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# Ovarian Hyperstimulation (OHSS) Policy

Document Owner: State Medical Director

Applicability: Repromed SA and NT

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In the event of a failure to or inability to comply with the process as described, users must follow the Emergency Procedures, as described. Failure to comply with these instructions may constitute misconduct, such instances will be investigated, and disciplinary action may be taken.

## This Document ensures compliance with:

*Legislation / Regulations / Standards*

- Current RTAC Code of Practice
- Current NHMRC Ethical Guidelines for the use of assisted technology in clinical practice and The Australian Commission on Safety and Quality in Healthcare
- Current National Safety and Quality in Healthcare Service Standards

## Definitions

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| *OHSS* | Ovarian Hyperstimulation is a complication of fertility treatment, which uses pharmacological ovarian stimulation to increase the number of oocytes and therefore embryos available during assisted reproductive technology (ART). |

## Related Documents

- Using GNRH agonist OI during IVF if OHSS Risk
- Luteal Phase Management
- Prevention of Severe OHSS Use of Cabergoline
- Repromed Patient Companion

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# Ovarian Hyperstimulation (OHSS) Policy

## Purpose and Scope

This document describes the processes to minimise the incidence of risk of Ovarian Hyperstimulation Syndrome (OHSS) and the management of patients with OHSS.

## Policy

It is Repromed Policy that:

- ✓ The risk of Ovarian Hyperstimulation Syndrome (OHSS) is minimised, and process exist to measure the risk and incidence
- ✓ Patients receive information on these risks, their symptoms and their management
- ✓ Patients receive information on how to access help, advice or care out of normal hours or in the event of a medical emergency
- ✓ All cases which involve re-hospitalisation that can be attributed directly to the ART procedure are reported to RTAC and the certifying body as a serious notifiable adverse event as defined in the RTAC Code of Practice
- ✓ All cases of OHSS requiring hospitalisation are reported to ANZARD

## MVF Specific Requirements

### Compliance

Compliance with this policy must be monitored by each business unit at intervals not exceeding 12 months by:

- ✓ Internal Audit/s
- ✓ Review of Adverse Events and Feedback by the Medical Director and local Leadership teams

### Non-Compliance with this policy

There is no tolerance to non-compliance with this policy.

Clinical guidelines may be altered to meet the needs of patients based on doctors' clinical decisions. Any non-compliance to clinical guidelines must be recorded in the patient's notes so that staff are aware of the authorised non-compliance.

## Responsibilities

State Medical Director is responsible for:

- Reviewing all cases of OHSS for evidence of compliance to policy and procedure and the purposes of corrective and preventative actions
- Reporting OHSS cases /trends to the Medical Advisory Committee for the purposes of review corrective /preventative actions /continual improvement and ongoing education

Quality Risk and Compliance Officer is responsible for:

- Reviewing and reporting all cases of OHSS to the Medical Director
- Reporting all OHSS cases requiring re hospitalising as described in the Adverse Event and Feedback policy
- Monitoring and auditing the OHSS rates at least annually

Clinicians are responsible for:

- Ordering of appropriate FSH dose based on patient history and test results
- Documenting any approved non-conformance to procedure in the patient notes
- Liaising with Medical Director or delegate regarding FSH dose if required
- Discussing OHSS risk with patients
- Management of patient with OHSS
- Reporting admission of patient to hospital with OHSS as an Adverse Event in RiskMan or to the Fertility Nurse team

Fertility Nurses are responsible for:

- Monitoring cycle of patients at risk for OHSS.
- Education patients regarding OHSS symptoms
- Reporting admission of patient to hospital with OHSS as an Adverse Event in RiskMan

Local Leadership Team are responsible for:

- Review all cases of OHSS for evidence of compliance to policy and procedure and the purposes of corrective and preventative actions

## When:

**Patients at anticipated higher risk of OHSS (prior starting IVF)**

- Diagnosis of PCOS especially thin PCOS
- Patients who have experienced OHSS in the past
- High AMH Levels with large antral follicle counts (AMH ≥ 30 pmol/L *or AFC (2-10mm) ≥ 40.
- Age ≤ 35 years* on first cycle IVF

* These risk indices are based on the medical literature and an audit of Repromed's hospitalised cases of OHSS in 2022. In that audit the median AMH of OHSS patients was 30pmol, with 90% of cases being aged under 35 years.

