Produced in Full Compliance with US FDA & EU Regulations

Cinnovex®

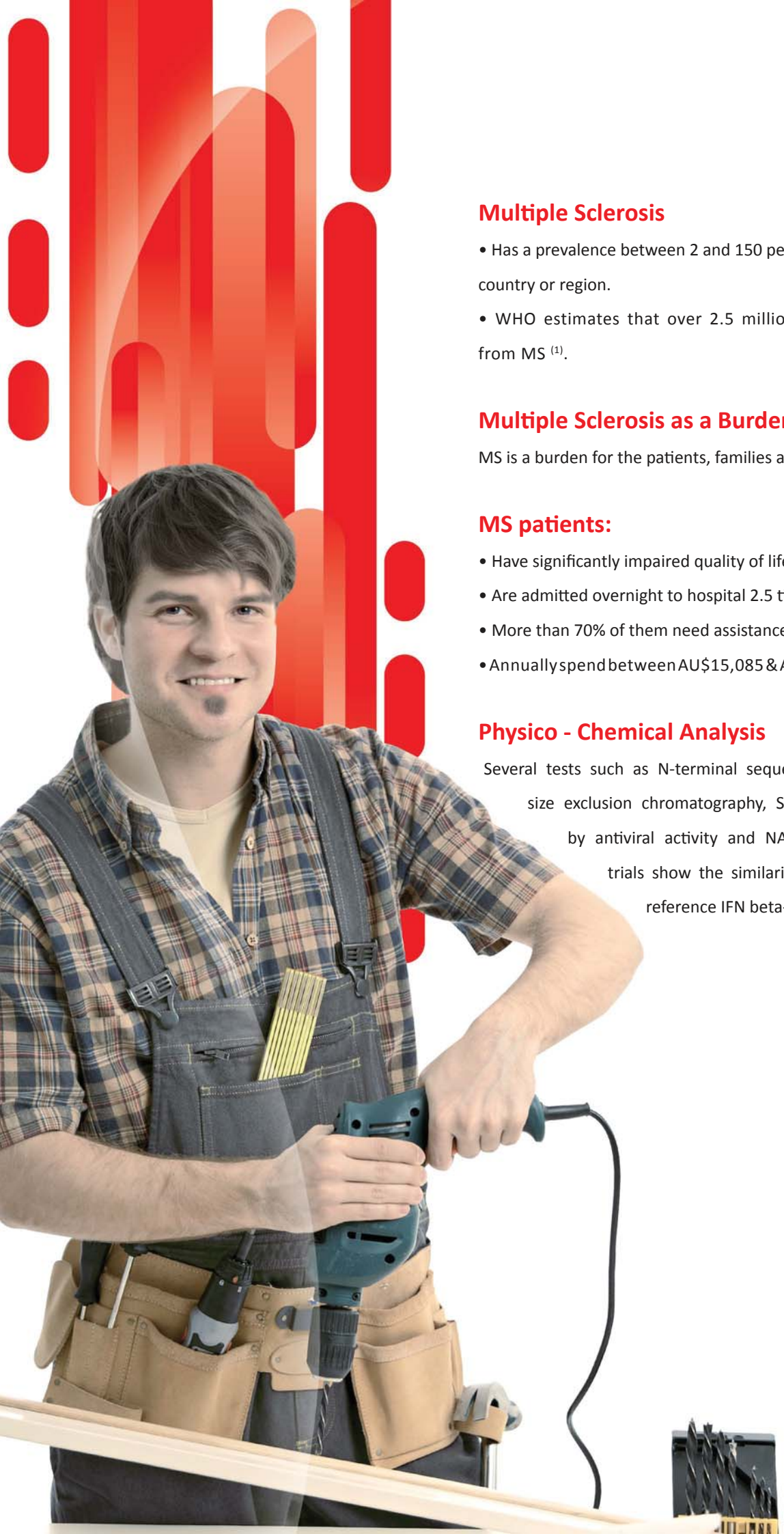
INTERFERON BETA - 1a

Once - a - Week

We offer
a better solution:

- Same Efficacy
- Cost Effectiveness

شرکت سیناژن
CinnaGen Co.



Multiple Sclerosis

• Has a prevalence between 2 and 150 per 100,000 according to the country or region.

• WHO estimates that over 2.5 million people globally suffer from MS [(1)].

Multiple Sclerosis as a Burden

MS is a burden for the patients, families and society.

