

IBSA Group

Institut Biochimique SA (IBSA)

Company Fact Sheet

IBSA Group is a privately owned pharmaceutical company that was founded in Lugano by a group of Swiss biologists. Today, the company's products are marketed on five continents and over 80 countries. IBSA is a world leader in hyaluronic acid-based products and the largest private pharmaceutical company in Switzerland. IBSA drugs for thyroid hormone replacement therapy are available in a wide range of strengths and formulations which have been developed for better compliance.

Founded 1945 (Current management took over in 1985)

Website www.ibsagroup.com

LinkedIn www.linkedin.com/company/ibsa-sa

Headquarters Via del Piano, 29
CH 6915
Pambio-Noranco, Lugano,
Switzerland



Headquarters in Lugano, Switzerland

Founder and CEO Arturo Licenziati

Employees 1,400

Branches (in order of establishment) Switzerland
Italy
Hungary
China
Slovakia
Turkey
Poland
Scandinavia
Russia
United States of America

Main Markets Switzerland, European Union, Middle East and North Africa, and the Americas

Research and Development 25 factories and laboratories in Switzerland, Italy and China

Manufacturing 11 manufacturing sites located in Switzerland, Italy and China. IBSA manufactures 14 million vials of hormones, 300 million soft gel capsules and 60 million packages of finished products every year.

Strategic Partner Laboratoires Genevrier in France

Patent Portfolio 65 exclusive registered patents. Examples include transdermic patches, which control the release of a drug for periods of time; NAHYCO[®] Hybrid Technology, which thermally stabilizes high molecular weight (H-HA) with low molecular weight (L-HA) hyaluronic acid; and PEARLtec[®], which dissolves the caps' delicate L-T4 active ingredient in a liquid formulation.

Therapeutic Areas

IBSA has a presence in nine therapeutic areas including:

- **Cardiometabolic:** IBSA recently launched new products aimed at assuring broad protection and prevention, in particular through the control of triglycerides and cholesterol, concentrating its efforts on the secondary prevention of heart attacks.
- **Dermatology:** IBSA's portfolio includes innovative products for the treatment of psoriasis and other skin conditions that respond to corticosteroids, as well as hyaluronic acid-based products, used to stimulate the healing process in wounds and burns that are difficult to heal.
- **Dermaesthetic:** A relatively recent product line, based mainly on ultra-pure hyaluronic acid obtained with a patented process.
- **Endocrinology:** IBSA has developed and patented a new process for the manufacture of the first and only liquid levothyroxine formulation for the treatment of hypothyroidism, available in both soft gel capsules in a wide range of doses and single dose vials for oral use. The company is also aiming to consolidate its leadership in the treatment of hypothyroidism with a complete portfolio of products, which includes the thyroid hormone Triiodothyronine (T3) and iodine and selenium supplements, which help the thyroid to function.
- **Osteoarticular:** IBSA's key product for osteoarthritis contains highly purified chondroitin sulphate and is extremely effective in treating pain and functional impairment caused by osteoarthritis. In order to counter pain or reduced mobility due to degenerative processes, post-traumatic diseases or the wear and tear of joint alterations, IBSA has also developed a highly purified hyaluronic acid-based solution in a ready-to-use syringe for intra-articular injection.
- **Pain and Inflammation:** In this therapeutic area IBSA is developing various formulations containing diclofenac epolamine, a well-known anti-inflammatory that effectively treats a wide range of painful disorders. The most widely sold IBSA product in this area is the non-steroidal anti-inflammatory patch (NSAID) for the local treatment of inflammation and acute pain caused by bruising, strains and sprains.
- **Reproductive Medicine:** IBSA's portfolio in this field offers innovative and quality tools for controlled ovarian stimulation and support during the luteal phase in medically assisted reproductive programs (ARP). An innovative platform to identify the possible presence of chromosomal abnormalities in the embryo prior to implantation is another of the recent additions to IBSA's portfolio.
- **Respiratory:** IBSA offers a complete range of mucolytics, recently enriched with hyaluronic acid-based products for various respiratory pathologies.
- **Urology:** IBSA has created a product to counter the effects of interstitial cystitis that, by combining hyaluronic acid, the main component of the epithelium tissue, with chondroitin sulphate, which is found in abundance in the extra-cellular matrix, plays an important role in maintaining the structural integrity of the tissues and can prevent serious damage to the inner lining of the bladder wall, encouraging the healing process. More recently, IBSA has been focusing its interest on male disorders like erectile dysfunction (ED) by developing an innovative sildenafil oral disintegrating film (ODF).

