

# NEUROSCIENCES

Ipsen has a long-standing commitment to treat mobility impairment in adult and pediatric patients. The Group has made a commitment to support and improve the quality of life of patients who are affected by conditions that restrict mobility. Interdependent treatment approaches must be used to deliver optimal benefits to patients seeking recovery. The Group's preliminary contribution supporting a multi-modal approach in managing patient care was initiated with the introduction of its botulinum neurotoxins, twenty-five years ago.

## DYSPORT® INDICATIONS\*

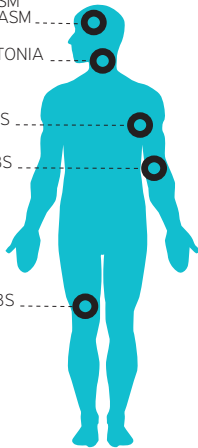
GLABELLAR LINES  
BLEPHAROSPASM  
HEMIFACIAL SPASM

CERVICAL DYSTONIA

HYPERHIDROSIS

SPASTICITY  
OF UPPER LIMBS

SPASTICITY  
OF LOWER LIMBS



## CLINICAL TRIALS

### AESTHETIC MEDICINE

#### 3 PHASE III

TRIALS (IN COLLABORATION  
WITH GALDERMA)  
ARE IN PROGRESS

#### 2 TRIALS

WITH DYSPORT®  
SOLUTION (CLINICAL  
CENTERS MAINLY  
IN EUROPE)

#### 1 TRIAL

WITH THE EXISTING  
FORMULATION  
OF DYSPORT®  
IN CHINA

### THERAPEUTICS

#### 1,000

ADULT AND CHILDREN  
PATIENTS WITH SPASTICITY  
IN PHASE III CLINICAL  
TRIALS PERFORMED IN  
150 CLINICAL CENTERS  
WORLDWIDE

#### 800

PATIENTS TARGETED FOR  
RECRUITMENT  
IN 200 SITES WORLDWIDE  
IN THE NEUROGENIC  
DETRUSOR OVERACTIVITY  
PHASE III  
PROGRAM INITIATED  
IN MARCH 2016

\* Indications may vary according to country.

**S**ince 1990 Ipsen has dedicated its focus on pioneering research in neurotoxins and recombinant neurotoxin engineering.

Dysport® is a drug treatment based on the type-A botulinum toxin, which inhibits the transmission of nerve impulses to the muscle. Botulinum toxin injections cause contracted muscles to relax, relieving patients' symptoms and contributing to improvements in the quality of their daily lives.

The recent approval of Dysport® for the treatment of upper limb spasticity in adults in the United States will complement the Groups' focus over the next five years. Clinical trials are underway to generate additional data in support of the therapeutic uses of Dysport®. In areas where national labels are currently in place, the Group will submit evidence in support of improved Dysport® labelling for spasticity in adults and pediatrics. Ipsen aims to further explore and develop additional Dysport® indications in neurology (hypersalivation) and urology (neurogenic detrusor overactivity) conditions often associated with

spasticity patients. Research is also underway on a liquid formulation of Dysport®. The Group has advanced the consolidation of its innovative toxin platform and has actively focused on developing the next generation of neurotoxins.

### OUR ENGAGEMENTS FOR PATIENTS

Ipsen has built a strong, long-term partnership with Dystonia Europe, an organization dedicated to representing dystonia patients across the continent, as well as with the American Dystonia Society. The Group also continues to support initiatives for physicians who seek further research in cervical dystonia, disease awareness campaigns for patients and the creation of patient networks in Europe. Fully committed to improving spasticity management for patients, Ipsen launched I-CAN, an innovative spasticity management program that engages patients in their treatment to improve outcomes. To support this innovative approach, the Group recently launched a digital application called "i-GSC" to assist patients performing guided self-rehabilitation, in complement of their traditional physiotherapy.

### OUR COMMITMENT FOR HEALTH CARE PROFESSIONALS

Ipsen provides ongoing training and medical education at local and regional levels for physicians who want to improve treatment outcomes using Dysport®. For years, Ipsen has delivered an elite-level medical training program, "Ixcellece Network", which supports specialists who wish to expand their





practical expertise and improve outcomes in support of better patient management. In aesthetics, educational masterclasses are critical to elevate clinical and practical expertise and improve outcomes for customers and their clients.

