RECORDATI S.p.A.

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PHARMA CHEMICALS

For almost 100 years

EMPLOYEES
>4,450

REVENUE 2023
2,082.3
Million Euros

MARKETS
~150
Across EMEA, Americas and APAC regions

RECORDATI GROUP AT A GLANCE

With its beginnings in a family-run pharmacy in Correggio, Italy in the 1920s, Recordati is now a global pharmaceutical group, listed on the Italian Stock Exchange.

We are a group of like-minded, passionate individuals who go to extraordinary lengths for our partners, customers, investors, and the people we serve across the globe.

We develop and commercialise medicines to serve people living with common diseases, as well as those living with some of the rarest.

GROUP HIGHLIGHTS

2 pharmaceutical **chemical** plants.
7 pharmaceutical **manufacturing** plants,
1 packaging and **distribution** centre dedicated to products for Rare Diseases.

Ecovadis 2024

GOLD | Top 5% ecovadis Sustainability Rating JUN 2024

We pursue a sustainable growth model by integrating social and environmental aspects into our corporate strategy.

We work on **reducing our environmental impact** and continuing to fight against climate change, increasing our efforts towards a circular economy and promoting waste reduction initiatives.

In 2023, **100% of electricity** purchased for Group plants comes **from renewable sources**, in countries where this was possible.

[This figure excludes Tunisia, where renewable energy is not available]

We have established a roadmap for **installing renewable energy production systems** at our main plants.

PHARMA CHEMICALS KEY DATA

1926

The manufacturing of active ingredients has been closely linked with pharmaceutical activities since the beginning of Recordati's history: as early as 1926, Giovanni Recordati transformed the family-run pharmacy and adjoining chemical laboratory into the "**Laboratorio Farmacologico Reggiano**", resulting in the birth of Recordati as a Chemical Pharmaceutical Industrial Company.

1952

Pharmaceutical production and research moved from Correggio (RE, Italy) to Milan. Since then, **innovation** and **internationalization** have always been Recordati's objectives.

1963

The new pharmaceutical chemicals plant in Campoverde di Aprilia is born, replacing the chemical plant in Correggio. Here, Recordati produced and continues to produce flavoxate, the first Italian drug to receive FDA approval in the US.

Under the new name **Recordati Industria Chimica e Farmaceutica**, the company grew internationally with products such as **flavoxate**, **fenticonazole** and **lercanidipine** and outlined its development strategy.

2005

Recordati establishes the **new pharmaceutical chemical plant in Cork** (Ireland) to guarantee adequate and continuous supplies of active ingredients and in **2007 enters into the Rare Diseases sector.**

Today our pharmaceutical chemicals business is an important company asset, exporting around **90% of its production of APIs and intermediates**, **selling directly in over 50 countries** and manufacturing intermediates and active ingredients for Recordati pharmaceutical brands.

Recordati is also engaged in the exclusive and custom manufacturing business, serving **major innovator and big pharma organizations**.

01.
PLANTS AND FACILITIES

CAMPOVERDE

KEY FIGURES
- **Total Area: 375,000 m²**
- **Building Area: 35,000 m²**
- **Output: 600 MT/y**
- **In-process intermediates: more than 4,000 MT/y**

MANUFACTURING EQUIPMENT
- **Reactors: 820 m³, glass lined (30%) and stainless steel (70 %), from 0.4 m³ to 25 m³ each**
- **Total storage volume: 2,600 m³**

CORK

KEY FIGURES
- **Total area: 43,400 m²**
- **Production Area: 2,100 m²**
- **Production: Lercanidipine API**

MANUFACTURING EQUIPMENT
- **Reactors: 17 m³ (35% glass lined; 65% stainless steel)**
- **Storage vessels: 395 m³ (60% solvents; 40% utilities)**

THE CAMPOVERDE SITE IS FOCUSED ON SUPPLYING HIGH QUALITY ACTIVE PHARMACEUTICAL INGREDIENTS AND INTERMEDIATES TO THE PHARMA MARKET AND TO RECORDATI'S PHARMACEUTICAL OPERATIONS, IN THE FRAMEWORK OF A STRONG VERTICAL INTEGRATION.

