Infertility Injectables (Cetrotide®, chorionic gonadotropin, Follistim® AQ , ganirelix acetate, Gonal F®/RFF®/Redi-ject®, leuprolide acetate solution, Menopur®, Novarel®, Ovidrel®, Pregnyl®)

(Intramuscular/Subcutaneous)

Document Number: IC-0067

Last Review Date: 02/01/2022

Date of Origin: 11/28/2011

Dates Reviewed: 12/2011, 11/2012, 02/2013, 03/2014, 08/2014, 07/2015, 04/2016, 09/2016, 04/2017, 04/2018, 05/2019, 05/2020, 02/2021, 02/2022

I. Length of Authorization

Coverage will be provided for 3 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

Drug	QL	Frequency
Cetrotide	1 vial	Daily
Follistim AQ	1 cartridge	Per 2 days
ganirelix acetate	1 prefilled syringe	Daily
Gonal-f/RFF	1 vial	Per 2 days
Gonal-f RFF Redi-ject	1 pen	Per 2 days
leuprolide acetate solution	Two 14-day kits	28 days
Menopur	6 vials	Daily for up to 20 days
Novarel/Pregnyl/ human chorionic gonadotropin (hCG)	One 5,000 unit vial	Per 1.25 days
	One 10,000 unit vial	Per 2.5 days
Ovidrel	1 prefilled syringe	Daily; once per cycle

B. Max Units (per dose and over time) [HCPCS Unit]:

Drug	HCPCS	MU	Frequency
Cetrotide	J3490	0.25 mg	Daily
Follistim AQ	S0128/ J3590	4	Daily (female infertility)
		7	Daily (ART)
		6	Weekly (spermatogenesis)
ganirelix acetate	S0132/ J3490	1	Daily

Gonal-f	J3590	4	Daily (female infertility)
		6	Daily (ART)
		4	Three times weekly (spermatogenesis)
Gonal-f RFF/RFF Redi-ject	S0126/ J3590	4	Daily (female infertility)
		6	Daily (ART)
leuprolide acetate solution	J9218	1	Daily
Menopur	S0122/ J3590	6	Daily for up to 20 days (female infertility)
		6	Weekly (spermatogenesis)
Novarel/Pregnyl/human chorionic gonadotropin (hCG)	J0725	10	Daily; once per cycle (female infertility)
		100	90 days (cryptorchidism)
		144	90 days (hypogonadism)
Ovidrel	J3590	250 mcg	Daily; once per cycle

III. Initial Approval Criteria

Coverage is provided in the following conditions:

Infertility in Females † [1-12]

- Patient of child-bearing age; **AND**
- Patient in whom clomiphene alone does not result in fertilization (unless contraindicated or participating in a Assisted Reproductive Technology (ART) program); **AND**
- Patient meets the additional drug-specific criteria below:

Drug	Criteria
– Ganirelix – Leuprolide – Cetrotide	• Patient is undergoing controlled ovarian stimulation (COS)
– Novarel – Pregnyl – hCG	• Used for the induction of ovulation in the anovulatory infertile patient in whom the cause of infertility is not due to primary ovarian failure; **OR** • Patient's treatment is part of an ART program; **OR** • Treatment of corpus luteum dysfunction (i.e., luteal phase support) after receiving ovulation induction protocol with FSH/LH (menotropins)
– Ovidrel	• Used for the induction of ovulation in the anovulatory infertile patient in whom the cause of infertility is not due to primary ovarian failure; **OR** • Patient's treatment is part of an ART program
– Menopur	• Used for the development of multiple follicles as part of an ART program
– Gonal-f/ RFF/RFF Redi-ject	• Used for the induction of ovulation in the anovulatory infertile patient in whom the cause of infertility is not due to primary ovarian failure; **OR** • Patient's treatment is part of an ART program
– Follistim AQ	• Used for the induction of ovulation in the anovulatory infertile patient in whom the cause of infertility is not due to primary ovarian failure; **OR** • Patient's treatment is part of an In Vitro Fertilization (IVF) or Intracytoplasmic Sperm Injection (ICSI) Cycle

Spermatogenesis Stimulation in Males † (Φ Gonal-f only) [2,4,5]

