Saudi Public Assessment Report

Baclon®

Active Pharmaceutical Ingredient(s): Baclofen

ATC code/CAS no.: M03B X01

Pharmaceutical/Dosage Form: Tablets

Dosage Strength: 10 mg – 25 mg

Marketing Authorization Holder: Alrai Pharmaceutical industry Co. (L.L.C)

Shelf life: 24 months

Storage conditions: Do not store above 30 °C. Store in original Package.

Registration No.: 2702221770 - 2702221771

Decision and Decision Date: Approved on 7/02/2022

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Terms, Definitions, Abbreviations

Terms	Definitions
AUC_{0-t}	Area under the concentration-time curve (time 0 to time of last quantifiable concentration
$AUC_{0-\infty}$	Area under the serum concentration-time curve from time 0 to infinite time
C.I	Confidence Intervals
C_{max}	Maximum serum concentration
GCC	Gulf Cooperation Council
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
INN	International Nonproprietary Names
KSA	Kingdom of Saudi Arabia
SA	Saudi Arabia
SDI	Saudi Drug Information System
SFDA	Saudi Food and Drug Authority
SPC	Summary of Product Characteristics
USAN	United States Adopted Names

2. Background

2.1 Submission Details

Type of submission: Human Generic Drug

Reference product in SA: Lioresal 25 mg Tablet

Pharmacological class: Antispastic with spinal site attack

Submitted Indication:

Baclon is indicated for the relief of spasticity of voluntary muscle resulting from such disorders as multiple sclerosis, other spinal lesions e.g. tumours of the spinal cord, syringomyelia, motor neurone disease, transverse myelitis, and traumatic partial section of the cord. Baclon is also indicated in adults and children for the relief of spasticity of voluntary muscle arising from e.g. cerebrovascular accidents, cerebral palsy, meningitis, traumatic head injury.

Patient selection is important when initiating Baclon therapy; it is likely to be of most benefit in patients whose spasticity constitutes a handicap to activities and/or physiotherapy. Treatment should not be commenced until the spastic state has become stabilized.

Paediatric population:

Baclon is indicated in patients 0 to <18 years for the symptomatic treatment of spasticity of cerebral origin, especially where due to infantile cerebral palsy, as well as following cerebrovascular accidents or in the presence of neoplastic or degenerative brain disease.

Baclon is also indicated for the symptomatic treatment of muscle spasms occurring in spinal cord diseases of infectious, degenerative, traumatic, neoplastic, or unknown origin such as multiple sclerosis, spastic spinal paralysis, amyotrophic lateral sclerosis, syringomyelia, transverse myelitis, traumatic paraplegia or paraparesis, and compression of the spinal cord.

Submitted Dosage: 10 mg – 25 mg

2.2 Regulatory Background

This product is considered a human generic drug for Saudi regulatory purposes. Furthermore, this product is qualified to follow the regular review pathway.

2.3 Product Information

The officially approved Summary of Product Characteristics (SPC) can be accessed via Saudi Drug Information System (SDI) at: https://sdi.sfda.gov.sa/

3. Scientific discussion about the product:

3.1 Quality Aspects

3.1.1 Drug Substance

- Baclofen is a white to off-white, Crystalline powder is odorless or practically odorless. Baclofen is slightly soluble in water, very soluble in methanol and insoluble in chloroform. Baclofen does not have any chiral centers. Polymorphism has been observed.
- The drug substance is manufactured by a multiple-step chemical synthesis.
- The structure of Baclofen has been fully elucidated using several spectroscopic techniques.
- The drug substance specification includes relevant tests for proper quality control. The control methods are validated according to international guidelines.
- Appropriate stability data have been presented and justify the established re-test period.

3.1.2 Drug Product

- Baclon drug product is available in two strengths:

1. 10 mg tablets: White, or almost white compact, biconvex, round 7.0 mm, embossed “D8” with break line.
2. 25 mg tablets: White, or almost white compact, biconvex, round 8.0 mm, embossed “D9” with break line.

- Each tablet contains 10 mg or 25 mg of Baclofen. The composition of the drug product is adequately described, qualitatively and quantitatively. Suitable pharmaceutical development data have been provided for the finished product composition and manufacturing process.

- The manufacturing process is described narratively and in sufficient detail, taking into account pharmaceutical development data. Batch manufacturing formulas and in-process controls are included.
- The drug product specification covers appropriate parameters for this dosage form, which allow for proper control of the finished drug product. The control methods are validated according to international guidelines. Batch data show consistent quality of the drug product.
- The drug product is packaged in a carton box, containing 5 white PVC/PVDC – Alu blisters, containing 10 tablets in each blister.
- Appropriate stability data have been generated in the packaging material intended for commercial use and following relevant international guidelines. The data show good stability of the finished product and support the shelf life.

3.2 Clinical Aspects

3.2.1 Bioequivalence study

A randomized, open label, two treatment, two period, two sequence, single dose, crossover, bioequivalence study of Baclon® (Baclofen) 25 mg of Alrai pharmaceutical industries Co. (L.LC), KSA, and Lioresal® (Baclofen) 25 mg of Novartis Pharma GmbH/90327 Nürnberg, Germany, in healthy human adult subjects, under Fed condition. The study was conducted in accordance with Gulf Cooperation Council (GCC) Guidelines for Bioequivalence, standards of Good Clinical Practice (GCP) and Good Laboratory Practices (GLP).