It was one of **the first Italian chemical pharmaceutical plants authorized to export to the United States**, and it is the manufacturer of flavoxate HCl, the first Italian synthetic drug to be approved by the U.S. Food and Drug Administration. Many different therapeutical areas are covered, in both Specialty & Primary Care, with relevant contributions in the field of Rare Diseases treatment. An outstanding level of technical expertise, combined with a dynamic and purpose-oriented organization, enables the full management of a reliable production chain, from raw materials supply to finished API. The wide range of technologies and the extensive know-how acquired over the years allow the Campoverde plant to produce to high quality standards. All operations are carried out **firmly integrating environmental, social, and governance (ESG) activities into our business strategy** and ensuring a positive relationship with the local community, located in the beautiful green fields south of Rome.

CAMPOVERDE CORE CAPABILITIES

- A wide range of competencies in the field of organic synthesis enables **quick and effective study of new processes** from research to final industrialisation.
- The Research and Development department is fitted with an **extremely versatile pilot plant** equipped for c-GMP compliant scale-up tests and small scale productions.
- The site has **expertise and technical capabilities** enabling execution of many different types of chemical reactions and purifications, safely utilizing highly dangerous chemicals.
- All operations are carried out in compliance with current **Good Manufacturing Practices** (cGMP) and to the most stringent international environmental regulations.
- The Plant Environmental Management System is certified by Det Norske Veritas Italy according to the **ISO 14001**: **2015 standard**.
- Investments are continuously made to enhance the technological and production capacity of the plant; over the last decade, these projects have resulted in the installation of more than **25 new reactors, a latest generation three-stage distillation unit for liquids unstable at high temperatures, two thin film evaporators, four filters for the isolation of solid products and an anti-acid dryer**.
- Specific sustainability projects are implemented to continuously **reduce the environmental footprint of the site**, by pursuing reduction of emissions and resource utilization.
- Recordati has started a three-year project aimed at the installation of a **10 MW photovoltaic power generation facility** and the downsizing of the methane-based cogeneration unit currently in use. These measures will provide a **significant reduction of Recordati's carbon footprint**.

CORK CORE CAPABILITIES

- Our plant in Cork is dedicated to the continuous supply of a single active ingredient, **Lercanidipine** HCl, fully researched and developed by Recordati.
- The manufacturing process is controlled through an automated systems that allows maintaining the **highest Safety and Quality standards**.
- The site operates in accordance with **GMP** (Good Manufacturing Practices).
- It received the **2012 National Energy Efficiency Award** promoted by the sustainable Energy Authority of Ireland (SEAI) and in 2013 received the **European Energy Efficiency Award** promoted by the Chemical European Federation Industry Council (CEFIC).
- An extension completed in 2016 allowed for additional space in the **Quality Control Laboratory** and in the Administration Building.
- **Photovoltaic panels** for the generation of electricity were installed in 2022 for a total area of 1,100 sq.m. **providing 10% of the site electricity demand**.

02. MANUFACTURING

A HUGE VARIETY OF VERTICALLY INTEGRATED OPERATIONS ENSURE TOP QUALITY PRODUCTS THAT START FROM VERY SIMPLE RAW MATERIALS BY MANAGING EXTREMELY COMPLEX CHEMICAL PROCESSES.

One of Recordati's most important manufacturing expertise areas are the capabilities related to the utilization of substances requiring special risk management measures and carrying out reactions in extreme conditions, such as high temperatures and pressures. A constant effort is made to keep all production lines and areas at the forefront of technology, with relevant investments aimed to continuously improve **QHSE management** and to **develop production capacity, efficiency and flexibility**.

MANUFACTURING FACILITIES AND UTILITIES

- 4 Synthesis Departments, producing intermediates and APIs wet cakes
- 1 Finishing Department, in charge of drying, milling, micronising and packaging intermediates and products
- Multipurpose Equipment, with a high level of flexibility
- Waste Water Treatment Plant, performing chemical-physical and biological processes
- Thermo-electrical Power Station, able to supply the entire energy requirements of the site
- Reverse Osmosis System for Purified Water
- Internal nitrogen production, for blanketing equipment with no significant risks of operations interruption
- A large variety of cooling and heating fluids, covering a wide range of operating conditions

PROCESS CAPABILITY

- Oxidations
- Chloromethylations
- Friedel-Crafts and Fries reactions
- High temperature condensations
- High and low pressure catalytic reductions
- Alkylations and dealkylations
- Cyanations
- Halogenations
- Phase-transfer catalytic reactions
- Esterifications
- Amidations
- Hydrogenations and dehydrogenations
- High OEB chemicals in small scale
- Medium to high vacuum distillations for thermally sensitive compounds

03.

