

# **Adjuvant Therapy Information & Consent Form**

Adjuvant therapy, also referred to as adjunct therapy or "add-ons," includes a range of medical treatments that are administered in addition to the standard IVF/fertility treatment, either alone or in combination. However, it is crucial to note that for most of these add-ons, there is limited or no evidence demonstrating their effectiveness in enhancing live birth rates.

The medications prescribed by your doctor to improve outcomes are not part of the standard Monash IVF protocol drugs and are based off the recommendations of Dr Nicholas Lolatgis, a fertility specialist and immunologist within infertility. There is no evidence-based medical reports that support the use of these drugs, but there is anecdotal evidence supporting their effectiveness. Although no randomized controlled trials have been conducted in some cases, the drugs are licensed by the TGA and are safe with minimal side effects and allergic reactions. However, the cost of these medications may vary from pharmacy to pharmacy and will be an additional expense on top of your treatment cycle.

If you have any inquiries about these drugs, please contact the nursing team on (07) 55191602.



## **Medications**

**Medication: Testogel (Androgen Cream)** 

**Definition:** Testogel is available by prescription that has the potential to enhance the number of eggs collected, embryos formed, and pregnancy rates during in vitro fertilization (IVF) treatment. It may also improve the quality of eggs. By increasing the activity of the follicle stimulating hormone (FSH) receptor and insulin-like growth factor 1 (IGF1), Androgen Cream may affect the granulocytes in the follicles.

It's essential to note that Testogel is an off-label prescription, and its use in IVF treatment is not authorized. Additionally, testosterone, which is the active ingredient in testogel, is classified as a Category D drug. Therefore, it should be avoided during pregnancy and breast-feeding as it has been linked to an increased incidence of human fetal malformations or irreversible damage. Women should not use testosterone during pregnancy as it could potentially result in the development of male traits in a female fetus.

**Dose:** 12.5mg

Frequency: Applied once daily on the inside of the upper arm

**Type:** Topical Cream

**Duration:** Commenced 3-4 weeks prior to your cycle and ceased on Day 1 of your treatment

cycle.

**Side Effects:** Possible common side effects of testogel include burning, itching, redness, skin rash, swelling, soreness and skin irritation at the site of application where the gel is applied. To minimize the risk of transmission of Testogel, it is advisable to cover the application site with clothing to prevent skin-to-skin contact with other individuals. Additionally, increased acne; headaches; sweating, increased hair growth; mood swings, high blood pressure, unusual weight gain/loss, increased red blood cell count may occur. It's also possible for a change in sex drive to occur.

Rare side effects can include but are not limited to increased risk of blood clots in the legs or lungs, increased risk of heart attack or stroke; swelling of your ankles, feet, or body, with or without heart failure; enlarged or painful breasts and having problems breathing while you sleep.



**Medication: Melatonin** 

**Definition:** Melatonin is available over the counter that has the potential to improve egg quality. Melatonin is a hormone that your brain produces in the response to darkness to help with timing of your circadian rhythms and with sleep. There has also been an association noted between higher levels melatonin in the follicular fluid improving egg quality.

Dose: 4mg

Frequency: Once Daily

We recommend taking this medication at night approximately 30 minutes before bed.

**Type:** Oral medication taken with water

**Duration:** This medication is safe to consume throughout your entire treatment cycle. Upon pregnancy please consult with your treating specialist.

**Side effects:** An allergic reaction to this drug is rare. Side effects include drowsiness, sleepiness, headaches, dizziness and nausea.

#### **Medication: Aspirin**

**Definition:** As a non-steroidal anti-inflammatory drug (NSAID), aspirin is utilized to alleviate mild to moderate pain and decrease fever. In addition, low dose aspirin (100mg) functions as a blood thinner and minimizes the likelihood of stroke by reducing blood clotting. This medication can also enhance blood flow to the ovary and uterus, thereby increasing pregnancy implantation rates and assisting in the thickening of the endometrium. Aspirin is classified as a Category A drug and is deemed safe for consumption during pregnancy.

