BIOSIDUS
MULTIPLE SCLEROSIS

Quality Treatments for Multiple Sclerosis

Delivering long-term efficacy and safety

BLASTOFERON®
Interferon ß1a 22 and 44 mcg

esclerOFERON®
interferon beta 1a 30 mcg

BiOMONAR®
Fingolimod

Choosing the Best Treatment

- Multiple sclerosis is the most common neurological disease in young adults and it represents a leading cause of neurological disability throughout life.[1]

- Due to MS prolonged progression, it is key to determine the initial prognostic factors and to choose long-term effective and safe therapy strategies.[2]

BLASTOFERON® Interferon ß1a 22 and 44 mcg

esclerOFERON® interferon beta 1a 30 mcg

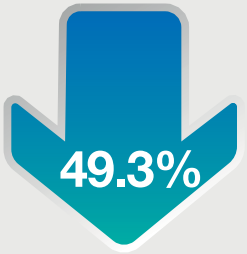
BIOMONAR® Fingolimod

Blastoferon® Efficacy
Short-term

- Clinical studies in patients with RRMS treated with interferon beta 1a show its efficacy measured with different endpoints.[3]
- Non-clinical and clinical studies conducted with BLASTOFERON® show biosimilarity with the reference product.[4]

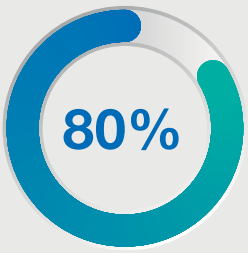
Efficacy of Interferon beta 1a in RRMS

Relapse-free patients



relative reduction of relapse risk with interferon beta 1a TIW 44 µg *vs.* placebo

Patients without disability progression



of patients treated with interferon beta 1a showed no disability progression

Benefits of subcutaneous interferon beta 1a TIW 44 µg after one year from PRISMS[3] study ($p < 0.05$ compared with placebo)

TIW: three times weekly
Prepared from Traboulsee *et al.*, 2018

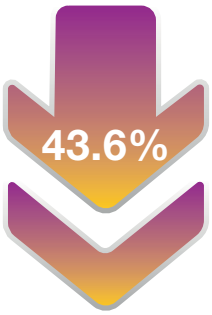
- These clinical benefits were evident as early as 2 months regardless of age, sex, baseline EDSS score, and disease progression time.[3]

Blastoferon® Efficacy
Medium-term

- Benefits were sustained for longer periods, even in patient subgroups with high disease activity.[5]

ARR relative reduction adjusted at 2 years of treatment[5]

All patients
(44 µg TIW *vs* placebo)



Patients with high activity
(44 µg TIW *vs.* placebo)

Pooled analysis from studies PRISMS/SPECTRIMS; n = 706
High activity: either ≥ 1 relapse within the 2 years prior to initiation or ≥ 1 gadolinium-enhancing lesion at baseline.

ARR: annualized relapse rate; TIW: three times weekly
Prepared from Freedman *et al.*, 2020

- This way, BLASTOFERON® therapy effectively reduces risk, disease progression, and lesion burden in MRI, even in patients who seem to be transitioning from RRMS to SPMS.[5]

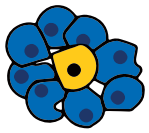
Based on the evidence available, BLASTOFERON® has been added as a Chemical Reference Substance to the European Pharmacopeia by the European Directorate for the Quality of Medicines & HealthCare (EDQM).[6]

The selection of BLASTOFERON® as a reference substance in the European Pharmacopeia reinforces Biosidus' commitment to the compliance of rigorous quality standards.

Blastoferon® Efficacy and Safety
Long-term

- In the 15-year follow-up of the patients of the original PRISMS study, the cumulative dose and treatment duration was found to be associated with better outcomes in different relevant indicators.[2]
- These benefits are joined by an appropriate tolerability profile, with safety and bioequivalence data for Blastoferon® over decades of experience.[7-10]

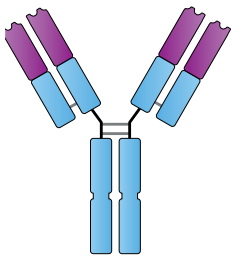
Blastoferon® Safety, Tolerability, and Bioequivalence[10]



No reports of malignancies over 16 years

Use during pregnancy and breastfeeding

BLASTOFERON®
Interferon ß1a 22 and 44 mcg



No differences in immunogenicity with other interferon beta 1a

Laboratory-confirmed pharmacogenomic effects

Escleroferon® Efficacy and Safety

Medium-term

The administration of ESCLEROFERON® to MS patients is related to high efficacy and tolerability rates, initially evidenced in pivotal studies and confirmed in the long-term follow-up.[11]