QUALITY ASSURANCE

RECORDATI'S PHARMACEUTICAL CHEMICALS BUSINESS UNIT IS COMMITTED TO ESTABLISHING AND MAINTAINING A QUALITY SYSTEM THAT MEETS INTERNATIONAL GUIDELINES.

Recordati's Pharmaceutical Chemicals Business Unit is committed to establishing and maintaining a Quality System that meets international guidelines, including – but not limited to – ICH Q7 "**Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients**", Eudralex Volume 4 Good Manufacturing Practice (GMP) Guidelines: Part II - "**Basic Requirements for Active Substances used as Starting Materials**", Part III "GMP - related document", Annex 11 "Computerized systems", CFR 21 part 11 and ANVISA Resolution RDC 654/2022. Recordati is recognised as a leader in several high purity **APIs** and a reliable provider for compendial reference standards. The company's cooperation with the pharmacopoeia expert committees began **more than 20 years ago** with the proposal for the compendial monographs for the APIs developed by Recordati and, more recently, the company cooperated in the revision of several compendial monographs to introduce highly selective methods for related substances determination.

GMP AND EHS COMPLIANCE

- Approved by the Italian Ministry of Health since 1964
- Last AIFA inspection was held in September 2022
- FDA inspected since 1969
- Last FDA Inspection was held in June 2018
- Approved by Korean Ministry of Health since 2006
- Accredited by Japanese Ministry of Health since 2009
- Last renewal of the PMDA accreditation in September 2019
- Approved by the Brazilian Ministry of Health since 2011
- Last ANVISA inspection in 2015
- UNI EN ISO 14001 Certification by DNV since 2003
- Integrated Pollution Prevention and Control Autorisation (AIA) according to European Directive 2010/75/UE
- Compliant to Directive 2012/18/UE *"on the control of major-accident hazards involving dangerous substances"*