Key Products

Cardiometabolic

- Cardioral[®]
- Colesia[®]
- Omegaoil[®]

Dermatology

- Ialuset[®]/Ialugen[®]
- Ialuset[®] Plus/Ialugen[®] Plus
- Ialuset[®] Gel
- Ialuset[®] Spray
- Betesil[®]

Dermaesthetic

- Viscoderm[®]
- Prophilo[®]
- Aliaxin[®]

Endocrinology

- Tirosint[®]
- Tirosint-Sol[®]

Osteoarticular

- Condrosulf[®]/Chondrosulf[®]/Condral[®]
- Sinovial[®]/Intrage[®]/Yara[®]/Gelsyn-3[™]
- Sinovial[®] HL

Pain and Inflammation

- Flector Tissugel[®]/Flector[®] Patch/Flectormed[®]
- Flector[®] Gel/Flector Effigel[®]/
- Flectorartro[®]
- Akis[®]/Dicloin[®]

Reproductive Medicine

- Fostimon[®]
- Meriofert[®]
- Choriomon[®]
- Prolutex[®]
- Chromoscreen[®]

Respiratory

- Solmucol[®]
- Yabro[®]
- Yabro[®] Spray-Sol

Urology

- Ialuril
- Ialuril[®] Prefil
- Ialuril[®] Soft Gels
- Nebycrom[®]
- Ialuna[®]
- Silandy[®]/Rabestrom[®]/Xybilun[®]/Silvir[®]
- Sildenafil Ibsa

Fundamental Pillars

- People and caring for them
- Innovation. The constant search for more practical and effective therapeutic solutions
- Quality. The main objective in all areas of the business
- Responsibility toward the individual and the environment

Foundations

IBSA Foundation for Scientific Research: An international nonprofit organization set up in Lugano in 2012, which promotes research, spreads scientific culture and educates young students through forums, workshops, study grants and publications. It plays an active role in increasing public awareness of healthcare issues, quality of life and care of the individual.
www.ibsafoundation.org

IBSA Foundation for Children: The main goal of this foundation is the management of the Primi Passi IBSA day-care facility for 30 children ages 4 months to 4 years old, created to offer practical help to IBSA employees in the Canton of Ticino and the local population. www.nidoprimipassi.ch

IBSA Foundation for the Management of the Social Security Fund for Personnel: Founded in 1958, well before it was obliged to do so by law, its aim is to manage assets of the pension fund of IBSA employees in the Canton of Ticino. The social security services offered are superior to those required by Swiss law for company pension funds and guarantee employees financial peace of mind during retirement and in the event of health-related problems.

"Small companies can prosper only if they are smart, that is if they adapt, gradually, to situations that are often insignificant and unprofitable for large pharmaceutical companies. For us, in this field, the road to be taken in order to transform an idea into a tangible and productive project is performing research aimed at practical needs together with the tendency to address the everyday real issues linked to the needs of doctors and patients.

Our goal is to direct our interest toward pharmaceutical substances with already-known properties and to identify their unexploited potential. On the basis of market studies that highlight certain gaps in certain therapeutic areas, we commit ourselves to understanding the real needs of the individual and then find the best and most easy-to-use pharmaceutical forms that improve people's lives."

– Arturo Licenziati, founder and CEO of IBSA, on his entrepreneurial vision

IBSA Pharma Inc.

