**Purpose:** To define the most clinically efficacious and cost effective treatment for unexplained infertility and mild male factor.

### Detailed Steps/Screen Shots

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| **1. Background Information** | • Unexplained infertility accounts for 20% of infertility cases.  
• Historically, super-ovulation with clomiphene citrate or gonadotropins combined with intrauterine insemination (IUI) has provided less invasive options before proceeding to IVF.  
• A traditional approach involved 3 cycles of clomiphene/IUI followed by 3 cycles of gonadotropin/IUI before pursuing IVF.  
• Gonadotropin/IUI is associated with an increased risk multiple gestation (30%) including high-order multiple births (8.1%).  
• The pregnancy rate per cycle for gonadotropin/IUI is 9%.  
• The pregnancy rate per cycle for clomiphene/IUI is 7%.  
• Conception, when it occurs, is achieved within 3-4 clomiphene or gonadotropin/IUI cycles in 90% of cases.  
• The cumulative pregnancy rate for gonadotropin/IUI treatment is 33%.  
• The cumulative pregnancy rate for clomiphene/IUI treatment for women <35 is 25%.  
• Skipping gonadotropin/IUI in the traditional approach and moving instead directly to IVF yields a significant increase in pregnancy rate and time to conception while decreasing overall costs.  
• Gonadotropin/IUI should not be used for treatment given the increased cost of medication, risk for a multiple gestation and a cumulative pregnancy rate that is only slightly higher compared to clomiphene/IUI.  
• SET will most likely further reduce the overall cost of treatment. |
| **2. Client/Target Population** | • This guideline applies to all couples/individuals with unexplained infertility |

### Clinical Management

| 3. Diagnosis | • Mild male factor, for the purpose of this guideline, may be considered to include cases where the sperm count is >15 million/ml, motility is > 40% and morphology is > 20% |
| 4. Treatment | • Clomiphene Citrate 50-100 mg per day, on cycle days 5-9 or 3-7 may be utilized for women <35. A single IUI should be performed the day after either a positive ovulation predictor kit result or after hCG administration given when the lead follicle is ≥18-20mm. |
| 5. Best Practices and Medical Director Escalation | • All cases of gonadotropin/IUI should be reviewed by the medical director.  
• All cases of clomiphene/IUI for women ≥35 should be reviewed by the medical director.  
• All cases of clomiphene/IUI for women <35 progressing beyond 3 cycles should be reviewed by the medical director.  
• Members with unexplained infertility or mild male factor should be encouraged to pursue IVF with SET as the initial course of treatment. |
6. **Case Example**

A 34 year old member presents with secondary infertility of 2 years duration. This is her second marriage. She has one child from her previous marriage. Her current husband has no children and comes from a large family. The initial infertility evaluation, including a semen analysis, hysterosalpingogram and tests of ovarian reserve were all within normal limits. The member has limited infertility coverage and financial resources and would like to maximize her odds for conception. She states that she would be delighted to have twins.

Although a brief course of clomiphene/IUI might be considered for this member, the odds for conception are no greater than 25% over a cumulative 3-4 cycles. In addition, the utilization of her healthcare benefits for a process with limited success will deplete her resources should she require additional therapy. Increasing the aggressiveness of treatment to the use of gonadotropin/IUI only minimally increases the chance for conception and runs the risk of multiple gestation and increased depletion of financial resources. This member is an ideal candidate for IVF with single embryo transfer. The member would need to be counseled as to the benefits of SET as well as the minimization of the risks of a multiple gestation.

7. **Bibliography**