AIFA AGENZIA ITALIANA DEL FARMACO

Pmda Pharmaceuticals and Medical Devices Agency, Japan

FDA U.S. FOOD & DRUG ADMINISTRATION

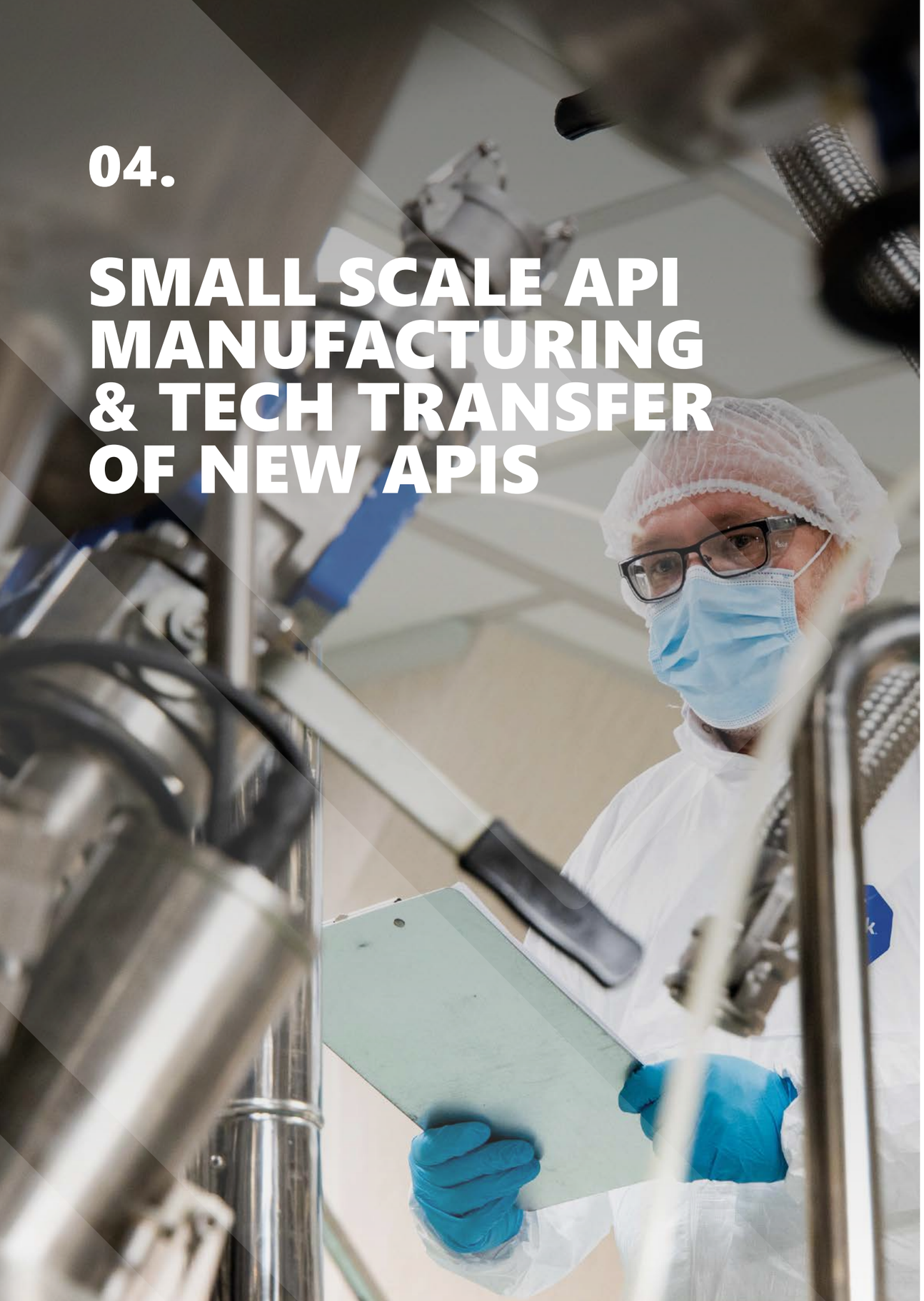
EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH

edqm European Directorate for the Quality of Medicines & HealthCare

ICH Member

ANVISA Agência Nacional de Vigilância Sanitária

KFDA Korea Food & Drug Administration 식품의약품안전청



04.

SMALL SCALE API MANUFACTURING & TECH TRANSFER OF NEW APIS

THE R&D DEPARTMENT'S MAIN ROLE IS SUPPORTING RECORDATI BUSINESS DEVELOPMENT THROUGH THE FINE-TUNING OF NEW PRODUCTS AND THE MANUFACTURING OF APIS BOTH FOR RECORDATI AND OTHER PHARMACEUTICAL COMPANIES.

To this end, a complete set of manufacturing facilities is available both at lab and pilot plant scale, combined with the use of **suitable software for process development and tech transfer from the lab to the production plant**.

SMALL SCALE CGMP MANUFACTURING FACILITIES: KG-LAB

- Small scale production in cGMP compliance
- GMP Kg-Lab
- GMP isolator for API manufacturing: handling of Toxic, air/moisture sensitive compounds and HPAPI (OEL< 1 µm/ m^3)
- Isolator Total Capacity: 25 L
- API batch size: from 200 gr up to 1 Kg
- Kg-lab Glass reactors: 0,5 to 10 L
- Operative conditions: -90°C to 220°C
- GMP kg-lab Vacuum-Filter/Dryer (100 mL to 1000 mL capacity)
- GMP glovebox for packaging under inert atmosphere (argon, nitrogen)

PLANT

- Pilot Plant Reactors: 100 - 1400 L (Glass lined, AISI 316, Hastelloy reactor with Cryogenic capability)
- Pilot Plant under SCADA control, equipped with mass flow controllers and load cells
- Hydrogenation Autoclaves: 200 L (100 bar) - - AISI 316
- Operative conditions: -90°C to 140°C
- Pilot Plant Equipment for batch Distillation
- Pilot Plant Total Capacity: 7500 L
- Isolating Equipment: Pressure Filter-Dryer, Centrifuges
- Tray Dryer; Crusher; Seaving Mill
- Controlled areas for APIs isolation and finishing
- High containment for HPAPI handling (OEL< 1 µm/ m^3)

