Anthem

Clinical UM Guideline

Subject: Intracytoplasmic Sperm Injection (ICSI)
Guideline #: CG-SURG-35
Status: Revised

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Description

This document addresses the use of intracytoplasmic sperm injection (ICSI) during an infertility treatment cycle. This technique can allow some infertile individuals to attain live birth rates similar to those achieved with in vitro fertilization (IVF) using conventional methods of fertilization.

Note: Please see the following related documents for additional information:

- CG-MED-66 Cryopreservation of Oocytes or Ovarian Tissue
- CG-MED-88 Preimplantation Embryo Biopsy
- CG-SURG-34 Diagnostic Hysteroscopy for Infertility
- LAB.00045 Selected Tests for the Evaluation and Management of Infertility

Clinical Indications

Medically Necessary:

A maximum of three cycles of ICSI per attempted pregnancy is considered **medically necessary** in covered individuals who meet **ANY** of the following criteria:

A. Severe infertility due to **any** of the following semen analysis parameters;
   1. Asthenozoospermia (less than 40% moving sperm) (see definition section); **or**
   2. Oligozoospermia (less than 15 million/ml); **or**
   3. Teratozoospermia (normal morphology in 4% or fewer observed sperm); **or**

B. Previous IVF treatment cycle has resulted in failed or poor fertilization (equal to or greater than 50% of oocytes unfertilized in a prior cycle); **or**
C. Anti-sperm antibodies have been documented; **or**
D. Spinal cord injury individuals requiring electroejaculated sperm; **or**
E. Surgically retrieved sperm (epididymal or testicular); **or**
F. When using cryopreserved sperm for individuals in remission from cancer; **or**
G. When completing preimplantation genetic testing (PGT) (for example, for single gene defect).

Note: Two semen analyses are required prior to categorization of the infertility. A comprehensive semen analysis must be completed prior to infertility treatment cycles.

Not Medically Necessary:

A. More than three cycles of ICSI per attempted pregnancy is considered **not medically necessary.**
B. ICSI is considered **not medically necessary** when the criteria above are not met including, but not limited to all of the following:
   1. Unexplained infertility;
   2. Tubal occlusion;
   3. Advanced maternal age;
   4. Low oocyte yield at retrieval;
   5. Routine insemination of oocytes for IVF.

Coding

The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT	
89280	Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
89281	Assisted oocyte fertilization, microtechnique; greater than 10 oocytes

ICD-10 Diagnosis	
	All diagnoses

When services are Not Medically Necessary:
For the procedure codes listed above when criteria are not met or for situations designated in the Clinical Indications section as not medically necessary.

Discussion/General Information

The American Society of Reproductive Medicine (ASRM) (2020) defines infertility as a disease of the reproductive system with the inability to achieve a successful pregnancy after 12 months or more of regular unprotected intercourse. Infertility can be caused by the inability to ejaculate or an insufficient number of sperm. Work-up for the diagnosis of infertility should include a comprehensive medical, reproductive, and family history and a physical exam. Laboratory testing and diagnostic evaluation may also be appropriate

with emphasis on a systematic, expeditious manner and the least invasive method for diagnosis of infertility.

According to the National Institutes of Health (NIH), approximately one in six couples has difficulty conceiving. It is estimated that infertility related to sperm factors occurs in about 30–40% of these cases. The most common cause for reduced sperm production is an enlarged mass of veins in the spermatic cord within the scrotum. The spermatic cord is made up of veins, arteries, lymphatic vessels, nerves, and the duct that carries sperm from the testes to the seminal vesicles.

Normal semen parameters established by the World Health Organization (WHO) laboratory manual for the examination and processing of human semen (2021) are as follows:

- Semen volume: 1.4 ml or more;
- Sperm concentration: 15 million spermatozoa per ml or more;
- Total sperm number: 39 million spermatozoa per ejaculate or more;
- Total motility (percentage of progressive motility and non-progressive motility): 42% or more motile or 30% or more with progressive motility;
- Vitality: 54% or more live spermatozoa;
- Sperm morphology (normal forms): 4% or more.