MS patients:

• Have significantly impaired quality of life

• Are admitted overnight to hospital 2.5 times more frequently

• More than 70% of them need assistance with one or more tasks

• Annually spend between AU$15,085 & AU$20,396 respectively[(2)].

Physico - Chemical Analysis

Several tests such as N-terminal sequencing, peptide mapping, size exclusion chromatography, SDS-PAGE, ELISA, bioassay by antiviral activity and NAb tests and also clinical trials show the similarity of **CinnoVex®** to the reference IFN beta-1a.

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Clinical Efficacy and Safety

In a double blind randomized clinical trial study 60 patients with relapsing remitting multiple sclerosis (RRMS) with Expanded Disability Status Scale (EDSS) score of 0-5.5 were randomly allocated to two groups. 31 patients in the Avonex and 29 patients in the Cinnovex® group completed full 24 months of study period. There was no statistically significant difference in attack number between two groups (1.0±1.2 in Avonex and 1.2±1.3 in Cinnovex®; p=0.46). Regarding frequency and duration of most considerable side effects, there were no significant differences between 2 groups, as well and neutralizing antibodies were not positive in any patients.

So Cinnovex® can be used as a safe and effective alternative to Avonex in treatment of RRMS.[3]

Post marketing study

CINA Study (Cinnovex® Iranian National Assessment) as a post marketing study was conducted from 2007 to 2008 in cities of Tehran, Isfahan, Mashhad, Tabriz and Shiraz. A total of 1050 patients with RR-MS and EDSS of <4 entered the study. Mean age was 30.7±8.6 and 82% were female. This study showed that Cinnovex® could prevent progression and improve clinical course of MS and conventional side effects of beta interferon therapy also are observed with this drug.[4]

PK/PD study

In a single- center, double treatment, crossover study, 20 healthy male volunteers aged between 25 and 35 years old with no past medical history were randomly allocated to this trial. Pharmacokinetics was assessed by AUC_{0-48}, peak concentration and time to peak concentration of both Cinnovex® and Avonex and pharmacodynamics by evaluation of serum neopterin and beta-2 microglobulin concentration profile. Data shows that there is no significant difference between AUC_{0-48} values, Cmax values and time to maximum concentration for both Avonex and Cinnovex®. (p=0.64, p=0.71, p=0.69). Also there is no significant difference between neopterin and beta2 microglobulin AUC_{0-144} values following either products injection. (p=0.37, p=0.86)

Observation of no difference in pharmacokinetics and pharmacodynamics parameters suggest that both products are interchangeable and have the same efficacy.

References:

1 www.Leaddiscovery.co.uk / Reports/ Multiple Sclerosis Market Analysis & Forecast Report 2007-2022

2 Bruce Taylor a, Elizabeth McDonald b, Bruno Fantino c, Les Sedal d, Richard MacDonnell e, Fotini Pittas a, Trish Groom. The cost of multiple sclerosis in Australia. J Clin Neurosci.2007 june:14(6):532-9.

3 Nafissi S, Azimi A, Amini-Harandi A, Salami S, shahkarami MA, Heshmat R. Comparing efficacy and side effects of a weekly intramuscular biogeneric/biosimilar interferon beta-1a with Avonex in relapsing remitting multiple sclerosis: a double blind randomized clinical trial. Clin Neurol Neurosurg. 2012 Sep;114(7):986-9.

4 Masood Etemadifar, Mehrdokht Mazdeh, Hamid Reza Torabi, Majid Ghaffarpour, Mojtaba Azimian, Shiva Salami, Sayyed Mohammad Amir Shahkarami. A report of multiple sclerosis patients treated by CinnoVex in Iran. Tehran University Medical Journal: Vol. 68, No. 1, Apr 2010: 30-36

CinnoVex®

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30 mcg Lyophilized Powder Vial

Use
Treatment of patients with relapsing forms of MS.
Patients with MS in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

Dosing
30 mcg injected IM once a week.