Aspirin should not be used if you have a bleeding disorder like haemophilia, a recent history of gastrointestinal bleeding, or if you are allergic to non-steroidal anti-inflammatory drugs (NSAIDs).

Dose: 100mg

Frequency: Once Daily

**Type:** Oral medication taken with water

**Duration:** From day 2 of your treatment cycle (unless specified by your treating specialist) or upon positive pregnancy testing until 10-12 weeks gestation. Cessation of this medication is under the guidance and control of your treating specialist.

**Side Effects:** Side effects may include an upset stomach, heartburn, bruising, drowsiness, ringing in the ears, nausea, vomiting, and rash. It is possible for individuals with asthma or



who are susceptible to asthma attacks to experience worsened symptoms. Allergic reactions are uncommon.

Serious but rare side effects can include ringing in your ears, confusion, hallucinations, rapid breathing, seizure (convulsions); severe nausea, vomiting, or stomach pain; bloody or tarry stools, coughing up blood or vomit that looks like coffee grounds; fever lasting longer than 3 days; or swelling, or pain lasting longer than 10 days.

**Medication: Clexane (Enoxaparin)** 

**Definition:** Clexane is an anti-coagulant and is used to treat blood clots, certain types of heart disease and the prevention of blood clots. In fertility it thins the blood and aids implantation. Clexane is a medication available by prescription.

Dose: 40mg

Frequency: Once Daily

We recommend administering this medication at night.

**Type:** Subcutaneous injection that is injected into the and around the abdomen.

**Duration:** From day of embryo transfer or insemination (IUI) of your treatment cycle (unless specified by your treating specialist) or upon positive pregnancy testing until 10-12 weeks gestation. Cessation of this medication is under the guidance and control of your treating specialist.

**Side Effects:** The most common side effect from enoxaparin is bleeding and bruising, pain and/or irritation at the injection site and hard inflamed nodules at injection site.

An allergic reaction is rare, rare side effects include shortness of breath, swelling and rashes.

Some other side effects from long-term use include, hair loss, thinning of your bones, haematomas – collection of blood under the skin, prolonged bleeding – from minor cuts, gum or nose bleeding, or periods, severe headaches or back pain, swelling, bruising or tender areas with no cause, blood appears in any bodily fluid – urine, stools, vomit or secretions.

**Medication: Dexamethasone** 



**Definition:** Dexamethasone is a corticosteroid and prescription medication that mimics the natural hormone produced by the adrenal glands. It is commonly used to supplement the body's production of this hormone when it is deficient. This medication effectively reduces inflammation, which includes symptoms such as swelling, heat, redness, and pain. Dexamethasone is prescribed to treat a range of health conditions including certain forms of arthritis, blood disorders, kidney disorders, eye disorders, thyroid disorders, and intestinal disorders such as colitis. Additionally, it is utilized to treat severe allergies, asthma, and certain types of cancer.

Dexamethasone has also been found to improve egg quality in individuals with polycystic ovarian syndrome (PCOS) and protect the embryo by suppressing the immune system.

This drug falls under Category A, which means that it has been taken by many pregnant women and women of childbearing age without any harmful effects on the fetus. However, there is a slightly increased risk of congenital heart defects, cleft lip/palate (which is six times higher than normal), and incomplete formation of the anus in infants born to mothers who have taken steroids during pregnancy, particularly in the first trimester.

It is dangerous to suddenly stop corticosteroid treatment, especially if the treatment has lasted for 4 or more weeks. This type of medication needs to be withdrawn slowly under medical supervision.

Dose: 2mg

Frequency: Once Daily

We recommend taking this medication in the morning due to its potential effect on sleep.

**Type:** Oral medication taken with water

**Duration:** From day 2 of your treatment cycle (unless specified by your treating specialist) or upon positive pregnancy testing until 10-12 weeks gestation. Cessation of this medication is under the guidance and control of your treating specialist.

