Drug Therapy Guidelines

| Medical Benefit | Effective: 6/21/17 |
| Pharmacy- Formulary 1 | x | Next Review: 6/18 |
| Pharmacy- Formulary 2 | x | Date of Origin: 7/00 |
| Pharmacy- Formulary 3/Exclusive | x | Review Dates: 7/12/00, 5/8/01, 1/15/02, 5/6/03, 12/16/03, 6/8/04, 12/16/05, 2/1/06, 10/15/06, 7/20/07, 11/5/07, 12/15/08, 12/09, 9/10, 1/11, 9/11, 9/12, 9/13, 9/14, 6/15, 6/16, 6/17 |
| Pharmacy- Formulary 4/AON | x |

I. Medication Description

Gonadotropin Releasing Hormone (GnRH) Agonists are indicated for the inhibition of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian stimulation. GnRH Antagonists are indicated for inhibition of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian stimulation. Gonadotropins, FSH, or combination of FSH/LH are indicated for stimulation of ovarian follicular growth. Human chorionic gonadotropins (hCG) are indicated for inducing ovulation.

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Agents</th>
</tr>
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<tbody>
<tr>
<td>GnRH Agonists</td>
<td>leuprolide</td>
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<tr>
<td>GnRH Antagonists</td>
<td>Cetrotide®, Ganirelix®</td>
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</tbody>
</table>
| Gonadotropins | *Follitropin alfa*: Gonal-F®, Gonal-F RFF® (non-preferred)  
*Follitropin beta*: Follistim AQ® (preferred)  
*Menotropins*: Menopur®  
*Urofollitropins*: Bravelle® |
| hCG | human chorionic gonadotropin, Novarel®, Ovidrel®, Pregnyl® |
| Progestins | progesterone oil for injection |

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

Contractual limitations may also apply to coverage of injectable fertility medications:

- Artificial means to induce pregnancy such as IVF (in-vitro fertilization), GIFT (gamete intra-fallopian transfer), embryo transfer, and costs related to the processing/acquisition of donor sperm samples may not be covered under a particular contract. In most cases, injectable fertility drugs used in any of these procedures also may not be covered.
- These exclusions can also apply to unmanaged contracts per the NYS Infertility Mandate.
- The NYS Infertility Mandate supports coverage for women 21 through 44 years of age only.
Uses outside of infertility treatment will be considered on a case-by-case basis depending on FDA approval or the corporate Off Label Drug Use Policy and Procedure.

III. Policy

Coverage can be provided when the following criteria are met:

Female Infertility:
- Coverage is requested by an appropriate fertility specialist AND
- Prior to starting sequential hormone therapy for female infertility:
  - An infertility work-up needs to be performed (if not previously done) AND
  - Primary ovarian failure and tubal obstruction are ruled out AND
  - Complete semen analysis is performed and sample is deemed appropriate for use AND
- One of the following apply, based on the medication requested:
  - For coverage of hCG: Medication is being used as part of a covered procedure OR
  - For coverage of gonadotropins: Hypothalamic amenorrhea (HA) is documented OR
  - For coverage of GnRH antagonists, GnRH agonists, progestins, or gonadotropins, at least ONE of the following conditions is met:
    - Documented severe (Stage 4) endometriosis is confirmed OR
    - Documented diminished ovarian function (DOR) such as elevation in 3-day FSH level (above 10-14 mIU/ml) is confirmed OR
    - Documented oral therapy failure (with clomiphene, metformin, or letrozole) is confirmed, as defined by one of the following:
      - Failure to become pregnant after 3 ovulatory cycles of therapy
      - Failure to ovulate after 3 consecutive cycles of therapy
      - Patient experienced intolerable side effects from oral therapy

- Coverage of non-preferred medication Gonal-F® or Gonal-F RFF® can be considered only after a trial with plan-preferred medication Follitropin AQ® has resulted in either a treatment failure or intolerable side effects OR when the following criteria have been met:
  - When requesting coverage of a brand medication for which an A/B rated generic is available, there is sufficient evidence that the use of the A/B rated generic equivalent has resulted in inadequate results AND
  - At least one of the following is met:
    - The plan-preferred medications are contraindicated or will likely cause an adverse reaction by or physical or mental harm to the member.
    - The plan-preferred medications are expected to be ineffective based on the known clinical history and conditions of the member and the member’s prescription drug regimen.
    - The member has tried the plan-preferred medications or another prescription drug in the same pharmacologic class or with the same mechanism of action and such prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event.
The member is stable on the medication selected by their healthcare professional for the medical condition under consideration (where “stable” is defined as receiving the medication for an adequate period of time, have achieved optimal response, and continued favorable outcomes are expected UNLESS the medication was initially selected due to the availability of a drug sample or a coupon card).