Blood samples were taken pre-dose (0.0) and at a specified time points up to 24 hours after administration of test or reference product. Plasma levels of Baclofen were detected by a validated LC-MS/MS method.

Twenty-seven (27) volunteers completed the study and all data were analyzed. No significant protocol deviations were reported. There were no serious adverse events reported in the study.

The ratio and 90% Confidence Intervals of Test versus Reference for Baclofen are tabulated below:

Table 1: Ratio and 90% Confidence Intervals (C.I) of Test versus Reference for Baclofen:

Pharmacokinetic Parameter	**Point Estimate**	**90% Confidence Intervals (%)**
C_{max}	99.22	94.51 – 104.16
AUC_{0-t}	98.92	96.29 – 101.62
$AUC_{0-\infty}$	98.67	96.03 – 101.39

Based on the results obtained in this study, Baclon® (Baclofen) 25 mg of Alrai pharmaceutical industries Co. (L.LC), KSA, is **bioequivalent** to Lioresal® (Baclofen) 25 mg of Novartis Pharma GmbH/90327 Nürnberg, Germany, under Fed Conditions.

4. Risk Management Plan

4.1 Artwork and Trade Name assessment (Artwork available in appendix)

Proposed trade Name	**Dosage Form**
Baclon	Tablet

Look –alike/Sound-alike (LA/SA) Error Risk Potential:

Baclon name LA/SA confusion risk potential has been assessed based on the evaluation of LA/SA similarities from our data sources (SFDA registered Drug List, Martindale, ISMP Confused Drug Name List, INN International Nonproprietary Names and USAN United States Adopted Names STEM) and the pharmaceutical characteristic of the product:

LA/SA for Product name	SFDA	Shared File/ Excel Sheet	Martindale	Stem Book 2018
Baclon	NO	NO	NO	NO

Trade Name Recommendation:

Based on the submitted data, the proposed name Baclon is accepted.

Outer and Inner Package:

Based on the submitted data, the proposed artwork is accepted.

5. Overall Conclusion

Based on a review of data on quality, safety and efficacy, SFDA considered that the benefit/risk profile of Baclon was favorable and decided to grant the marketing authorization of Baclon to indicated for the relief of spasticity of voluntary muscle resulting from such disorders as multiple sclerosis, other spinal lesions e.g. tumours of the spinal cord, syringomyelia, motor neurone disease, transverse myelitis, traumatic partial section of the cord. Baclon is also indicated in adults and children for the relief of spasticity of voluntary muscle arising from e.g. cerebrovascular accidents, cerebral palsy, meningitis, traumatic head injury.

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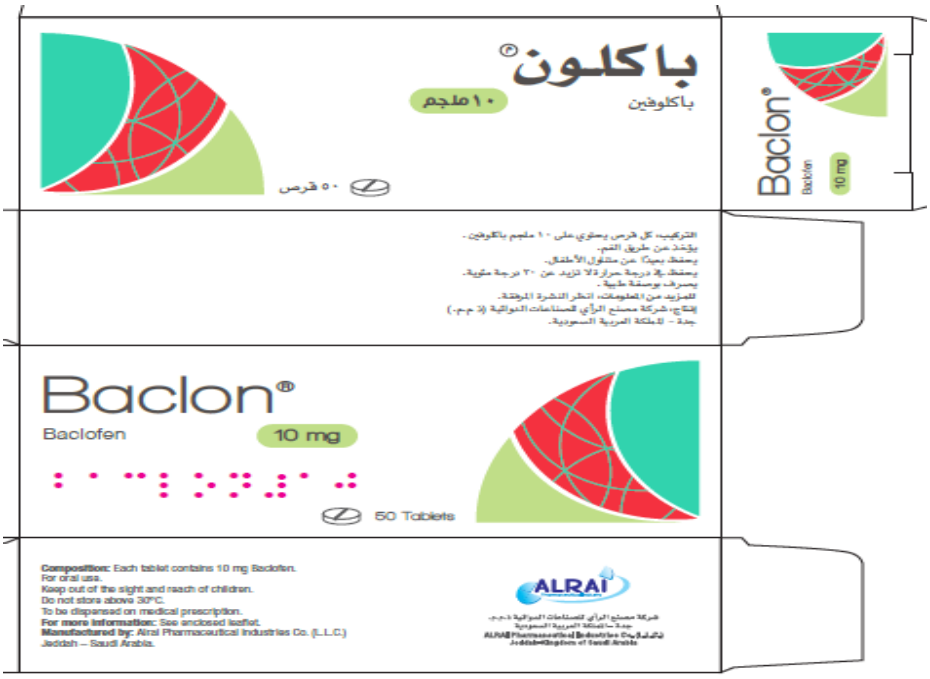
6. Appendix



Baclon®

The date of revision of this text corresponds to that of the Saudi PAR. New information concerning the authorized medicinal product in question will not be incorporated into the Saudi PAR. New findings that could impair the medicinal product's quality, efficacy, or safety are recorded and published at (SDI or Summary Saudi-PAR report).

For inquiry and feedback regarding Saudi PAR, please contact us at Saudi.PAR@sdfa.gov.sa