### OUR MILESTONES

- > **February 2015:** Option agreement to acquire Canbex Therapeutics Ltd upon completion of the phase IIa study of Canbex's VSN 1 6R lead candidate for the treatment of spasticity in patients with multiple sclerosis (MS).
- > **April 2015:** Joint collaboration agreement with Hannover Medical School to test recombinant botulinum neurotoxin proteins to affect intracellular molecular pathways with targeted secretion inhibitors (TSIs).
- > **July 2015:** The US Food and Drug Administration approved Dysport® for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors, wrist flexors and finger flexors. This differentiated label is a testimony to the quality of the clinical research. In most European countries, the Dysport® adult spasticity label was strengthened to incorporate these data.
- > **August 2015:** *The Lancet Neurology*\* published results from the Ipsen-sponsored phase III study demonstrating the efficacy and safety of Dysport® in post-stroke and traumatic brain injury patients with upper limb spasticity.
- > **January 2016:** Scientific journal *Pediatrics*\*\* published detailed results of a phase III study that confirm the efficacy and safety profile of Dysport® in the treatment of lower limb spasticity in children with cerebral palsy and demonstrate improvement in functional benefit after a single injection of Dysport®. Also known as pediatric lower limb spasticity, this debilitating condition is the most common cause of chronic motor disability in childhood.
- > **January 2016:** Ipsen and Galderma expanded the geographical scope of their neurotoxin partnership, whereby Galderma acquired the exclusive rights to develop, promote and distribute Dysport® in the aesthetic indications in some key Asia-Pacific markets, including China, India, South Korea and Indonesia.

### OUR PARTNERSHIP WITH GALDERMA

Ipsen has granted the rights to distribute Dysport® as an aesthetic treatment in several countries to strategic partner Galderma Pharma SA, a specialty pharmaceutical company focused on dermatology. Ipsen markets therapeutic indications for Dysport® while under the terms of the collaboration, Galderma distributes aesthetic treatment under the brand names of Dysport® and Azzalure® depending on the country of registration. Ipsen and Galderma continue to collaborate on the future development and commercialization of new neurotoxin therapies. The partnership with Galderma now covers over 75% of the world's aesthetics market including the United States, Canada, Europe, Brazil and Australia.

### OUR SOLUTIONS

#### DYSPORT®, ONE PRODUCT FOR A RANGE OF INDICATIONS

**Dysport® is a type-A botulinum neurotoxin complex.** It inhibits the transmission of nerve impulses responsible for muscle contraction and allows the muscle to relax temporarily, without affecting normal function.

Dysport® was first registered for the treatment of blepharospasm in the United Kingdom in 1990 and has been marketed since 1991.

Today, Dysport® is primarily used for patients with spasticity, cervical dystonia, hemifacial spasm, blepharospasm, and hyperhidrosis. In aesthetic medicine, Dysport® is indicated for the reduction of glabellar lines depending on the territory. Dysport® is authorized in more than 80 countries for 7 therapeutic and aesthetic indications.

#### NEXT-GENERATION NEUROTOXINS

**Botulinum toxins** have the potential for very broad applications across multiple therapeutic areas, such as urology, oncology, endocrinology, and regenerative medicine.

\* Online at <http://www.thelancet.com/neurology>

\*\* Online at <http://pediatrics.aappublications.org/content/early/2016/01/24/peds.2015-2830>



Ipsen Bioinnovation is focused on the discovery of new recombinant botulinum toxins, mainly for therapeutic indications, in addition to the promising area of targeted secretion inhibition.

The acquired technology platform has led to opportunities for collaborative research with renowned university research centers. Ipsen is currently in collaboration with Harvard University to identify new ways to deliver further neurotoxin innovations to meet patients' needs.

### COMMITMENT TO SPASTICITY IN MULTIPLE SCLEROSIS

**The Group and British company GW Pharmaceuticals** have signed an agreement under which Ipsen gained promotion and distribution rights in Latin America for Sativex®, a cannabis extract spray indicated as an add-on treatment for symptom improvement in patients with moderate to severe spasticity due to multiple sclerosis. GW Pharmaceuticals and Ipsen are conducting regulatory filings in selected countries in Latin America for this indication.

## “I-CAN” PROGRAM



### “I-CAN” IS A SPASTICITY MANAGEMENT PROGRAM

THAT ENGAGES PATIENTS IN THEIR TREATMENT TO INCREASE THEIR MOTIVATION AND IMPROVE TREATMENT OUTCOMES.

IT COMBINES DYSPORT® WITH NEW STANDARDS OF CARE IN SPASTICITY MANAGEMENT:

- THE AGREEMENT ON INDIVIDUALIZED TREATMENT GOALS BASED ON OPTIMAL PATIENT ASSESSMENT;
- THE EFFICIENT USE OF DYSPORT® IN THE RIGHT MUSCLES WITH THE RIGHT DOSE AT A PATIENT-TAILORED FREQUENCY;
- THE PARTNERSHIP BETWEEN THE MULTIDISCIPLINARY TEAM AND THE PATIENTS FOR THEIR GUIDED SELF-REHABILITATION PROGRAM, IN SYNERGY WITH PHYSICAL AND OCCUPATIONAL THERAPY.

THE “I-CAN” PROGRAM IS SUPPORTED BY THE DEVELOPMENT OF A DIGITAL APPLICATION CALLED “I-GSC” WHICH HELPS PATIENTS PERFORM GUIDED SELF-REHABILITATION IN COMPLEMENT OF THE TRADITIONAL PHYSIOTHERAPY. IT WILL BE AVAILABLE IN GERMAN, FRENCH, SPANISH, ENGLISH, RUSSIAN AND PORTUGUESE.