Administration
CinnoVex is intended for use under the guidance and supervision of a doctor. Patients may self-inject if their doctor determines that it is appropriate and with medical follow-up, as necessary, after proper training in intramuscular injection technique.
Sites for injection include the thigh or upper arm
A 25 gauge, 1" needle for intramuscular injection may be substituted for the 23 gauge, 1 ¼" needle by the prescribing physician, if deemed appropriate.
Use appropriate aseptic technique during the preparation of CinnoVex.
To reconstitute lyophilized CinnoVex , use a sterile syringe to inject 1.1 mL of the supplied diluent, Sterile Water for Injection, into the CinnoVex vial.
Gently swirl the vial of CinnoVex to dissolve the drug completely.
Do not shake.
The reconstituted solution should be clear to slightly yellow without particles. Inspect the reconstituted product visually prior to use. Discard the product if it contains particulate matter or is discolored.
Each vial of reconstituted solution contains 30 mcg/1.0 mL Interferon beta-1a.
Withdraw 1.0 mL of reconstituted solution from the vial into a sterile syringe.
Attach the sterile needle and inject the solution intramuscularly.
The CinnoVex and diluent vial are for single-use only; unused portions should be discarded.

Adverse Reactions
CNS: Headache, fatigue, fever, pain, chills, depression, dizziness
GI: Nausea, abdominal pain
Genitourinary: Urinary tract infection
Hematologic: Leukopenia
Hepatic: ALT and AST increased
Local: Injection site reaction
Neuromuscular & skeletal: Myalgia, back pain, weakness, skeletal pain, rigors
Ocular: Vision abnormal
Respiratory: Sinusitis, upper respiratory tract infection, Flu-like syndrome

Contraindications
Hypersensitivity to natural or recombinant interferons, human albumin, or any other component of the formulation

Warnings/Precautions
Bone marrow suppression: Use with caution in patients with bone marrow suppression.
Flu-like symptoms: Associated with a high incidence of flu-like adverse effects, use of analgesics and/or antipyretics on treatment days may be helpful.
Hepatic effects: Treatment should be suspended if jaundice or symptoms of hepatic dysfunction occur. Use with caution in patients with hepatic impairment or in those who abuse alcohol. Dosage adjustment may be necessary. Some reports indicate symptoms began after 1-6 months of treatment. Transaminase elevations may be asymptomatic, so monitoring is important.
Neuropsychiatric disorders: Avoid use in severe psychiatric disorders and use caution in patients with a history of depression; patients exhibiting symptoms of depression should be closely monitored and discontinuation of therapy should be considered.
Seizure disorder: Use with caution in patients with a history of seizure disorder.
Cardiovascular disease: Use with caution in patients with pre-existing cardiovascular disease, including angina, HF, and/or arrythmia.
Chronic progressive MS: Safety and efficacy have not been established for this use.
Pediatrics: Safety and efficacy have not been established in children.
Geriatrics: Clinical studies did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

Drug Interactions
No formal drug interaction studies have been conducted with interferon beta-1a.
Pregnancy Risk Factor: C
Lactation: Excretion in breast milk unknown/not recommended

Monitoring Parameters
Thyroid function tests, CBC with differential, transaminase levels, symptoms of autoimmune disorders, signs/symptoms of psychiatric disorder, signs/symptoms of new onset/worsening cardiovascular disease

Pharmacodynamics/Kinetics
Onset of action: 12 hours (based on biological response markers)
Peak biological response marker levels are typically observed 48 hours after dosing.
Duration: 4 days (based on biological response markers)
Half-life elimination: 10 hours
Time to peak, serum: I.M.: 3-15 hours

Dosage Forms
30 mcg Lyophilized Powder Vial
A vial of CinnoVex (interferon beta-1a) is formulated as a sterile, white to off-white lyophilized powder for intramuscular injection after reconstitution with supplied diluent (Sterile Water for Injection).
Each vial of reconstituted CinnoVex contains 30 mcg of Interferon beta-1a, Albumin (Human), Sodium Chloride, Dibasic Sodium Phosphate, and Monobasic Sodium Phosphate, in 1.0 mL at a pH of approximately 7.3 (7.0-7.5).
CinnoVex lyophilized vials are available in the following package configuration:
A package containing four Administration Dose Packs (each containing one vial of CinnoVex lyophilized powder for injection, one diluent vial for reconstitution , two alcohol wipes, one gauze pad, one syringe for reconstitution and injection and one separate needle for intramuscular injection.

Stability and Storage
Vials of CinnoVex (interferon beta-1a) should be stored in a 2-8°C refrigerator.
Do not expose to high temperatures.
Do not freeze.
Protect from light.
Do not use beyond the expiration date stamped on the vial.
Following reconstitution, it is recommended the product be used as soon as possible within 6 hours stored at 2-8°C.
Do not freeze reconstituted CinnoVex (interferon beta-1a).

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