- Patient meets the drug-specific criteria below:

Drug	Criteria
– Follistim AQ – Gonal-f – Menopur	• Primary or secondary hypogonadotropic hypogonadism not due to primary testicular failure; **AND** • Must be used in combination with hCG

Novarel; Pregnyl; human chorionic gonadotropin (hCG) ONLY:

Hypogonadotropic Hypogonadism in Males † [8,9,12]

- Patient has primary or secondary hypogonadotropic hypogonadism; **AND**
- Used alone or in combination with menotropins or follitropin therapy

Prepubertal Cryptorchidism † [8,9,12]

- Patient's condition is not due to anatomical obstruction

† FDA-labeled indication(s); ‡ Compendia recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-12]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include severe hypersensitivity reactions and anaphylaxis, abnormal ovarian enlargement, ovarian hyperstimulation syndrome (OHSS), ovarian torsion, ectopic pregnancy, severe pulmonary complications (e.g., atelectasis, acute respiratory distress syndrome, exacerbation of asthma, etc.), severe vascular complications (e.g., thrombosis, embolism, etc.), ovarian neoplasms, etc.

V. Dosage/Administration [1-12]

Drug	Indication	Dose
Cetrotide	Infertility in females (controlled ovarian stimulation)	0.25 mg subcutaneously once daily during the early- to mid-follicular phase. Administer on either stimulation day 5 or 6 and continue daily until the day of hCG administration.

Drug	Indication	Dose
Follistim AQ	Infertility in females	Up to 250 IU subcutaneously daily until the day of hCG administration.
	Patients undergoing IVF or ICSI Cycle	Up to 500 IU subcutaneously daily until the day of hCG administration.
	Spermatogenesis induction in males	Up to 450 IU subcutaneously per week (in 2 or 3 divided doses).
Ganirelix acetate	Infertility in females (controlled ovarian stimulation)	250 mcg subcutaneously daily during the mid to late portion of the follicular phase and continued daily until the day of hCG administration.
Gonal-f	Infertility in females	Up to 300 IU subcutaneously daily until adequate follicular development is indicated. In general, treatment should not exceed 35 days.
	Patients undergoing ART	Up to 450 IU subcutaneously daily until adequate follicular development is indicated. In general, therapy should not exceed 10 days.
	Spermatogenesis induction in males	Up to 300 IU subcutaneously three times a week in conjunction with hCG.
Gonal-f RFF/ RFF Redi-ject	Infertility in females	Up to 300 IU subcutaneously daily until adequate follicular development is indicated. In general, therapy should not exceed 35 days.
	Patients undergoing ART	Up to 450 IU subcutaneously daily until adequate follicular development is indicated. In general, therapy should not exceed 10 days.
leuprolide acetate solution	Infertility in females (controlled ovarian stimulation)	0.5 to 1 mg subcutaneously once daily
Menopur	Patients undergoing ART	Up to 450 IU subcutaneously daily until adequate follicular development is indicated. Therapy should not exceed 20 days.
	Spermatogenesis induction in males	Up to 150 IU subcutaneously three times per week
Novarel, Pregnyl, & chorionic gonadotropin	Infertility in females	5,000 to 10,000 USP units intramuscularly one day following the last dose of menotropins.
	Hypogonadotropic hypogonadism in males	Intramuscular injection: • 500 to 1,000 USP units three times a week for 3 weeks, followed by the same dose twice a week for 3 weeks; **OR**

Drug	Indication	Dose
		• 4,000 USP units three times weekly for 6-9 months, after which the dosage may be reduced to 2,000 USP units three times weekly for an additional 3 months
	Prepubertal cryptorchidism	Intramuscular injection: • 4,000 USP units three times a week for 3 weeks; **OR** • 5,000 USP units every 2nd day for 4 injections; **OR** • 15 injections of 500 to 1,000 USP units over a period of 6 weeks; **OR** • 500 USP units three times weekly for 4-6 weeks ○ If unsuccessful, another course is begun 1 month later, giving 1,000 units per injection
Ovidrel	Infertility in females & Patients undergoing ART	250 mcg subcutaneously one day following the last dose of the follicle stimulating agent.