Founded	2018
Headquarters	Parsippany, New Jersey
Additional Office	Washington, D.C.
CEO	Aldo Donati
Key Products	Tirosint® Tirosint-Sol® (launches in early 2019)
Media Inquiries	info@ibsapharma.com (908) 280-1596

Tirosint[®] (levothyroxine sodium) capsules

Fact Sheet

Product Details	Tirosint (levothyroxine sodium) is the first and only levothyroxine therapy in a liquid gel cap. Levothyroxine is a hormone that is normally produced by the thyroid gland.
FDA Approval	In February 2007, IBSA announced the market release of levothyroxine sodium soft gel capsules in the United States, following U.S. Food and Drug Administration (FDA) approval of the drug and of the Swiss manufacturing site of the drug. ¹
Formulation	Tirosint is produced to exacting standards with the highest-quality ingredients available. The small, golden capsule appears different from other levothyroxine therapies because it only contains four ingredients: levothyroxine, gelatin, glycerin and water. Tirosint does not contain sugars, dyes, alcohol, wheat starch (gluten) or lactose.
Usage	Tirosint is used as replacement or supplemental therapy for hypothyroidism and as the treatment or prevention of various types of euthyroid goiters. Tirosint is used to treat adults and children 6 years of age and older who suffer from hypothyroidism or inadequate levels of thyroid hormone.
Regimen	<p>Tirosint is available in 10 dosage strengths, including an exclusive 13-microgram dose. Tirosint is administered as a single daily dose, preferably one-half to one hour before breakfast. Tirosint should be taken at least four hours apart from drugs that are known to interfere with its absorption. Tirosint capsules cannot be cut or crushed. Due to the long half-life of levothyroxine, the peak therapeutic effect at a given dose of levothyroxine sodium may not be attained for four to six weeks.</p> <p>Tirosint capsules are housed in blister packs to protect them from light and moisture. Blister packs are clearly marked for daily dosing. Tirosint should be protected from light and moisture and stored at 25 degrees C (77 degrees F); excursions permitted to 15-30 degrees C (59-86 degrees F).</p>
Indication	<p>Levothyroxine sodium is L-thyroxine (T4) and is indicated for:</p> <ul style="list-style-type: none">• Hypothyroidism: As replacement or supplemental therapy in congenital or acquired hypothyroidism of any etiology, except transient hypothyroidism during the recovery phase of subacute thyroiditis• Pituitary Thyrotropin-Stimulating Hormone (TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer

¹ Medscape. Published online at: <https://www.medscape.org/viewarticle/552254>

IMPORTANT SAFETY INFORMATION

Warning: Not for the Treatment of Obesity or for Weight Loss

- Thyroid hormones, including TIROSINT, either alone or with other therapeutic agents, should not be used for the treatment of obesity or for weight loss.
- In euthyroid patients, doses within the range of daily hormonal requirements are ineffective for weight reduction.
- Larger doses may produce serious or even life-threatening manifestations of toxicity, particularly when given in association with sympathomimetic amines such as those used for their anorectic effects.

Contraindications

- Uncorrected adrenal insufficiency

Warnings and Precautions

- *Cardiac adverse reactions in the elderly and in patients with underlying cardiovascular disease.* Initiate TIROSINT at less than the full replacement dose because of the increased risk of cardiac adverse reactions, including atrial fibrillation
- *Myxedema coma:* Do not use oral thyroid hormone drug products to treat myxedema coma
- *Acute adrenal crisis in patients with concomitant adrenal insufficiency:* Treat with replacement glucocorticoids prior to initiation of TIROSINT treatment
- *Prevention of hyperthyroidism or incomplete treatment of hypothyroidism:* Proper dose titration and careful monitoring is critical to prevent the persistence of hypothyroidism or the development of hyperthyroidism
- *Worsening of diabetic control:* Therapy in patients with diabetes mellitus may worsen glycemic control and result in increased antidiabetic agent or insulin requirements. Carefully monitor glycemic control after starting, changing, or discontinuing thyroid hormone therapy
- *Decreased bone mineral density associated with thyroid hormone over-replacement.* Over-replacement can increase bone reabsorption and decrease bone mineral density. Give the lowest effective dose
- *Use for the suppression of nontoxic diffuse goiter or nodular thyroid disease:* Use is not recommended in iodine-insufficient patients