**Side Effects:** This drug makes you more susceptible to illnesses. The side effects are an upset stomach, stomach irritation, vomiting, headache, dizziness, insomnia, restlessness, depression/mood changes, anxiety, acne, increased hair growth, easy bruising, weight gain and in-creased appetite and irregular or absent menstrual periods.

More severe side effects include skin rash, swollen face/lower legs/ankles, vision problems, cold or infection that lasts a long time, muscle weakness, black or tarry stools and if you have diabetes, dexamethasone may increase your blood sugar level. An allergic reaction to this drug is rate. There is however a small increased risk of hair, lip and cleft palate.

**Medication: Prednisolone** 



**Definition:** Prednisolone is a prescription medication and a type of corticosteroid hormone that is naturally produced by the adrenal gland. This medication is used to treat a range of conditions, including arthritis, immune system disorders, skin, and eye disorders, breathing problems, and allergies. Prednisolone is known for its ability to suppress the immune system, and reduce pain, swelling and allergic-type reactions. Prednisolone has also been found to improve pregnancy rates.

This drug is categorized as a Category A medication, which means that it has been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other harmful effects on the fetus. However, there is a slightly increased risk of congenital heart defects, cleft lip/palate (which is reported to be six times higher than normal), and incomplete formation of the anus in babies born to women who have taken steroids during pregnancy, particularly in the first trimester.

It is dangerous to suddenly stop corticosteroid treatment, especially if the treatment has lasted for 4 or more weeks. This type of medication needs to be withdrawn slowly under medical supervision.

Dose: 10mg

Frequency: Once Daily

We recommend taking this medication in the morning due to its potential effect on sleep.

**Type:** Oral medication taken with water

**Duration:** From day 2 of your treatment cycle (unless specified by your treating specialist) or upon positive pregnancy testing until 10-12 weeks gestation. Cessation of this medication is under the guidance and control of your treating specialist.

**Side Effects:** Side effects include nausea, headache, dizziness, insomnia, extreme changes in mood including unusual happiness, changes in personality, acne, thin fragile skin, slowed healing of cuts and bruises, thinning of hair, increased appetite, changes in the way fat us spread around the body, increased sweating, irregular or absent menstrual periods, low sex drive and weak muscles. If you are diabetic, this drug may cause your blood sugar to rise.

There is a small risk of an allergic reaction to this drug.

Serious side effects include sore throat, fever, chills, cough or other signs of injection, seizures, muscle weakness, vision problems, depression, loss of contact with reality, sudden weight gain, stomach swelling, swelling of the eyes, lips, face, tongue, throat, arms, feet, ankles or lower legs, difficulty breathing or swallowing, rash, hives and itching. Prednisolone may increase the risk that you will develop osteoporosis.

Medication: Intravenous Immunoglobulin (IVIG)



**Definition:** The body's immune system produces natural antibodies known as immunoglobulins, which assist in combating infections and illnesses. Intravenous immunoglobulin (IVIg) therapy utilizes immunoglobulins contributed by multiple individuals to treat a variety of medical conditions. Administered through a drip, IVIG is produced from plasma, and is employed to mitigate the impact of certain immune system-related inflammatory ailments referred to as autoimmune diseases. Additionally, it is utilized to boost immunoglobulin levels in cases where they are insufficient or have decreased due to treatment with other drugs.

This treatment is to be completed by a Haematologist which will require you to have a consultation prior to starting your cycle.

We can refer you to

Dr Herman Lee Pindara Place 13 Carrara St Benowa, QLD, 4217 Phone: 07 5597 1211 Dr Greg Seeley Gold coast Private Hospital Ground Floor, Suite 17, 14 Hill Street Southport Qld 4215. Ph: 07 5532 7655

Dose: 400 to 600 milligrams per kilogram

**Frequency:** Once during cycle and 2 more; upon positive pregnancy and at 7 weeks following heartbeat at viability scan, or as advised by your treating specialist.