VI. Billing Code/Availability Information

HCPCS & NDC:

Drug	Company	HCPCS	1 Billable Unit	Package Size	NDC
Cetrotide	EMD Serono	J3490	N/A	0.25 mg vial	44087-1225
hCG	generic	J0725	1000 USP units	10,000 USP MDV	multiple
Follistim AQ	Merck	S0128/ J3590	75 IU	300 IU cartridge	00052-0313
				600 IU cartridge	00052-0316
				900 IU cartridge	00052-0326
ganirelix	generic	S0132/ J3490	250 mcg	250 mcg pfs	multiple
Gonal-f	EMD Serono	S0126/ J3590	75 IU	450 IU MDV	44087-9030
				1050 IU MDV	44087-9070
Gonal-f RFF	EMD Serono	S0126/ J3590	75 IU	75 IU vial	44087-9005
Gonal-f RFF Redi-ject	EMD Serono	J3590	75 IU	300 IU pen	44087-1115
				450 IU pen	44087-1116
				900 IU pen	44087-1117
leuprolide acetate	generic	J9218	1 mg	14 mg MDV	multiple
Menopur	Ferring	S0122/ J3590	75 IU	75 IU vial	55566-7501
Novarel	Ferring	J0725	1000 USP units	5,000 USP MDV	55566-1502
				10,000 USP MDV	55566-1501
Pregnyl	Merck	J0725	1000 USP units	10,000 USP MDV	00052-0315

Ovidrel	EMD Serono	J3590	N/A	250 mcg pfs	44087-1150
Note: S HCPCS codes are not payable by Medicare					

VII. References

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Appendix 1 – Covered Diagnosis Codes

Cetrotide, ganirelix, Gonal-f/RFF/Redi-ject, leuprolide acetate solution, & Ovidrel

ICD-10 Codes	ICD-10 Description
N97.0	Female infertility associated with anovulation
N97.1	Female infertility of tubal origin
N97.2	Female infertility of uterine origin
N97.8	Female infertility of other origin
N97.9	Female infertility, unspecified

Follistim AQ, Gonal-f, & Menopur

ICD-10 Codes	ICD-10 Description
N46.01	Organic azoospermia
N46.021	Azoospermia due to drug therapy
N46.022	Azoospermia due to infection
N46.023	Azoospermia due to obstruction of efferent ducts
N46.024	Azoospermia due to radiation
N46.025	Azoospermia due to systemic disease
N46.029	Azoospermia due to other extratesticular causes
N46.11	Organic Oligospermia
N46.121	Oligospermia due to drug therapy
N46.122	Oligospermia due to infection
N46.123	Oligospermia due to obstruction of efferent ducts
N46.124	Oligospermia due to radiation
N46.125	Oligospermia due to systemic disease
N46.129	Oligospermia due to other extratesticular causes
N46.8	Other male infertility
N46.9	Male infertility, unspecified
N97.0	Female infertility associated with anovulation
N97.1	Female infertility of tubal origin
N97.2	Female infertility of uterine origin
N97.8	Female infertility of other origin
N97.9	Female infertility, unspecified

Novarel, Pregnyl, & chorionic gonadotropin

ICD-10 Codes	ICD-10 Description
E23.0	Hypopituitarism
E29.1	Testicular hypofunction
N46.01	Organic azoospermia
N46.021	Azoospermia due to drug therapy
N46.022	Azoospermia due to infection
N46.023	Azoospermia due to obstruction of efferent ducts
N46.024	Azoospermia due to radiation
N46.025	Azoospermia due to systemic disease
N46.029	Azoospermia due to other extratesticular causes
N46.11	Organic Oligospermia
N46.121	Oligospermia due to drug therapy
N46.122	Oligospermia due to infection
N46.123	Oligospermia due to obstruction of efferent ducts
N46.124	Oligospermia due to radiation
N46.125	Oligospermia due to systemic disease
N46.129	Oligospermia due to other extratesticular causes
N46.8	Other male infertility
N46.9	Male infertility, unspecified
N97.0	Female infertility associated with anovulation
N97.1	Female infertility of tubal origin
N97.2	Female infertility of uterine origin
N97.8	Female infertility of other origin
N97.9	Female infertility, unspecified
Q53.9	Undescended testicle, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Article (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC