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About Pharm-Sintez

Pharm-Sintez Company was founded in 1997 by Mikhail Evgenievich Nazarenko.

Pharm-Sintez uses advanced technologies for manufacture of medicinal products according to GMP standard. We produce and sell highly effective medicinal products for oncology, neurology, abdominal surgery, obstetrics and gynecology developed by us and in partnership with other companies. Our highly qualified researchers, chemists, technologists and managers are guarantors of quality and the basis for dynamic strategic development of the company.

Pharm-Sintez CJSC is a part of the economic potential of Russia, one of the leading Russian manufacturers of prescription medicinal products in the segment of public procurement. The Company’s total sales exceeded 1.85 billion Rubles in 2015. The portfolio includes high-technology medicinal products. The majority of which are the first generics synthesised in the Russian Federation, and original medicines. Representatives of the company work all over the Russian Federation.

The Company pays key attention to the international partnership and development of new markets. We offer the following areas of cooperation for potential partners:

• R&D and pilot production of medicines;
• Contract manufacturing; In-license and Out-license projects;
• Registration of finished dosage forms and pharmaceutical substances in Russia, Kazakhstan, Belarus, and Uzbekistan;
• Promotion and sales of registered medicinal products all over Russia and in the EEU countries.
Catalogue
Rezoscan, $^{99m}$Tc
**Trade name:** Rezoscan, $^{99m}$Tc  
**International nonproprietary name:** Zoledronic acid.  
**Pharmaceutical form:** Lyophilisate for preparation of solution for intravenous administration.

A new original radiopharmaceutical product based on bisphosphonate of the last generation (zoledronic acid) for performing scintigraphy and single-photon emission computed tomography (SPECT) of the skeleton. The product is used for detection of foci of pathological changes in the skeleton of various genesis and extension.

**Indications:**

1. Detection of foci of pathological resorption and areas of increased metabolism in the bone tissue in different pathological processes in the skeleton (osteomyelitis, bone and joint tuberculosis, different bone and joint degenerative processes including arthritis and arthroses of diffuse origin);

2. Detection and identification of lytic, mixed and blast metastases in the skeleton in malignant tumors of different genesis and extension;


**Examination procedure:**

The examination is conducted by using gamma-chamber by the method of scintigraphy of the whole body in the anterior and posterior projections 1-2 hours after administration of the product with mandatory preliminary emptying of the urinary bladder.

*Rezoscan is the only radiopharmaceutical based on zoledronic acid.*
Octreotide, $^{111}\text{In}$
**Trade name:** Octreotide, $^{111}$In  
**International nonproprietary name:** Pentetreotid.  
**Pharmaceutical form:** Lyophilisate for preparation of solution for intravenous administration.

The only in Russia receptor-specific radiopharmaceutical product for SPECT studies of the basic tumor lesion and its metastases which have receptors of somatostatin.

The diagnostics with Octreotide $^{111}$In provides valuable clinical information for diagnosing, determining the receptor status of the tumor, choosing the tactics of therapy, evaluating the clinical effect of therapy.

**Indications:**
For radionuclide diagnostics of tumors with high density of somatostatin receptors (neuroendocrine tumors, tumors of the central nervous system, breast cancer, small cell carcinoma of the lung), and also for determination of the receptor status of the tumor to predict the clinical effect of treatment with Octreotide.

**Method of administration and doses:**
The product is administered as bolus in a dose of 111MBc for planar scintigraphy and 222MBc for SPECT. The obtained solution is intended for 1 patient and should be used within 6 hours after preparation.

* Octreotide $^{111}$In is the first Russian pentetreotid.
Buserelin-depo
Trade name: Buserelin-depo

International nonproprietary name: Buserelin.

Pharmaceutical form: Iyophilisate for preparation of suspension with extended release for intramuscular administration.

The first Russian analogue of gonadotropin-releasing hormone (GnRH).

Buserelin-depo, being a synthetic analogue of GnRH, is similar by its’ structure and pharmacological characteristics to natural hormones but possesses a greater metabolic stability and biological activity. The monthly administration of Buserelin-depo results in inhibition of secretion of gonadotropins and blockade of the hypothalamus-pituitary-testicle axis due to which the level of sex steroids decreases to the postcastration values. “Drug-induced pseudomenopause” and “pharmacological castration” occurring during prolonged use of Buserelin have the short-term and reversible character. Buserelin-depo possesses the direct antiproliferative action due to suppression of synthesis of receptors to GnRH in cells of endometrium. Subsequently this leads to suppression of autocrine stimulation of endometrial proliferation.

Indications:

• Hormone-dependent prostate cancer;
• Breast cancer;
• Endometriosis (pre- and postoperative periods);
• Uterine myoma;
• Hyperplastic processes of endometrium;
• Treatment of infertility (while implementing the program of extracorporeal fertilization).

* Buserelin depo is the first Russian buserelin.
Buserelin-spray
Trade name: BUSERELIN  
International nonproprietary name: Buserelin  
Pharmaceutical form: nasal spray  
Analog of gonadotropin-releasing hormone.

Nasal spray 17.5 mL.

The product is a synthetic analogue of natural gonadotropin-releasing hormone (GnRH). At nasal administration the product is completely absorbed through the nasal mucous membrane. It is excreted in the breast milk in insignificant amounts. The half-life is about 3 hours.

Indications:

Hormone-dependent pathology of the reproductive system due to absolute or relative hyperestrogenism: endometriosis (pre- and postoperative periods), uterine myoma, hyperplastic processes of the endometrium, treatment of infertility (while implementing the program of extracorporeal fertilization).

* Buserelin depo is the first Russian buserelin.
ActiGel
Trade name: Multi-Gyn® ActiGel
International nonproprietary name: None
Medical Device Product
Pharmaceutical form: gel 50 mL

Composition: Active ingredients: reticulate copolymer of galactoarabinan and polyglucuron acid*, xanthan gum, glycerin, caprylyl glycol – pH 4.1.
* - 2QR complex: patented complex of bioactive polysaccharides.

Due to the action of 2QR-complex of polysaccharides, ActiGel facilitates blocking of the mechanism of fixation of pathogenic bacteria, preservation of natural microflora of the vagina, improvement of the condition of the mucous membrane and recovery of optimal pH.

Used for prophylaxis and in complex treatment of bacterial vaginosis
• Decreases unpleasant odor and discharges.
• Exerts alleviating action in itching and irritation.
• Contributes to prevention of vaginal discomfort.

Gel Multi-Gyn ActiGel is safe at use in the period of pregnancy and breast feeding.

* ActiGel – the only product medical device with the 2 QR-complex
Manufactured by:
BioClin BV
Tamsulon
**Trade name:** Tamsulon®-FS  
**International nonproprietary name:** tamsulosin  
**Pharmaceutical form:** prolonged action capsules  
Active ingredient: Tamsulosin hydrochloride 0.4 mg

Tamsulosin is a specific blocker of postsynaptic $\alpha_1^A$-adrenoreceptors located in the smooth muscles of the prostate, urinary bladder neck and the prostatic part of the urethra. Blockade of $\alpha_1^A$-adrenoreceptors by tamsulosin leads to a decrease of tone of the smooth muscles of the prostate, urinary bladder neck and the prostatic part of the urethra and improvement of outflow of the urine. Concomitantly there occurs a reduction of both symptoms of emptying and symptoms of filling conditioned by increased tone of the smooth muscles and detrusor hyperactivity in benign hyperplasia of the prostate.

**Indications:**
Treatment of dysuric disturbances in benign hyperplasia of the prostate.

*Tamsulon – the first Russian generic of tamsulosin*
Octreotide
Trade name of the product: Octreotide
International nonproprietary name: Octreotide.
Pharmaceutical form: solution for intravenous and subcutaneous administration.

Active ingredient:
Octreotide 50 mcg or 100 mcg

Indications:
For treatment of acute pancreatitis, for prevention and treatment of complications after operations on the organs of the abdominal cavity, for stopping of ulcerative bleedings and bleedings from varicosities in patients with liver cirrhosis.

* Octreotide is the first Russian analogue of somatostatin.
Octreotide-Depo
Trade name: OCTREOTIDE-DEPO

International nonproprietary name: Octreotide.

Pharmaceutical form: Lyophilisate for preparation of suspension for intramuscular administration of prolonged action.

Active ingredient: Octreotide 10,0 mg 20,0 mg 30,0 mg

Octreotide is a synthetic octapeptide being a derivative of natural hormone somatostatin and possessing similar pharmacological effects but with a significantly greater duration of action.

Octreotide-depo is the first Russian analogue of somatostatin manufactured by Pharm-Sintez in the pharmaceutical form with extended release for intramuscular administration, which provides maintenance of stable therapeutic concentrations of Octreotide in blood for 4 weeks. Octreotide is an agent of pathogenetic therapy in tumors which actively express receptors to somatostatin. The product suppresses the pathologically increased secretion of growth hormone (GH) and also peptides and serotonin produced in the gastroenteropancreatic endocrine system.

Indications:

In therapy of acromegaly: when an adequate control of manifestations of the disease is performed by means of subcutaneous administration of Octreotide; in the absence of sufficient effect from surgical treatment and radiation therapy; for preparation for surgical treatment; for treatment between the courses of radiation therapy until development of persistent effect; in inoperable patients.

In therapy of endocrine tumors of the gastrointestinal tract and pancreas: carcinoid tumors with phenomena of the carcinoid syndrome; insulinoma. VIPoma; gastrinomas (Zollinger-Ellison syndrome); glucagonomas (for control of hypoglycemia in the preoperative period, and also for maintenance therapy); somatoliberinoma (the tumor characterized by hyperproduction of the releasing factor of the growth hormone).

Treatment of patients with secreting and non-secreting diffuse (metastatic) neuroendocrine tumors of the jejunum, ileum, caecum, ascending colon, transverse colon and the vermiform process, or metastases of neuroendocrine tumors without the primarily detected lesion.

In therapy of hormone resistant cancer of the prostate: together with combined therapy against the background of surgical or medical castration.

In prevention of development of acute postoperative pancreatitis during extensive surgeries on the abdominal cavity and during thoracoabdominal interventions (including cancer of the stomach, esophagus, colon, pancreas, primary and secondary damage of the liver).

* Octreotide depo is the first Russian analogue of somatostatin.
Octreotide
300 mcg/mL, 600 mcg/mL
**Trade name:** Octreotide 300 mcg/mL, 600 mcg/mL  
**International non-proprietary name:** Octreotide  
**Pharmaceutical form:** solution for intravenous or subcutaneously administration  
**Active ingredient:** Octreotide acetate equivalent to of 300 mcg or 600 mcg octreotide  
**Description:** clear, colourless liquid without odour

**Indications:**  
Acromegaly;  
Secreting endocrine tumours of GIT and pancreas;  
Carcinoid tumours with the presence of carcinoid syndrome;  
WDHH-syndrome;  
Glucagonomas;  
Zollinger-Ellison syndrome;  
GRFomas;  
Arrest of bleeding and prophylaxis of relapses of bleeding from varicose veins of the oesophagus and stomach in patients with liver cirrhosis.

*Octreotide 600 mcg/mL – unique dosage of octreotide*
Rezorba
**Trade name of the product:** Rezorba  
**International nonproprietary name:** zoledronic acid.  
**Pharmaceutical form:** Lyophilisate for preparation of solution for infusions.  
Active ingredient: zoledronic acid monohydrate 4.26 mg (equivalent to anhydrous zoledronic acid 4.0 mg)

Rezorba is the first Russian zoledronic acid manufactured by Pharm-Sintez. It belongs to the class of high effective bisphosphonates which possess the selective action on bone tissue. Suppresses the activity of osteoclasts, does not exert adverse effect on the formation, mineralization and mechanical properties of bone tissue. Possesses the direct anti-tumor properties which provide effectiveness in bone metastases. At hypercalcemia caused by a tumor it decreases the calcium concentration in serum. Rezorba may be combined with chemotherapy, radiation therapy methods and any variants of hormone treatment.

**Indications:**

- **Hypercalcemia** (concentration of serum calcium corrected by albumin $\geq 12$ mg/dL or $3 \text{ mmol/L}$) induced by malignant tumors.

- **Metastatic lesions of bones in malignant solid tumors and multiple myeloma** (to decrease the risk of pathological fractures, compression of the spinal cord, tumor-induced hypercalcemia and a reduction of the need in radiation therapy).

*Resorba is the first Russian zoledronic acid.*
ИМАТИБ
Иматиниб 100 мг
КАПСУЛЫ
120 капсул
Для приема внутрь

Imatib
Trade name of the product: Imatib  
International nonproprietary name: Imatinib.  
Pharmaceutical form: capsules.

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<th>Active component:</th>
<th>Dosage</th>
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<td>Imatinib</td>
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Imatinib is an inhibitor of protein tyrosine kinase. It inhibits the enzyme Bcr-Abl-tyrosine kinase on the cellular level, in vitro and in vivo. Suppresses selectively proliferation and causes apoptosis of Bcr Abl positive cell lines, and also young leukemia cells in Philadelphia chromosome-positive chronic myeloleukemia and in acute lymphoblastic leukemia.

Indications:

- Newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in children and adults;
- Philadelphia chromosome-positive (Ph+) CML in the chronic phase at failure of the previous therapy with interferon alpha or in the acceleration phase or blast crisis in children and adults;
- Newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) in adult patients in combination with chemotherapy;
- Relapsing or refractory Ph+ALL in adult patients as monotherapy;
- Myelodysplastic/myeloproliferative diseases (MDD/MPD) related to genetic transformations of growth factor receptor in adult patients;
- Systemic mastocytosis (SM) in adult patients with the absence of D816V c-Kit mutation or with the unknown c-Kit mutation status;
- Hypereosinophilic syndrome and/or chronic eosinophilic leukemia in adults with positive or negative abnormal FIP1L1-PDGRF alpha-tyrosine kinase;
- Inoperable and/or c-Kit (CD 117)-positive metastatic malignant gastrointestinal stroma tumors in adult patients;
- Adjuvant therapy of c-Kit (CD 117)-positive gastrointestinal stroma tumors in adult patients;
- Inoperable, relapsing and/or metastatic protruding dermatofibrosarcoma in adult patients
Cabecyn
Trade name: Cabecyn
International nonproprietary name: capecitabine
Pharmaceutical form: film-coated tablets
Active ingredient: capecitabine – a derivative of fluoropyrimidine carbamate, oral cytostatic activating in tumor tissue and exerting the selective cytotoxic action on it. In vitro capecitabine does not possess the cytotoxic effect. In vivo it is converted into fluorouracil (FU), which undergoes further metabolism. The formation of FU takes place predominantly in tumor tissue under the action of tumor angiogenic factor – thymidine phosphorylase that minimizes the systemic impact of FU on healthy tissues of the body.

Indications:

Breast cancer
- combined therapy with docetaxel of locally advanced or metastatic breast cancer in inefficacy of chemotherapy including a product of anthracyclin group;
- monotherapy of locally advanced or metastatic breast cancer resistant to chemotherapy with taxines or products of anthracyclin group in the presence of contraindications for their use.

Colorectal cancer
- adjuvant therapy of stage III colon cancer after surgical treatment;
- therapy of metastatic colorectal cancer.

Stomach cancer
- first-line therapy of diffuse stomach cancer.
Миланфор
Trade name of the product: Milanfor
International nonproprietary name: bortezomib.
Pharmaceutical form: lyophilisate for preparation of solution for intravenous administration.
Active ingredient: Bortezomib 3.5 mg.

Milanfor is the first Russian Bortezomib manufactured by Pharm-Sintez.

Bortezomib is a high selective reversible inhibitor of the activity of proteasome 26S; it is a modified boric acid.

Proteasome 26S is present in the nucleus and cytosol of all eukaryotic cells and is the key component which catalyzes degradation of the main proteins involved in control of the life cycle of cells. Bortezomib inhibits chymotripsin-like action of proteasome, causes inhibition of proteolysis and leads to apoptosis.

Myeloma cells are almost 1000 times more susceptible to apoptosis caused by bortezomib than normal cells of the plasma.

Indications:

- multiple myeloma (included into combination therapy of line 1);
- multiple myeloma in the patients earlier receiving therapy of line 1 (therapy of line 2);
- mantle cell lymphoma in the patients earlier receiving therapy of line 1.

*Milanfor is the first Russian bortezomib.
Целлекс
Раствор для подкожного введения 0,1 мг/мл
5 ампул по 1 мл
Sterильно

Cellex
**Trade name:** Cellex®

**International nonproprietary name:** absent.

**Pharmaceutical form:** solution for subcutaneous administration.

**Composition per 1 mL:**
Active ingredient: Cellex® substance-solution calculated with reference to protein 0.100 mg

Cellex is a novel product consisting of the balanced and stable mixture of biologically active proteins and polypeptides which possess the aggregate multifunctional action.

The product activates secondary neuroprotection due to stimulation of the processes of synaptogenesis, restoration of signals of autophagia, improvement of tissue immune regulation with inhibition of immunogenic cytotoxicity of macrophages. This is accompanied by tissue specific and systemic reparative action of the product with restoration of the regenerative and reparative potential of the brain cells, a decrease of the number of damaged cells and extent of perifocal edema in the area of penumbra (makes it possible to achieve a significant limitation of the focus of necrosis of the cerebral tissue) with restoration of microcirculation and total perfusion.

The restoration and regulatory stimulation of different compartments of CNS with the systemic action of growth factors, differentiation and signal molecules provides a reduction of the period of recovery and rehabilitation of patients with lesions of the central and peripheral nervous system of the vascular genesis and restoration of motor, sensory and cognitive functions.

The therapeutic effect usually develops 3-5 days after the beginning of the use of the product.

**Indications:**
Acute disorders of cerebral circulation in the acute and early rehabilitation period in the course of disease as a part of complex treatment.

* Cellex is a unique product in its class.
Theranostics*

Theranostics in management of neuroendocrine tumors, peptide receptor platforms for radionuclide diagnostics and therapy

Membrane of tumor cell expressing somatostatin receptors

Peptide receptor platform

Therapeutic isotope

Diagnostic isotope

*Theranostics (theranostics) [Gr. thera (peia) - caring, care, treatment, and (diag) nostikos - can recognize] a new approach pharmaceutical companies, consisting in a complex therapeutic problem solving - the simultaneous creation of medicine and the appropriate means of early diagnosis of the disease.
Theranostics

Theranostics in management of metastatic lesions in the skeleton, **bisphosphonate platforms** for radionuclide diagnostics and therapy

Specific accumulation in a metastasis is provided by target carrier – zoledronic acid which provides accumulation of isotope in a metastasis

**ZOLEREN, $^{188}\text{Re}$**
(ZOLEDRONIC ACID, 4 mg + 45.0 MBq/kg)
Radiopharmaceutical agent for systemic radionuclide therapy – the only agent in the world with double radiometabolic action

Absorbed dose for a metastasis 5-44 Gy

**REZOSCAN, $^{99m}\text{Tc}$**
(ZOLEDRONIC ACID, 0.4 – 1.5 mg)
Radiopharmaceutical agent for diagnostics of metastatic lesions in the skeleton by methods of single photon emission tomography and planar scintigraphy of the skeleton
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