The World Health Organization (2021) considers infertility due to sperm factors to be severe when any of the following semen analysis parameters are present:

- Oligozoospermia (less than 15 million/ml)
- Asthenozoospermia (less than 40% moving sperm)
- Teratozoospermia (normal morphology in 4% or fewer observed sperm)
- Positive anti-sperm antibodies
- Spinal cord injury individuals requiring electroejaculated sperm
- Surgically retrieved sperm (epididymal or testicular)

ICSI is a potential component of an IVF cycle. This technique has expanded treatment options for infertility, allowing previously infertile individuals to conceive. The procedure is completed under a microscope using a microscopic glass needle to inject a single sperm directly into the egg. Once the egg is fertilized, it is transferred to the uterus. ICSI is used for individuals who have very poor semen quality or lack of sperm in the semen caused by an obstruction or testicular failure. In some cases, sperm may be surgically extracted from the testicles or epididymis for this procedure.

According to the Society for Assisted Reproductive Technology (2008):

> If a woman gets pregnant naturally, there is a 1.5% to 3% chance that the baby will have a major birth defect. The chances of birth defects after ICSI are rare. Certain conditions that have been associated with the use of ICSI (Beckwith-Wiedemann syndrome, Angelman syndrome, hypospadias, or sex chromosome abnormalities) are thought to occur in far less than 1% of children conceived using this technique. Some of the problems that caused your infertility may be genetic. Therefore, boys conceived with the use of ICSI may have infertility issues as adults.

Smith and colleagues (2010) reported results from a prospective fertility cohort study of 408 couples undergoing cycle-based treatment in the United States. The authors concluded that cycle-based fertility treatments offer clinically significant increases in the pregnancy rate; however, this benefit does not persist indefinitely.

> Couples not achieving a pregnancy with medications alone after two cycles or intrauterine insemination (IUI) after three cycles may be best counseled to pursue a higher level of infertility treatment. Those failing IVF after two cycles may want to consider other treatment strategies, such as donor sperm, donor egg, or further modifications in the IVF or ICSI protocol because additional cycles seem less likely to increase reproductive success as much as earlier cycles.

A 2020 committee opinion of the American Society of Reproductive Medicine and Society for Assisted Reproductive Technology stated that ICSI is a safe and effective treatment for infertility due to sperm factors. The document also stated that ICSI for unexplained fertility, low oocyte yield and advanced maternal age does not improve clinical outcomes. Their opinion included a statement that ICSI may be beneficial for individuals undergoing IVF with PGT, fertilization after *in vitro* matured oocytes and cryopreserved oocytes. The authors concluded that the use of ICSI is a safe and effective therapy for the treatment of infertility related to sperm factors; currently there is no data to support the routine use of ICSI for other causes of infertility.

Definitions

Azoospermia: Lack of live spermatozoa in the semen; classified as obstructive or nonobstructive depending on whether cause is blockage of the tubules or ducts.

Infertility: A disease of the reproductive system with the inability to achieve a successful pregnancy after 12 months or more of regular unprotected intercourse.

Intracytoplasmic sperm injection (ICSI): A fertility treatment that is used to treat sperm related problems by injecting a single sperm into a mature egg. The fertilized egg is then placed in a woman's uterus or fallopian tube.

Oligospermia: Decreased number of spermatozoa in the semen.

Teratozoospermia: The sperm shape is abnormal and incapable of fertilizing the egg, with normal morphology observed in 4% or fewer sperm.

References

Peer Reviewed Publications:

1. Anderson JE, Farr SL, Jamieson DJ, et al. Infertility services reported by men in the United States: national survey data. Fertility and Sterility. 2009; (6):2466-2470.
2. Boulet SL, Mehta A, Kissin DM, et al. Trends in use of and reproductive outcomes associated with intracytoplasmic sperm injection. JAMA. 2015; 313(3):255-263.
3. Kathiresan AS, Ibrahim E, Aballa TC, et al. Comparison of in vitro fertilization/intracytoplasmic sperm injection outcomes in male factor infertility patients with and without spinal cord injuries. Fertil Steril. 2011; 96(3):562-566.
4. Pandian Z, Bhattacharya S, Ozturk O, et al. Number of embryos for transfer following in-vitro fertilization or intra-cytoplasmic sperm injection. Cochrane Database of Systematic Reviews 2009;(2):CD003416.
5. Smith JF, Eisenberg ML, Millstein SG, et al. Fertility treatments and outcomes among couples seeking fertility care: data from

a prospective fertility cohort in the United States. Fertil Steril. 2011; 95:79-84.