In the medium-term:

- Weekly intramuscular interferon beta 1a (30 µg) significantly extended the time to disability progression *vs*. placebo, with a relative reduction of 37%.[10]
- In addition, the probability of multiple relapses decreased 32% compared to placebo.[10]
- Interferon beta 1a therapy also had beneficial effects on radiological activity and cognitive function.[10]
- Probability of progression in the weekly intramuscular interferon beta 1a arm was estimated at 12.5% at the first year (*vs*. 22% for placebo) and 21.9% at the second year (*vs*. 34.9% for placebo). One in eight patients treated with interferon beta 1a was free from disease progression at 2 years of treatment.[12]

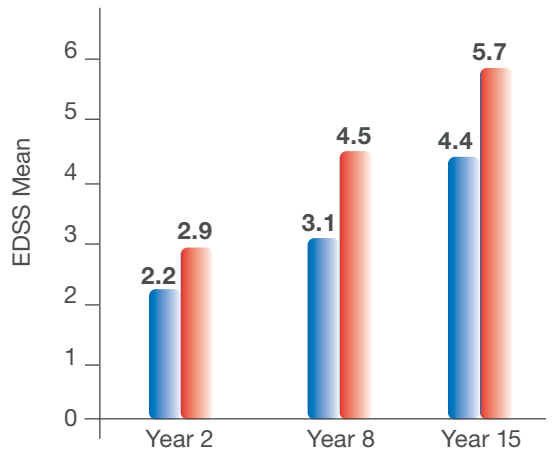
Escleroferon® Efficacy and Safety
Long-term

The outcomes described in the long-term follow-up of the clinical study cohorts, as well as real-world studies, confirm the efficacy and safety endpoints of ESCLEROFERON® in patients with MS.

In the long-term:

- In the 10-year follow-up extension of the CHAMPIONS study, 81% of patients treated maintained an EDSS score < 3.0.[13]
- The incidence of anti-interferon antibodies was only 5% after 8 years of follow-up.[10]
- In 15-year follow-up models, interferon beta 1a therapy was associated with lower disability levels and improved quality of life, compared with untreated patients.[14]

Intramuscular interferon beta 1a (30 µg) reduces disability in the long-term.



EDSS score from randomization to intramuscular interferon beta 1a (30 µg) or other long-term treatment in the ASSURANCE study[14] (p < 0.05 in all comparisons *vs.* other treatments)

- Interferon beta 1a
- Other treatments

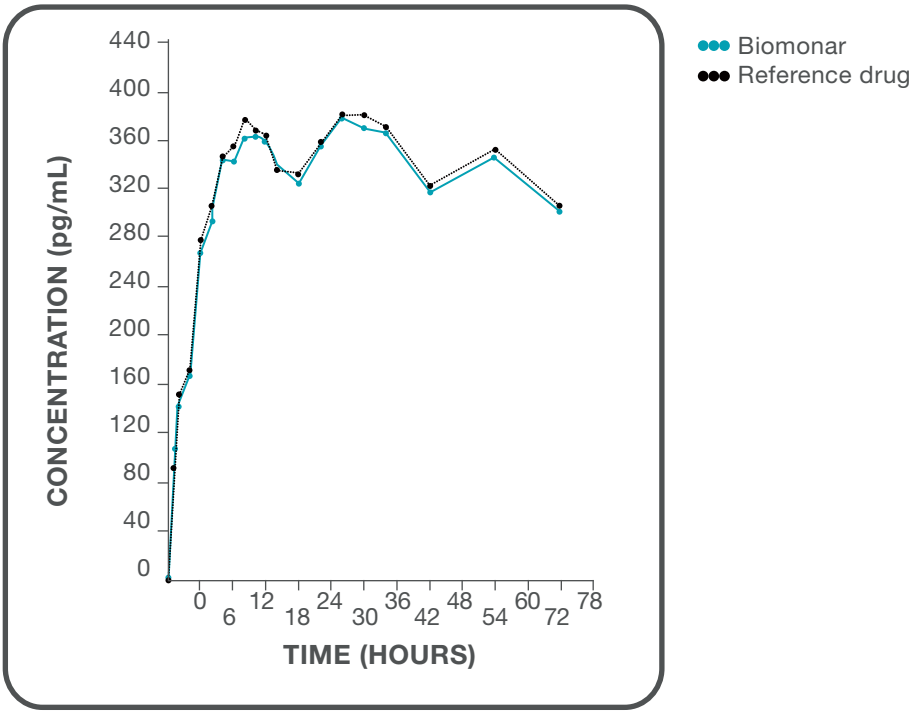
Prepared from Bermel *et al.*, 2010

Biomonar® Efficacy and Effectiveness

- Biomonar® is an oral tool for treatment of relapsing-remitting multiple sclerosis.[15]
- Its efficacy has been evidenced in Phase 3 clinical studies of up to 2 years, with a relative reduction of 54% in the relapse rate compared to placebo.[16]