## How:

**Minimisation of OHSS Risk**

- Patients diagnosed with increased risk of OHSS MUST be placed on an antagonist cycle to allow for the use of a GnRH agonist trigger. Long down regulation MUST NOT be used in patients at high risk of OHSS.
- Patients at very high risk of OHSS (first cycle IVF, age ≤ 35 years and AMH ≥ 30 pmol and AFC > 20 per ovary – total 40) must be consented for an antagonist cycle, GnRH agonist trigger and elective embryo freeze all *at the time of their IVF cycle planning clinic consultation.* This approach is not only safer for the patient, but also likely to maximize cumulative pregnancy rates as excessive COH response has been linked to reduced fresh embryo transfer success (Bosdou 2019, Yu 2020, Venetis 2022). Furthermore, if planned electively, rather than as a last-minute decision at the time of OPU or trigger, a freeze all strategy causes less patient confusion and stress.
- In patients at very high risk of OHSS a reduced starting dose of FSH should be considered (for example 100-112 IU/day in a normal BMI woman under 35 years of age). However, for high BMI patients a normal starting dose (150 IU/day age ≤ 35) may be considered optimal provided a freeze all embryo approach is taken. Long acting FSH (Elonva) is best avoided in patients at risk of OHSS.
- Review of previous history prior to ordering FSH dose.

**Clinical Management of IVF Cycle to Minimise / Prevent OHSS**

**a)** Previous OHSS on FSH 150iu, start 100-125iu FSH

- Senior clinician to decide FSH dose.
- Measure estradiol levels on day 6 of cycle. If E2 > 2500 pmol reduce dose of FSH. If E2 < 800 pmol consider increasing dose.

If on the Day 9 scan or later there is evidence of high OHSS risk:

- > 15 follicles of ≥ 14mm in size
- E2 > 8 nmol
- Patient symptoms of OHSS

**Then a mandated agonist trigger** once 3 or more follicles ≥ 17mm in size (see agonist trigger protocol) is used, unless there are contra-indications to its use (LDR cycle, known or suspected pituitary dysfunction, past poor response GnRH agonist trigger). If lead follicles on D8/9 scan are > 1 day from trigger criteria – consideration to halve the dose of an FSH stimulation should be made.

GnRH agonist triggers may be used for lesser risk patients, but fresh embryo transfer is not possible (see GnRH Agonist Policy).

If a patient has an unexpected high response (15 + oocytes collected at OPU, despite a smaller response being predicted on Day 9 scan), *and they were given a hCG trigger*, Cabergoline should be commenced at the time of OPU and a freeze all embryo approach taken. Cabergoline is NOT usually required if a GnRH agonist was used for trigger.

Decision on proceeding with a fresh ET in patients at borderline increased risk of OHSS (9-14 oocytes collected at OPU, schedule E2 > 6, and having received a hCG trigger):

- SET is mandated. DET should not be performed if aged ≤ 38 and good embryo quality.
- Luteal support MUST be HRT based (progesterone), not hCG.
- Embryo transfer should be delayed as late as possible (Day 5 preferable) to allow best assessment of patient's status.
- OHSS bloods (LFE/LFTs, CBE, Coag) should be performed the day before planned transfer so that these results are available at E/T time for consideration by Dr.
- If patient has significant OHSS symptoms suggesting hospitalization is required, or a PCV >0.45, a transfer must not proceed. LFTs exceeding twice the upper limit of normal range also precludes embryo transfer, irrespective of how well the patient feels.
- Difficult decisions of "transfer v freeze all" will need discussion with Medical Director or CREI consultant.
- Freeze all is mandated in hCG trigger cycles when 15 or more oocytes are collected, or if an agonist trigger is used.
- To minimise the financial impact of this "freeze all" OHSS safety policy, the patient will be charged a reduced amount (50% of the usual up-front fee) for their first FET treatment cycle. Subsequent FET cycles will be charged at the usual rate. This cost reduction policy does not extend to elective freeze all cycles in the context of planned PGT, or elective freeze all for other non-OHSS reasons (e.g., planned hysteroscopy/ polypectomy at OPU).
- Given that recent studies have shown that pregnancy rates are not reduced by allowing an ET in the menstrual cycle immediately following a stimulated cycle (Bergenheim et al 2021), patients can elect to have a FET in that immediate cycle. **OHSS Management**

Risk of OHSS: Non-Compliance to Policy and Procedure could result in a patient with OHSS.