**Type:** Intravenous infusion in a hospital setting.

**Duration:** The infusion is usually required to be done between days 7-12 of your cycle (after intralipids) but 7 days prior to an embryo transfer.

**Side Effects:** Although IVIG is generally well-tolerated, some individuals may experience mild side effects such as headaches, chill or fevers, muscle or joint discomfort, stomach pain, nausea, vomiting, low back pain and tiredness. However, there is a slight chance of an allergic response to IVIG, which can lead to anaphylactic shock.

Some people may also experience rarer symptoms of a rash, liver problems, kidney failure, inflammation of the brain, known as aseptic meningitis and haemolytic anaemia, a condition with different causes, that destroys red blood cells.

Medication: Filgrastim (Neupogen)



**Definition:** Filgrastim is a substance that triggers the production of white blood cells by the body. In cases of infertility, it promotes the growth of the endometrial lining, facilitating the attachment and implantation of the embryo. This cytokine is present in the follicular fluid of the ovary, and studies have demonstrated that it can enhance the quality of eggs produced.

**Dose:** 75-300 mcg

**Frequency:** To be determined by your treating specialist

**Type:** Subcutaneous injection or intrauterine (IUI)

Duration: IUI 1-5 days before transfer, subcutaneous 1 hour before transfer or day 1

FSH/HRT until pregnancy test

**Side Effects:** These can include redness, swelling, bruising, itching or a lump in the place where the medication was injected, bone, joint, back, arm, leg, mouth, throat, or muscle pain, headache, rash, constipation, diarrhea, nausea, vomiting, loss of appetite, difficulty falling asleep or staying asleep, decreased sense of touch, hair loss, nosebleeds, tiredness, lack of energy, feeling unwell and dizziness.

Some side effects can be serious and can include pain in the left upper part of the stomach or the tip of the left shoulder, fever, shortness of breath, trouble breathing, fast breathing, trouble breathing, coughing up blood, fever, abdominal pain, back pain, feeling unwell, swelling of stomach area or other swelling, decreased urination, trouble breathing, dizziness, tiredness, rash, hives, itching, swelling of the face, eyes, or mouth, wheezing, shortness of breath, unusual bleeding or bruising, purple markings under the skin, red skin, decreased urination, dark or bloody urine, swelling of the face or ankle, painful, urgent, or frequent urination.

#### **Medication: Humira (Adalimumab)**

**Definition:** Humira works by blocking a protein called tumour necrosis factor (TNF) which is found in the body's immune system. It is used to treat certain types of arthritis and is also used to treat Ulcerative colitis and Crohn's disease. It suppresses the immune system.

You should not start taking HUMIRA if you have any kind of infection.

Dose: 40mg

Frequency: Twice in-cycle

**Type:** Subcutaneous injection

**Duration:** Day 2 of treatment cycle + 14 days later



**Side Effects:** Side effects include redness, itching, pain, bruising or swelling at the injection site. Sore throat, rash cough fever, chills, night sweats, trouble breathing, upper respiratory infections, headaches, nausea and frequent micturition can also occur. It is a Category C drug but does not cause malformation and can be used in pregnancy until 32 weeks. An allergic reaction is rare.

### **Medication: Intralipid Infusion**

**Definition:** The composition of Intralipids consists of 1.2% egg yolk phospholipids, 10% soybean oil, 2.25% glycerin, and water.

The immune system regulates natural killer cells, which may react abnormally to a fertilized egg in women with autoimmune issues, treating it as a foreign body and signaling the immune system to attack it. Research has shown that Intralipids can deactivate natural killer cells, promoting the successful implantation and growth of the embryo in the uterine wall. The deactivation of natural killer cells can be sustained until the pregnancy can override signals from the immune system.

Dose: 200mls or 500mls

**Frequency:** Intralipids is usually administered around the time of a procedure (IUI, ovulation, transfer or FET) and/or upon confirmed pregnancy with a HCG level of 100 or more, then possibly every two weeks until 10-12 weeks of pregnancy or longer depending on the recommendation of the specialist who is looking after your care.

**Type:** Intravenous Infusion performed at day hospital or infusion clinic

**Duration:** Intralipids can take anywhere from 2 hours to 4 hours for the infusion to be complete.

**Side Effects:** Headache, dizziness, flushing, drowsiness, nausea, vomiting, or sweating may occur. If any of these effects last or get worse, tell your doctor or pharmacist promptly.

Serious side effects can include: signs of infection (such as sore throat that doesn't go away, fever), pain/swelling/redness at injection site, pain/swelling/redness of arms/legs, bluish skin, sudden weight gain, shortness of breath, back/chest pain, mental/mood changes, bone pain, muscle weakness, easy bruising/bleeding, signs of liver disease (such as nausea/vomiting that doesn't stop, loss of appetite, stomach/abdominal pain, yellowing eyes/skin, dark urine).

A very serious allergic reaction to this drug is rare. However, a serious allergic reaction can include: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.



**Medication: Naltrexone** 

**Definition:** Naltrexone is a medication used to prevent people who have been addicted to certain drugs, such as opiates, from taking them again. It is an opiate antagonist. However, when used in a low dose, Naltrexone has been also shown to modulate the immune system and help a variety of conditions including Infertility and hormonal balance.

Dose: 4.5mg

Frequency: Once daily

**Type:** Oral medication taken with water

**Duration:** From day 2 of your treatment cycle (unless specified by your treating specialist) or upon positive pregnancy testing until 10-12 weeks gestation. Cessation of this medication is under the guidance and control of your treating specialist.

**Side Effects:** Side effects include nausea, headache, dizziness, anxiety, tiredness, and trouble sleeping may occur. In a small number of people, mild opiate withdrawal symptoms may occur, including abdominal cramps, restlessness, bone/joint pain, muscle aches, and runny nose.

Sudden opiate withdrawal symptoms can occur within minutes after taking naltrexone. Tell your doctor right away if any of these withdrawal symptoms occur: abdominal cramps, nausea/vomiting, diarrhea, joint/bone/muscle aches, mental/mood changes (such as anxiety, confusion, extreme sleepiness, visual hallucinations), runny nose.

Naltrexone has rarely caused serious liver disease. The risk is increased when larger doses are used. Discuss the risks and benefits with your doctor. Stop using this medication and tell your doctor right away if you develop symptoms of liver disease, including: nausea/vomiting that doesn't stop, severe stomach/abdominal pain, dark urine, yellowing eyes/skin.

**Medication: Tacrolimus** 

**Definition:** Tacrolimus is classified as an immunosuppressant medication that operates by inhibiting the activity of the immune system in the body. By doing so, Tacrolimus helps to reduce the function of natural killer cells, which have been associated with decreased pregnancy rates and increased instances of pregnancy loss.

Dose: 1mg

Frequency: Twice daily

Type: Oral medication taken with water



**Duration:** Medication is taken 3 days prior to transfer/IUI and then continued on to 12-14 weeks of pregnancy.

**Side Effects:** Shaking, headache, diarrhea, nausea/vomiting, upset stomach, loss of appetite, trouble sleeping, and numbness/tingling of the hands/feet may occur.

Serious side effects, including: mental/mood changes, dizziness, signs of kidney problems (such as change in the amount of urine), pounding heartbeat, symptoms of heart failure (such as shortness of breath, swelling ankles/feet, unusual tiredness, unusual/sudden weight gain), hearing problems (such as hearing loss, ringing in the ears), pain/redness/swelling of arms or legs, easy bruising/bleeding, muscle pain/cramp/weakness, yellowing skin/eyes, dark urine, persistent nausea/vomiting, severe stomach/abdominal pain, severe leg pain.

