	22	5.10	37	4.95	37	2.59
Pericardial effusion	4	0.93	4	0.54	4	0.28
Cardiac Arrhythmia	19	4.40	32	4.48	32	2.24
Hemolysis	7	1.62	11	1.47	11	0.77
Hepatic Dysfunction	17	3.94	35	4.68	35	2.45
Psychiatric Episode	3	0.70	5	0.67	5	0.35
Thromboembolism-Arterial Non CNS	4	0.93	7	0.94	8	0.56
Thromboembolism-Venous	5	1.16	8	1.07	8	0.56
Other	70	16.22	99	13.25	104	7.27

All of the adverse events had an effect that is listed in the table below.

Adverse Event	**Effects of the Event** (note: some children were sedated and so the doctors were not able to determine the effect)
Major Infection	Antibiotics given
Major Bleeding	Transfusion given or operation performed to stop bleeding
Hypertension	High blood pressure
Neurological Dysfunction-Ischemic CVA	Weakness, Speech problems
Respiratory Failure	Tube placed
Right Heart Failure	Need for support of the right ventricle
Renal Dysfunction-Acute	Kidney not functioning properly
Pericardial Fluid Collection	Pressure on the heart
Pericardial Effusion	Drainage of fluid
Cardiac Arrhythmia-Sustained SVT	Medications given to control the fast heart beat
Hemolysis-Late	Lower level of red blood cells in blood
Hepatic Dysfuction	Bilirubin not being sent out from body
Psychiatric Episode	Agitation, feeling of panic
Arterial Non-CNS Thromboembolism	Blood clot in an artery with no effect
Venous Thromboembolism Event	Swelling
Other	Depends on event

www.berlinheart.com
Berlin Heart Inc • 200 Valleywood • Suite B-100 • The Woodlands, TX 77380
Phone: (281) 863-9700 • Fax: (281) 863-9701 • E-mail: info@berlinheart.com

RCN 1086 Version 4 – 3 July 2017