ANALYTICAL R&D CAPABILITIES

- Bruker AvanceNeo 400MHz NMR with H, C and other nuclei
- LC-MS - ion trap detector, equipped with ESI and APCI sources
- GC-MS with head-space capability
- Polarimeter
- FT-IR with NIR capability, UV-Vis spectroscopy
- HPLC with ELS detector
- DSC and Mettler melting point
- GMP certified GCs with-head space capability
- GMP certified HPLCs
- GMP certified UPLC with multiple columns comparison
- Classic titration equipment
- KF titrators
- Other equipment available at QC: Malvern for particle size, microscope for crystal studies, muffle for ashes

PROCESS R&D CAPABILITIES

- Hel Multi-reactor for process development, optimization and critical parameters studies
- Multi-reactor Capability for Calorimetric Study
- Crystal 16 for solubility and crystallization studies
- Lab. Hydrogenation Autoclaves with dosing system up to 60 bar
- Flasks and Lab Reactors from 100 mL up to 10 L, with operative range from -90°C to 220°C
- VisiMix software for mixing simulation to study scale-up parameters
- Flow reactor for flow chemistry studies
- Isolator for handling toxic reagents and air/moisture-sensitive products
- Standard distillation and kilo-scale Short Path Distillation Equipment
- Laboratory Pressure-Filter/Dryers and Ovens

05.

R&D PROCESS DEVELOPMENT

THE R&D DEPARTMENT IS COMPOSED OF A TEAM OF HIGHLY SPECIALIZED RESEARCHERS AND TECHNICIANS, WHO HAVE MASTERED MOST ORGANIC CHEMISTRY REACTIONS AND PRODUCTION TECHNOLOGIES AS WELL AS SHORT PATH DISTILLATION, HIGH PRESSURE HYDROGENATION AND FLOW CHEMISTRY.

Thanks to highly efficient discovery programs, as well as alliances with other pharmaceutical and research institutes, **Recordati has always been able to successfully introduce new products into its portfolio**. Commitment, scientific rigor and availability of technological capability in the R&D department, allow Recordati to develop new treatments and to build an innovative product pipeline. To constantly ensure high API quality and robustness of the production, the R&D group is involved in a continuous performance improvement cycle; however, the main research and development activities are mainly focused on generating innovative treatments with special attention to rare diseases.

R&D EXPERTISE

EXPERTISE IN HAZARDOUS AND HIGHLY TOXIC CHEMICALS HANDLING:
Na_2S, NaCN (not gaseous HCN), $POCl_3$, $SOCl_2$, formaldehyde, methylbromide, dimethylsulfate, other H350, liquid ammonia, peroxyacids.

ORGANOMETALLIC REACTIONS:
Grignard reagents, organolithium and lithium derivatives.

REDUCTIONS:
Catalytic hydrogenation (homogeneous and heterogeneous), metal hydrides (NaBH4, LiAlH4), Raney-Nickel, hydrogen transfer.

ASYMMETRIC REACTIONS:
Transition metal catalysts (hydrogenation, oxidation), biocatalysts, racemate resolution, use of chiral building blocks.

OXIDATIONS:
Peroxyacids, bichromate, inorganic salts, dehydrogenations.

REACTIONS UNDER SPECIAL CONDITIONS:
high-temperature reactions (+250°C) high-pressure reactions (10–100 bar) Flow-chemistry

ANALYTICAL R&D:
Specification set-up, Method development and validation, Solubility & Crystallization studies, Operative stability and Material Compatibility studies.