Government Agency, Medical Society, and Other Authoritative Publications:

1. The American College of Obstetricians and Gynecologists (ACOG). ACOG Committee on Obstetric Practice Committee on Gynecologic practice. Committee on Genetics. Number 671, September 2016, Reaffirmed 2020. Perinatal risks associated with assisted reproductive technology. Obstet Gynecol. 2016; 128:e61-68.
2. Boitrelle F, Shah R, Saleh R, et al. The sixth edition of the WHO manual for human semen analysis: a critical review and SWOT analysis. 2021. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8706130/pdf/life-11-01368.pdf. Accessed on July 6, 2023.
3. Cooper TG, Noonan E, von Eckardstein S, World Health Organization reference values for human semen characteristics. Human Reproduction Update. 2010; 16, (3)231-245.
4. Practice Committee of American Society for Reproductive Medicine and Society for Assisted Reproductive Technology. Intracytoplasmic sperm injection (ICSI) for non-male factor infertility: a committee opinion. Fertil Steril. 2020; 114:239-245.
5. Practice Committee of the American Society for Reproductive Medicine in collaboration with the Society for Male Reproduction and Urology. Evaluation of the azoospermic male. Fertil Steril. 2008; 90:74-77.
6. Practice Committee of the American Society for Reproductive Medicine in collaboration with the Society for Male Reproduction and Urology. The management of infertility due to obstructive azoospermia. Fertil Steril. 2008; 90:121-124.
7. Schlegel PN, Sigman M, Collura B, et al. Diagnosis and treatment of infertility in men: AUA/ASRM Guideline. October 2020. Available at: https://www.asrm.org/globalassets/_asrm/practice-guidance/practice-guidelines/pdf/diagnosis-and-treatment-of-infertility-in-men-aua-asrm.pdf. Accessed on July 6, 2023.
8. World Health Organization (WHO) Department of Reproductive Health and Research. WHO laboratory manual for the examination and processing of human semen. Sixth edition. 2021. Available at: https://www.who.int/publications/i/item/9789240030787. Accessed on July 6, 2023.

Websites for Additional Information

1. American Society for Reproductive Medicine. Available at:http://www.asrm.org/. Accessed on July 6, 2023.
2. Medline Plus. Male Infertility. Updated August 19, 2015. Available at:http://www.nlm.nih.gov/medlineplus/maleinfertility.html. Accessed on July 6, 2023.

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Intracytoplasmic sperm injection (ICSI)

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

History

Status	Date	Action
Revised	08/10/2023	Medical Policy & Technology Assessment (MPTAC) review. Revised terminology in MN criteria to replace preimplantation genetic diagnosis (PGD) with preimplantation genetic testing (PGT). Updated Discussion/General Information, References and Websites for Additional Information sections.
Reviewed	05/11/2023	MPTAC review. Updated Description, Discussion/General Information, References and Websites for Additional Information sections.
Reviewed	05/12/2022	MPTAC review. Updated Description, Discussion, References and Websites sections.
Revised	05/13/2021	MPTAC review. Removed reference of sex in MN clinical indications section. Updated Description, Discussion, References and Websites sections. Reformatted Coding section.
Reviewed	05/14/2020	MPTAC review. Updated References and Websites sections.
Revised	06/06/2019	MPTAC review. Updated formatting in Clinical Indications section. Clarified MN criteria for severe male factor infertility diagnosed based on semen analysis parameter, teratozoospermia. Updated Description, Discussion, Definition, References and Websites sections.
Reviewed	07/26/2018	MPTAC review. The document header wording updated from “Current Effective Date” to “Publish Date”. Updated References and Websites sections.
Reviewed	08/03/2017	MPTAC review. Updated Discussion, References and Websites sections.
Reviewed	08/04/2016	MPTAC review. Discussion and Websites sections updated. Removed ICD-9 codes from Coding section. Updated formatting in Clinical Indications section.
Revised	08/06/2015	MPTAC review. Clarified medically necessary abbreviation. Discussion and Websites sections updated.
Reviewed	08/14/2014	MPTAC review. Websites updated.
New	08/08/2013	MPTAC review. Initial document development.