- Hospitalisation
- Pleural effusion
- Deep Vein thrombosis
- Ascites
- Decreased renal perfusion
- Hypoalbuminemia
- Electrolyte imbalance
- Pulmonary embolism
- Death

- The principle of management is conservative care until the condition spontaneously resolves. Vaginal examination should be avoided as the risk of rupturing ovarian cysts and causing bleeding outweighs the merits. An ultrasound scan is the best method of determining the size of the ovaries and presence of ascites. Surgery is only indicated where ovarian torsion or a ruptured ovarian cyst occurs and must be discussed with the appropriate Repromed consultant.
- The underlying pathology is that of an endotheliosis resulting in hypoalbuminemia, ascites, haemoconcentration, electrolyte imbalance and decreased renal perfusion. Pleural effusion can occur in severe cases. Rarely are peritoneal or pleural taps indicated. There is also a risk of DVT with haemoconcentration and tense ascites impairing the venous return from the legs, and renal blood flow.

**In Patient Treatment**

1. *Fluid Balance*
   - Aim for a **total** input of 2-3 litres / 24 hours, either orally or if nausea and vomiting then with I.V. fluids. The aim is to correct haemoconcentration. **Beware of giving excess fluids, which will exacerbate third space fluid collection.**
   - Moderate OHSS - alternate Normal Saline and Hartman's and consider a volume expander eg: albumex 4.
   - Severe OHSS - alternate albumex 4 and normal saline 2L / 24 hrs initially and review each 24 hours.
   - Aim for a minimum average hourly urine output of 30mls/hour and catheterise if less.
   - Check PCV and if haemoconcentration remains uncorrected and/or a urine output <30mls/hour, then consider 2 x 100mls concentrated albumin I.V. (25gms). If available this may be repeated as necessary. Red Cross may restrict availability.
   - Under most circumstances if a patient requires concentrated I.V. Albumin a physician should be consulted to supervise patient management.
   - Check urea and electrolytes and replace as necessary.
   - Subcutaneous Clexane 40mgm daily with severe haemoconcentration
   - A patient with a tense ascites may develop renal vein compression with decreased urine output. HDU opinion should be sought and an ascitic drain may be appropriate.

2. *Pain Relief*
   - Paracetamol or Paracetamol + Codeine is safe whether the patient is pregnant or not. Beware of ↑pain from constipation with opiate use.
   - I.V. Maxalon PRN or Navoban.

It is essential to use TED stockings and encourage leg mobilisation to minimise risk of DVT.

Ascertain if the patient has a family history of thromboembolism.

3. *Investigations and Observations*

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| CBP, Urea and electrolytes - LFT's every 1-2 days | *Depends on severity of OHSS |
| INR + APTT | As indicated |
| Oestradiol & Progesterone | Every 2-3 days* |
| Quantitative Serum HCG | 16 days after embryo transfer |
| Four Hourly | Blood pressure, pulse, Respiratory rate |
| Daily | Abdominal girth - mark abdomen. Check legs for DVT Weight / Fluid balance chart |

## References

Bergenheim SJ, Saupstad M, Pistoljevic N, Andersen AN, Forman JL, Løssl K, Pinborg A. Immediate versus postponed frozen embryo transfer after IVF/ICSI: a systematic review and meta-analysis. Hum Reprod Update. 2021 Jun 22;27(4):623-642.

Bosdou JK, Venetis CA, Tarlatzis BC, Grimbizis GF, Kolibianakis EM. Higher probability of live-birth in high, but not normal, responders after first frozen-embryo transfer in a freeze-only cycle strategy compared to fresh-embryo transfer: a meta-analysis. Hum Reprod. 2019 Mar 1;34(3):491-505.

Ovarian Stimulation TEGGO, Bosch E, et al. ESHRE guideline: ovarian stimulation for IVF/ICSI Hum Reprod Open. 2020 May 1;2020(2)

Venetis CA. Pro: Fresh versus frozen embryo transfer. Is frozen embryo transfer the future? Hum Reprod. 2022 Jun 30;37(7):1379-1387.

Yu Y, Zhao S, Li Y, Niu Y, Wei D, Zhang S, Chen ZJ, Zhang H, Legro RS. Live birth after a freeze-only strategy versus fresh embryo transfer in three randomized trials considering progesterone concentration. Reprod Biomed Online. 2020 Sep;41(3):395-401.

## Emergency Procedures

Non-conformance to Policy and OHSS patient admission to hospital and must be reported to the Medical Director and entered into RiskMan as an Adverse Event to enable review of OHSS rates and management, including compliance to Policy.