SOLID STATE MANAGEMENT:
Polymorphysm studies: detection, characterization and interconversion mapping.
Particle size studies

PRODUCT LIST PHARMACEUTICAL ACTIVES

RECORDATI PHARMACEUTICAL ACTIVES

PRODUCT	THERAPEUTIC CATEGORY
Acyclovir	Antiviral
Benidipine HCl	Calcium channel blocker
Dimenhydrinate	Antiemetic
Diphenhydramine HCl	Antihistaminic
Diphenhydramine Citrate	Antihistaminic
Dobutamine HCl	β-Adrenergic Agonist
Dopamine HCl	β-Adrenergic Agonist
Ketorolac	Anti-inflammatory
Manidipine	Calcium channel blocker
Mebeverine HCl	Antispasmodic
Methenamine Hippurate	Antibacterial (Synthetic)
Papaverine HCl	Antispasmodic
Phenytoin	Anticonvulsant
Phenytoin Sodium	Anticonvulsant
Pyridoxal-5-phosphate	Enzyme co-factor vitamin B6
Sertraline HCl	Antidepressant
Tribenoside	Vasoprotective
Verapamil HCl	Calcium channel blocker

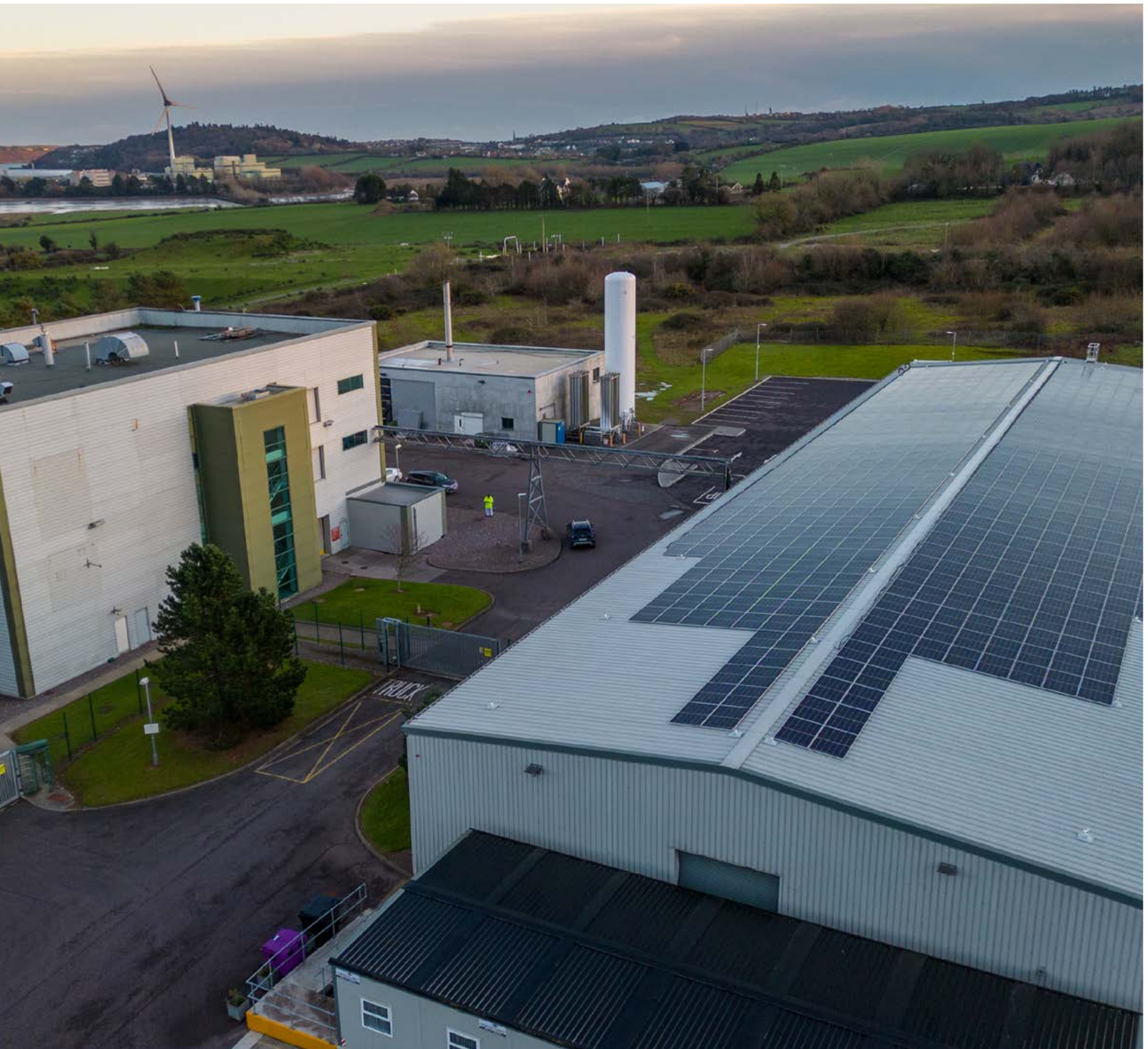
RECORDATI INTERMEDIATES

PRODUCT
(R)-Tetrahydropapaverine
Tetrahydropapaverine
Homoveratric Acid

SALES & MARKETING
Email: pharmachemicals@recordati.it Ph +39 02 48787336
https://recordati.com/our-business-chemical-business/our-business-chemical-business-products/

PRODUCT LIST FDF
(FINISHED DOSAGE FORM)

Alongside Recordati's Pharmaceutical Chemicals Business unit, Recordati's International Pharma Sales manage out-licensing and supply agreements in over 120 countries.
The range of partnerships varies:
- API trading with a trademark license;
- selling finished products under the trademark with local partners being also Recordati's regulatory representative and taking care of distribution and promotion;
- as well as, in some cases, local manufacturing.



RECORDATI PRODUCTS AVAILABLE FOR OUT-LICENSING

MOLECULE	TRADEMARK	INDICATION
Lercanidipine	ZANIDIP	Treatment of mild to moderate essential hypertension in adults
Lercanidipine/Enalapril	ZANIPRESS/ ZANEXTRA	Treatment of essential hypertension in patients whose blood pressure is not adequately controlled by lercanidipine or enalapril alone
Pitavastatin	LIVAZO/ALIPZA	Indicated for the reduction of elevated total cholesterol (TC) and LDL-C, in adults, adolescents and children aged six years or older with primary hypercholesterolaemia