Limitations of Use

- Not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients
- Not indicated for treatment of transient hypothyroidism during the recovery phase of subacute thyroiditis

Adverse Reactions

Common adverse reactions with levothyroxine therapy are primarily those of hypothyroidism due to therapeutic overdosage. They include the following:

- *General:* fatigue, increased appetite, weight loss, heat intolerance, fever, excessive sweating
- *Central Nervous System:* headache, hyperactivity, nervousness, anxiety, irritability, emotional lability, insomnia
- *Musculoskeletal:* tremors, muscle weakness
- *Cardiovascular:* palpitations, tachycardia, arrhythmias, increased pulse and blood pressure, heart failure, angina, myocardial infarction, cardiac arrest
- *Respiratory:* dyspnea
- *Gastrointestinal (GI):* diarrhea, vomiting, abdominal cramps, elevations in liver function tests
- *Dermatologic:* hair loss, flushing
- *Endocrine:* decreased bone mineral density
- *Reproductive:* menstrual irregularities, impaired fertility

Adverse reactions in Children

Pseudotumor cerebri and slipped capital femoral epiphysis have been reported in children receiving levothyroxine therapy. Overtreatment may result in craniosynostosis in infants and premature closure of the epiphyses in children with resultant compromised adult height. Seizures have been reported rarely with the institution of levothyroxine therapy.

Hypersensitivity Reactions

Hypersensitivity reactions to inactive ingredients (in this product or other levothyroxine products) have occurred in patients treated with thyroid hormone products. These include urticaria, pruritis, skin rash, flushing, angioedema, various GI symptoms (abdominal pain, nausea, vomiting and diarrhea), fever, arthralgia, serum sickness and wheezing. Hypersensitivity to levothyroxine itself is not known to occur.

For full prescribing information, visit www.Tirosint.com

Tirosint[®]-Sol (levothyroxine sodium) oral solution

Fact Sheet

Product Details	Tirosint-Sol (levothyroxine sodium) oral solution is the first and only FDA-approved levothyroxine therapy available in a liquid form. It is expected to launch in the United States in early 2019.
FDA Approval	In February 2017, IBSA announced that the U.S. Food and Drug Administration (FDA) approved Tirosint-Sol for two conditions: hypothyroidism and TSH suppression in the management of some thyroid cancers.
Formulation	<p>Tirosint-Sol is a liquid solution of levothyroxine, a hormone normally produced by the thyroid. It is a mixture of purified water and glycerol and is free of gluten, lactose, dyes, sugar and alcohol.</p> <p>By having its active principle already dissolved in the solution, the liquid formulation does not therefore require a release phase in the gastrointestinal tract. The absorption of T4 (levothyroxine sodium) in liquid form is faster than in tablets.</p>
Usage	Tirosint-Sol is indicated for the treatment of hypothyroidism in patients who may have difficulty swallowing. It will offer an important new treatment option for clinicians and patients of all ages with hypothyroidism.
Regimen	Treatment schedule consists of a daily oral dosage of LT4 in replacement therapy. Dosages depend on the severity of the hypothyroidism, its etiology and the age, sex and comorbidities of the patient.
Indication	<p>Levothyroxine sodium is L-thyroxine (T4) and is indicated for:</p> <ul style="list-style-type: none">• Hypothyroidism: As replacement or supplemental therapy in congenital or acquired hypothyroidism of any etiology, except transient hypothyroidism during the recovery phase of subacute thyroiditis• Pituitary Thyrotropin-Stimulating Hormone (TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer

IMPORTANT SAFETY INFORMATION

Warnings

- Thyroid hormones, including TIROSINT-SOL, either alone or with other therapeutic agents, should not be used for the treatment of obesity or for weight loss.
- In euthyroid patients, doses within the range of daily hormonal requirements are ineffective for weight reduction.
- Larger doses may produce serious or even life-threatening manifestations of toxicity, particularly when given in association with sympathomimetic amines such as those used for their anorectic effects.