Biomonar® **bioequivalence** has been evidenced in a comparative bioavailability study *vs.* the reference product, in both male and female patients, conducted in Ontario, Canada.[17]

Average concentration of Fingolimod (Biomonar® and reference drug) showing the bioequivalence between both products[17]

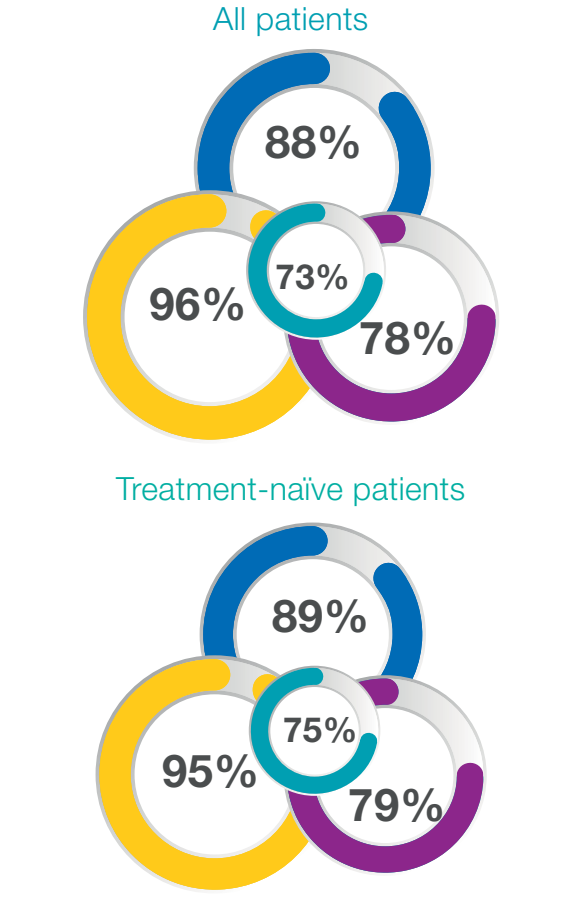


Adapted from Faulkner *et al.*, 2016

Biomonar® Effectiveness: NEDA-3 Status

- NEDA-3 (No Evident Disease Activity) status is defined as the absence of relapses, worsening of disability, and MRI activity.[18]
- In a real-world study (n = 483 MS patients) with an indication of Fingolimod over a median of 18 months, a high percentage of patients achieved NEDA-3 status, both treatment-naïve patients and those switching to Fingolimod from injectable drugs.[1]

Real-world NEDA-3 status in patients treated with Fingolimod[19]



Adapted from Prosperini *et al.*, 2018.

Effectiveness of Fingolimod in the real world in Argentine patients with previous treatment failure[15]

Adapted from Patrucco *et al.*, 2019

Biomonar® Safety

- In long-term extension studies (up to 4.5 years), tolerability was similar to clinical trials, without unexpected safety findings.[20]

- In post-marketing surveillance models, the drug was reported to be well tolerated and occasional cardiologic adverse events are usually self-limiting in the long-term.[21]

- According to real-world experience with 804 relapsing-remitting multiple sclerosis patients from 56 health centers treated during a mean of 2.2 years:[22]

  - The adherence rate was 93.9% during the first year.
  - 98.3% of participants experienced no adverse events with the first dose of Fingolimod.
  - The incidence of bradycardia was 0.2% following the first dose and zero for subsequent doses.

Highlights and conclusions

- The choice of MS treatment needs to consider both efficacy and safety regarding long-term periods.[2]
- BLASTOFERON® is a first-choice treatment for RRMS patients with mild to moderate activity, and it allows for an efficient disease control, with a positive risk-benefit profile and over 15 years of real-world experience.[23]
- ESCLEROFERON® is also a treatment option for these patients, which allows for an efficient management of MS with lower administration frequency.
- BIOMONAR® is an effective treatment for RRMS patients with active disease, and it is the first oral treatment with over 10 years of real-world experience.
- BLASTOFERON®, ESCLEROFERON®, and BIOMONAR® represent efficient, safe, effective, and tolerable long-term established treatment strategies, with a vast post-marketing experience.[3-23]

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