Leuprorelin acetate	ELIGARD	Treatment of hormone-dependent advanced prostate cancer and for the treatment of high-risk localized and locally advanced hormone dependent prostate cancer in combination with radiotherapy
Fenticonazole	LOMEXIN/ GYNOXIN	Treatment of vulvovaginal candidiasis, trichomoniasis and mixed infections
Silodosin	UROREC/SILODYX	Treatment of the signs and symptoms of BPH in adult men
N-acetylcysteine	EXOMUC	Treatment of bronchial secretion disorders, especially during acute bronchial affections: acute bronchitis and acute episode of chronic broncho-pneumopathy
Ginkgo biloba extract, troxérutin, heptaminol	GINKGO BILOBA	Treatment of symptoms related to veno-lymphatic insufficiency (heavy legs, pain, impatience of the primodecubitus etc). Treatment of functional signs related to the hemorrhoidal crisis
Biclotymol	HEXASPRAY	Local symptomatic treatment of acute disorders of the oropharynx
Rifamycin	OTOFA	Local treatment of certain purulent otorrhea: with a transtympanic aerator, with a draining cavity, and chronic non-osteitic otitis with an open tympanic membrane
Neomycin, polymyxin B, dexamethasone	POLYDEXA	Local treatment of otitis externa due to bacterial infection (in particular, infectious eczema of the external auditory canal) as long as the tympanic membrane is intact
Ternidazole, neomycin, nystatin, prednisolone	TERGYNAN	Local treatment of sensitive germ vaginitis and non-specific vaginitis
Sodium picosulfate, light magnesium oxide, citric acid anhydrous	CITRAFLEET	Bowel cleansing prior to any diagnostic procedures requiring a clean bowel e.g. colonoscopy or x-ray examination
Disodium phosphate dodecahydrate sodium dihydrogen phosphate dihydrate	PHOSPHOSODA	Bowel cleansing prior to any diagnostic procedures requiring a clean bowel e.g. colon surgery, x-ray or endoscopic examination. Laxative for severe constipation only allowed in certain countries

Contact: https://recordati.com/contact-us/

Recordati. Unlocking the full potential of life.

Produced by Recordati S.p.A. Concept and graphic design by Graphicamente Photography: Archivio Recordati, Riccardo Sarri, iStock

Ed. 2024