ALLERGAN SOLSTICE IPSEN Innovation for patient care

IMPORTANT SAFETY INFORMATION
REGARDING BOTULINUM TOXIN PRODUCTS
Botox®, Dysport®, NeuroBloc®

RISK OF SERIOUS ADVERSE EVENTS DUE TO SPREAD OF TOXIN

Dear Doctor,

Following discussions with EU regulatory authorities, including the Irish Medicines Board, we would like to alert you to the following safety information:

- **Serious adverse events related to the distant spread of botulinum toxin, including muscle weakness, dysphagia and aspiration, have been reported very rarely with all botulinum toxin products.**

- **There is a need for extreme caution when administering botulinum toxin products to patients with neurological disorders or a history of dysphagia or aspiration.**

Three different botulinium toxin-containing products, Botox®, Dysport® and NeuroBloc® have a Marketing Authorisation.

Further information on the safety concern
Botulinum toxins act by preventing release of acetylcholine at the neuromuscular or other cholinergic junctions and produce a reversible partial denervation of the injected muscles or eccrine glands.

Serious adverse events suspected to be related to the spread of toxin have been reported very rarely with botulinum toxin preparations, including muscle weakness, dysphagia or aspiration pneumonia. There have been very rare reports of adverse events with fatal outcome. Patients with underlying neurological disorders or swallowing difficulties are at increased risk of these side effects and should be treated and monitored with extreme caution.

In the currently approved indications, the benefit-risk ratio is acceptable. In order to minimize the risk of serious reactions due to spread of effect of toxin, it is essential that the posology, warnings and precautions are strictly followed as stipulated in the Summary of Product Characteristics for the respective product.

Further information to health care professionals

- **Botulinum toxin products should only be administered by physicians with appropriate experience including use of the required equipment.**

- **Patients or caregivers should be informed about the risk of spread of toxins and be advised to seek immediate medical care if swallowing, speech or respiratory disorders arise.**

- **Botulinum toxin units are not interchangeable from one product to another.**

- **The recommended administration techniques and specific dosing guidance (including the recommendation to use the minimum effective dose and titrate according to individual requirements) should be followed.**

Changes of Summary of Product Characteristics (SPC)
The SPCs (Section 4.4 "*Special Warnings and Precautions for Use*" and section 4.8 "*Undesirable effects*") for all three botulinum toxin products (Botox®, Dysport® and NeuroBloc®) are being amended, regarding the risk of side effects related to spread of toxin. Current SPCs for the aforementioned products can be accessed on 'www.medicines.ie' and 'http://www.emea.europa.eu/humandocs/PDFs/EPAR/neurobloc/H-301-PI-en.pdf' for BOTOX®/Dysport® and NeuroBloc® respectively. The core elements of the amended SPC text are shown in Annex 1.

Call for Adverse Drug Reaction (ADR) reporting
Please remember that any adverse event following the use of botulinum toxin products should be reported to the marketing authorisation holder and/or local regulatory authorities, in the usual way.

Communication information
For further information, please contact:

For BOTOX®	**For NeuroBloc®**	**For Dysport®**
Medical Information	Solstice Neurosciences Ltd	Ipsen Medical Information
Allergan Ltd	----------	Ipsen Ltd.
Marlow International	----------	190 Bath Road
Marlow, SL7 1YL	----------	Slough, SL1 3XE
Tel: +44 (0)1628 494026	+44 (0)1202 653351	+44 (0)1753 627777
Fax: +44 (0)1628 494057	----------	----------
Email: UK_Medinfo@allergan.com	contact@solsticeneuro.com	medical.information.uk@ipsen.com

Yours sincerely

Dr Izabella Bossowska	**Miss Joanne Medlock**	**Dr Philip Weatherill**
EU Qualified Person	**EU Qualified Person**	**EU Qualified Person**
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ANNEX 1

SPC core elements

(*It should be noted that the final product specific SPC text, resulting from the finalized / ongoing SPC revision, may have small differences in wording as compared with the text below*)

Section 4.4 Special warnings and precaution for use

Botox, Dysport, NeuroBloc

Side effects related to spread of toxin distant from the site of administration have been reported (see section 4.8), sometimes resulting in death, which in some cases was associated with dysphagia, pneumonia and/or significant debility.
Patients treated with therapeutic doses may experience exaggerated muscle weakness. Patients with underlying neurological disorders including swallowing difficulties are at increased risk of these side effects. The botulinum toxin product should be used under specialist supervision in these patients and should only be used if the benefit of treatment is considered to outweigh the risk. Patients with a history of dysphagia and aspiration should be treated with extreme caution.
Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory disorders arise.

Section 4.8 Undesirable effects

Botox, Dysport, NeuroBloc

Side effects related to spread of toxin distant from the site of administration have been reported very rarely (exaggerated muscle weakness, dysphagia, aspiration pneumonitis with fatal outcome in some cases) (see section 4.4).