This medication may also increase your risk of getting a rare but very serious (sometimes fatal) brain infection (progressive multifocal leukoencephalopathy-PML). Rare but very serious side effects include: clumsiness, loss of coordination, weakness, sudden change in your thinking (such as confusion, difficulty concentrating), difficulty moving your muscles, problems with speech, seizure, vision changes.

#### Medication: Recombinant Growth Hormone (RGH/HGH)

**Definition:** Growth Hormone is used in specific endocrine disorders. In infertility it has an effect on the follicular fluid and egg quality. HGH can lead to better embryo quality and live birth rates.

Recombinant Growth Hormone is a Pregnancy Category B2 drug. This means it has been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Dose: 1 IU

Frequency: Once daily

**Type:** Subcutaneous injection

Duration: 7-10 days prior to day 1 of cycle with cessation of HGH on day of trigger

**Side Effects:** Nerve, muscle, or joint pain, swelling due to fluid in the body's tissues (oedema), carpal tunnel syndrome, numbness and tingling of the skin, high cholesterol levels

HGH can also increase the risk of diabetes and contribute to the growth of cancerous tumours. An allergic reaction to HGH is rare.



Medication: Viagra (Sildenafil)

**Definition:** Viagra is a brand name medication containing the active ingredient sildenafil citrate, which is used to treat erectile dysfunction (ED) in men. It works by increasing blood flow to the penis, which helps a man achieve and maintain an erection during sexual activity. Viagra can also be used in women to increase the blood flow to the uterus.

**Dose:** 50-100mg

Frequency: Once Daily

Type: Oral medication taken with water

**Duration:** From day 2 of your treatment cycle (unless specified by your treating specialist)

until your embryo transfer.

**Side Effects:** Side effects include dizziness, headaches, heartburn, diarrhea, flushing (feeling or warmth), nosebleeds, stomach upset, difficulty falling asleep or staying asleep, numbness, burning or tingling in the arms, hands, feet or legs. Muscle aches, changes in colour vision and sensitivity to light may also occur.

An allergic reaction can occur when taking Viagra.

Severe side effects include sudden loss of vision, blurred vision, sudden decrease or loss of hearing, ringing in the ears, fainting, light-headedness, worsening shortness of breath, itching or burning during urination and a rash.

#### **Medication: Progesterone**

**Definition:** Progesterone pessaries are a medication that contain natural progesterone, which is a hormone that is normally produced by the ovaries during the second half of the menstrual cycle. Progesterone is important for preparing the uterus (womb) for pregnancy and for supporting a developing fetus.

In some cases, women who are undergoing in vitro fertilization (IVF) may not produce enough progesterone on their own, or they may need additional progesterone supplementation to support the early stages of pregnancy. In these cases, progesterone pessaries can be used to supplement or replace the body's own natural progesterone levels.

Progesterone pessaries are typically inserted into the vagina, where they slowly dissolve and release progesterone over time. The medication is available only with a prescription from a



healthcare provider, and it is important to use it only as directed and to discuss any potential risks and side effects with a healthcare professional before use

**Dose:** 200-400mg

Frequency: Three Times Daily

**Type:** Pessary that is inserted into the vagina for absorption

**Duration:** From ovulation of your treatment cycle (unless specified by your treating specialist, e.g. Frozen embryo transfer cycle) or upon positive pregnancy testing until 10-12 weeks gestation. Cessation of this medication is under the guidance and control of your treating specialist

**Side Effects:** The most common side effects are cramps, abdominal pain or perineal pain around the genial and back passage, headache, breast enlargement or breast pain, feelings of sadness and emotional, decreased sex drive, sleepiness, constipation, cramps, nausea and passing urine at night.

Rare side effects may include bloating, pain, dizziness, vaginal discharge, itching of the vaginal area, vaginal bleeding, vaginal thrush, diarrhea, vomiting, painful sexual intercourse and painful joints.