The plan-preferred medication is not in the best interest of the member because it will likely cause a significant barrier to the member’s adherence or to compliance with the member’s plan of care, will likely worsen a comorbid condition of the member, or will likely decrease the member’s ability to achieve or maintain reasonable functional ability in performing daily activities.

Male Infertility:

- Coverage is requested by an appropriate fertility specialist AND
- Prior to starting sequential hormone therapy for male infertility:
  - An infertility work-up needs to be performed (if not previously done) AND
  - Complete semen analysis is performed AND
  - Resultant diagnosis is deemed amenable to hormonal infertility treatment AND
- One of the following apply, based on the medication requested:
  - For coverage of hCG: There is a confirmed diagnosis of hypogonadotropic hypogonadism not associated with primary testicular failure
  - For coverage of follitropins:
    - There is a confirmed diagnosis of hypogonadotropic hypogonadism not associated with primary testicular failure AND
    - Pretreatment with hCG has first normalized serum testosterone levels AND
    - Medication must be given in conjunction with hCG AND
    - Coverage of non-preferred medication Gonal-F® or Gonal-F RFF® can be considered only after a trial with plan-preferred medication Follistim AQ® has resulted in either a treatment failure or intolerable side effects OR when the following criteria have been met:
      - When requesting coverage of a brand medication for which an A/B rated generic is available, there is sufficient evidence that the use of the A/B rated generic equivalent has resulted in inadequate results AND
      - At least one of the following is met:
        - The plan-preferred medications are contraindicated or will likely cause an adverse reaction by or physical or mental harm to the member.
        - The plan-preferred medications are expected to be ineffective based on the known clinical history and conditions of the member and the member’s prescription drug regimen.
        - The member has tried the plan-preferred medications or another prescription drug in the same pharmacologic class or with the same mechanism of action and such prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event.
o The member is stable on the medication selected by their healthcare professional for the medical condition under consideration (where “stable” is defined as receiving the medication for an adequate period of time, have achieved optimal response, and continued favorable outcomes are expected UNLESS the medication was initially selected due to the availability of a drug sample or a coupon card).

o The plan-preferred medication is not in the best interest of the member because it will likely cause a significant barrier to the member’s adherence or to compliance with the member’s plan of care, will likely worsen a comorbid condition of the member, or will likely decrease the member’s ability to achieve or maintain reasonable functional ability in performing daily activities.

o For coverage of menotropins:
  • There is a confirmed diagnosis of hypogonadotropic hypogonadism not associated with primary testicular failure AND
  • Pretreatment with hCG has first normalized serum testosterone levels AND
  • Medication must be given in conjunction with hCG

IV. Quantity Limitations

Coverage is available for quantities to afford dosing within FDA-approved dosing regimens.

V. Coverage Duration

Coverage is provided for 6 months and may be renewed.

VI. Coverage Renewal Criteria

Re-evaluation will be required after the initial authorization period and consideration can be granted for extended therapy if:
  • Requested by a fertility specialist with clinical rationale for continuation AND
  • Eligibility for coverage still applies as outlined in the NYS Fertility Mandate

VII. Billing/Coding Information

n/a

VIII. Summary of Policy Changes

• 4/11/11: Follistim® becomes preferred agent over Gonal-F®
• 1/1/12: no changes
• 12/15/12: no changes
• 12/15/13: hCG now covered without failure of oral therapy when used for a covered procedure
• 1/1/15:
  o coverage of hCG clarified to include pretreatment workup and testing
  o appropriate fertility specialist prescriber required for coverage
  o discontinued meds (Lupron, Luveris) removed from policy; clarification of coverage criteria for the
treatment of male infertility made based on FDA approved indication
  o removal of azoospermia as a condition for which male infertility treatment is not covered
• 7/1/15: formulary distinctions made
• 9/15/15: progestins added to policy
• 7/19/16: no policy changes
• 5/3/17: step edit criteria added
• 6/21/17: clarified oral agents requirement

IX. References

1. Al-Inany H. Gonadotropin-releasing hormone antagonists for assisted conception (Cochrane Review)
   847-885.
   with isolated hypogonadotropic hypogonadism. Fertility and Sterility Feb 2002; 77(2):270-27
7. Management of Infertility caused by ovulatory dysfunction, Practice Bulletins-Gynecology #34. Obstet
   Gynecol 2002; 99:347
19. Patient education: Ovulation induction with clomiphene (Beyond the Basics). UpToDate web site.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment
reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with
closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary agent will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.