LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Lecapusa
(budesonide)

SE/H/2127/01/DC

This module reflects the scientific discussion for the approval of Lecapusa. The procedure was finalised on 2022-01-27. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Lecapusa, 3 mg, gastro-resistant capsule, hard.

The active substance is budesonide. A comprehensive description of the indication and posology is given in the SmPC.

For recommendations to the marketing authorisation not falling under Article 21a/22a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a/22a/ 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

The applications for Lecapusa, 3 mg, gastro-resistant capsule, hard, are hybrid applications made according to Article 10(3) of Directive 2001/83/EC. The applicant, Day Zero ehf., apply through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DE as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Budenofalk, 3 mg, hard capsule, authorised in BE since 1999, with Dr. Falk Pharma Benelux BV as marketing authorisation holder.

The reference product used in the bioequivalence studies is Budenofalk, 3 mg, gastro-resistant capsule, hard, from DE with Dr. Falk Pharma GmbH as marketing authorisation holder.

Potential similarity with orphan medicinal products
According to the application form and a check of the Community Register of orphan medicinal products there is no medicinal product designated as an orphan medicinal product for a condition relating to the indication proposed in this application.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of budesonide are well known. As budesonide is a widely used, well-known active substance, no further studies are required, and the applicant provides none. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Since Lecapusa is intended for substitution with marketed products containing the same active substance, it is unlikely to lead to an overall increased exposure to the environment. Supportive consumption data for the absence of consumption increase has been provided by the applicant (at least the last 4 years including the 4 concerned member states with the highest prevalence).

With regard to the SmPC 6.6., there exists CHMP/SWP recommendations since 2014 that disposal advice should be included in SmPC and package leaflet independent of the conclusions on the ERA. As such, the applicant has added the following disposal advice as per EMA template: "*Any unused medicinal product or waste material should be disposed of in accordance with local requirements*."

There are no objections to approval of Lecapusa et al. from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics
To support the marketing authorisation application the applicant has conducted two single-dose bioequivalence studies comparing Lecapusa with the reference product Budenofalk.

Pharmacokinetic properties of the active substance
The exact mechanism of budesonide in the treatment of Crohn's disease is not fully understood. Data from clinical pharmacology studies and controlled clinical trials strongly indicate that the mode of action of budesonide capsules is predominantly based on a local action in the gut. Budesonide is a glucocorticosteroid with a high local anti-inflammatory effect.

Absorption: The systemic availability in healthy volunteers as well as in fasting patients with Crohn's disease is about 9-13 %.

Budesonide 3 mg capsules, which contain gastric juice resistant granules, have, due to the specific coating of the granules, a lag phase of 2 - 3 hours. In healthy volunteers, as well as in patients with Crohn's disease, mean maximal budesonide plasma concentrations of 1-2 ng/ml were seen at about 5 hours following an oral dose of budesonide 3 mg gastro-resistant capsules at a single dose of 3 mg, taken before meals. The maximal release therefore occurs in the terminal ileum and caecum, the main area of inflammation in Crohn's disease.

Concomitant intake of food may delay release of granules from stomach by 2-3 hours, prolonging the lag phase to about 4-6 hours, without change in absorption rates.

Elimination: The average elimination half-life is about 3-4 hours.

Study BE-2037-20 FASTED

Methods

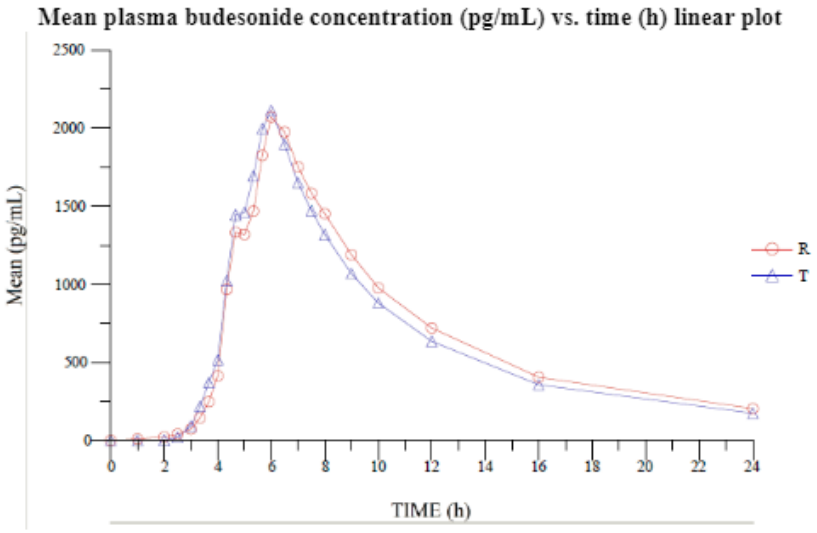
This was a randomised, two-treatment, four-period, two sequence, full replicate single-dose crossover bioequivalence study conducted in 80 healthy volunteers, comparing Budesonide 3 mg, gastro-resistant capsule, hard with Budenofalk, 3 mg, gastro-resistant capsule, hard under fasting conditions. Blood samples for concentration analysis were collected pre-dose and up to 24 hours post-dose. Plasma concentrations of budesonide were determined with an LC-MS/MS method. Analysis of variance (ANOVA) was performed on the log-transformed data for AUC_{0-t}, partial AUCs (AUC_{0-6}, AUC_{6-24}) and C_{max}. The study was conducted between 10 August 2020 and 4 September 2020.