Contraindications

- Hypersensitivity to glycerol
- Uncorrected adrenal insufficiency

Warnings and Precautions

- *Cardiac adverse reactions in the elderly and in patients with underlying cardiovascular disease.* Initiate TIROSINT-SOL at less than the full replacement dose because of the increased risk of cardiac adverse reactions, including atrial fibrillation
- *Myxedema coma:* Do not use oral thyroid hormone drug products to treat myxedema coma
- *Acute adrenal crisis in patients with concomitant adrenal insufficiency:* Treat with replacement glucocorticoids prior to initiation of TIROSINT-SOL treatment
- *Prevention of hyperthyroidism or incomplete treatment of hypothyroidism:* Proper dose titration and careful monitoring is critical to prevent the persistence of hypothyroidism or the development of hyperthyroidism
- *Worsening of diabetic control:* Therapy in patients with diabetes mellitus may worsen glycemic control and result in increased antidiabetic agent or insulin requirements. Carefully monitor glycemic control after starting, changing, or discontinuing thyroid hormone therapy
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For full prescribing information, visit

https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/206977s000lbl.pdf

Hypothyroidism

Fact Sheet

Hypothyroidism is one of the most common chronic disorders worldwide. It is an endocrine disorder with numerous causes resulting in a deficiency in thyroid hormone production.

Population More than 27 million adults have been diagnosed with hypothyroidism.²

Up to 13 million Americans have undiagnosed hypothyroidism.³

About 2 percent of the U.S. population has pronounced hypothyroidism, and as much as 10 percent has subclinical (mild) hypothyroidism.⁴

The condition is most common in women over 40 years of age and in the elderly of both sexes.⁴

Symptoms⁵ Hypothyroidism signs and symptoms may include:

- Fatigue
- Increased sensitivity to cold
- Constipation
- Dry skin
- Weight gain
- Puffy face
- Hoarseness
- Muscle weakness
- Elevated blood cholesterol level
- Muscle aches, tenderness and stiffness
- Pain, stiffness or swelling in your joints
- Heavier than normal or irregular menstrual periods
- Thinning hair
- Slowed heart rate
- Depression
- Impaired memory

Laboratory tests (TSH, FT3 and FT4) are the most common way hypothyroidism is detected.

Hypothyroidism Treatment⁵ Standard treatment for hypothyroidism involves daily use of the synthetic thyroid hormone levothyroxine. This oral medication restores adequate hormone levels, reversing the signs and symptoms of hypothyroidism.

Diagnosis⁵ A diagnosis of hypothyroidism is based on patient symptoms and the results of blood tests that measure thyroid hormone levels. The most commonly used test to detect hypothyroidism measures TSH (thyroid secretion hormone). A high level of TSH may indicate an underactive thyroid. TSH and other tests can be used to determine the amount of levothyroxine that may be necessary to control a patient's hypothyroidism.

² IMS Institute for Healthcare Informatics Report "Medicine Use and the Shifting Costs of Healthcare", 2014, pg. 46

³ Booth, M. Published online at: <http://www.reviewjournal.com/life/health/thyroid-disease-common-us>

⁴ Canaris GJ, Manowitz NR, Mayor G, Ridgeway EC, "The Colorado Thyroid Disease Prevalence Study", Archives of Internal Medicine, 2000; 160: 526- 534

⁵ Mayo Clinic. Published online at: <https://www.mayoclinic.org/diseases-conditions/hypothyroidism/symptoms-causes/syc-20350284>

Causes⁵

Hypothyroidism results when the thyroid gland fails to produce enough hormones. This may result from a number of factors including:

- Autoimmune disease
- Treatment for hyperthyroidism
- Thyroid surgery
- Radiation therapy
- Medication

Less often, hypothyroidism may result from one of the following:

- Congenital disease
- Pituitary disorder
- Pregnancy
- Iodine deficiency