Results

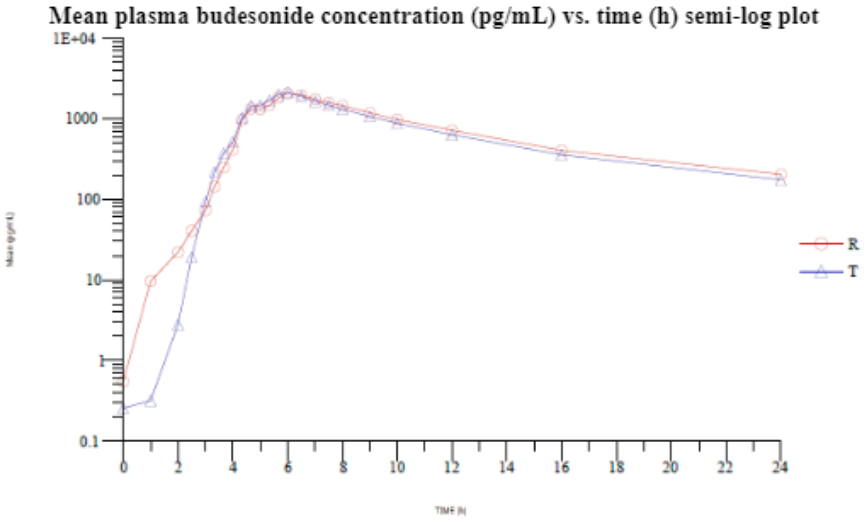
The linear and semi-log plots of mean plasma budesonide concentrations vs. time are presented in Figure 1 below.

Figure 1. The Linear and Semi-Log plots of Mean Plasma Budesonide Concentrations vs. Time

Linear plot:



Semi-Log plot:



The results from the pharmacokinetic and statistical analysis are presented in Table 1 and Table 2 below.

Table 1. Summary of Pharmacokinetic and Statistical Results for Budesonide

	Reference (R)				Test (T)			
Pharmacokinetic Parameter(s)	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**
AUC(0-t) (pg.h/mL)	149	15110.10	10354.005	68.52	152	14273.04	9713.721	68.06
AUC(0-6) (pg.h/mL)	149	2989.11	2612.890	87.41	152	3302.12	2664.867	80.70
AUC(6-24) (pg.h/mL)	149	12121.23	9007.592	74.31	152	10971.27	8436.885	76.90
Cmax (pg/mL)	149	2664.50	1606.252	60.28	152	2717.38	1684.555	61.99
*Tmax (h)	149	6.00 (3.68-12.00)			152	5.67 (3.33-12.00)		
Thalf (h)	146	6.07	1.978	32.61	149	5.86	1.627	27.77
Kel (1/h)	146	0.12	0.027	22.52	149	0.13	0.030	23.53
*: Median & range reported.								

	Reference Product (R)				Reference Replicate Product (R)			
Pharmacokinetic Parameter(s)	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**
$AUC_{(0-t)}$ (pg.h/mL)	75	14480.11	7915.492	54.66	74	15748.61	12369.867	78.55
$AUC_{(0-6)}$ (pg.h/mL)	75	2726.60	2260.439	82.90	74	3255.16	2918.785	89.67
$AUC_{(6-24)}$ (pg.h/mL)	75	11752.39	7452.556	63.41	74	12495.06	10388.142	83.14
C_{max} (pg/mL)	75	2508.33	1455.704	58.03	74	2822.79	1741.327	61.69
*T_{max} (h)	75	5.67 (3.68-12.00)			74	6.00 (4.33-9.00)		
T_{half} (h)	74	6.14	2.321	37.78	72	5.99	1.563	26.10
K_{el} (1/h)	74	0.12	0.027	22.03	72	0.12	0.028	23.14
*: Median & range reported.								

	Test Product (T)				Test Replicate Product (T)			
Pharmacokinetic Parameter(s)	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**
$AUC_{(0-t)}$ (pg.h/mL)	76	13576.31	10236.640	75.40	76	14969.77	9175.959	61.30
$AUC_{(0-6)}$ (pg.h/mL)	76	3023.63	2210.830	73.12	76	3580.61	3041.835	84.95
$AUC_{(6-24)}$ (pg.h/mL)	76	10554.39	8963.592	84.93	76	11388.15	7912.833	69.48
C_{max} (pg/mL)	76	2477.63	1530.871	61.79	76	2957.14	1803.669	60.99
*T_{max} (h)	76	5.67 (4.33-12.00)			76	5.67 (3.33-10.00)		
T_{half} (h)	74	5.87	1.642	27.99	75	5.85	1.624	27.75
K_{el} (1/h)	74	0.13	0.032	25.59	75	0.13	0.027	21.44
*: Median & range reported.								

Table 2. Statistical Summary of the comparative Bioavailability data for Budesonide

						90 % C.I (%)						
Pharmacokinetic Parameter(s)	**Test**	**N**	**RLD**	**N**	**Ratio (%)**	**Lower**	**Upper**	**Intra CV% - Ref**	**Intra CV% - Test**	**Intra CV% - Pooled**	**Lower Acceptance Limit**	**Upper Acceptance Limit**
$AUC_{(0-t)}$ (pg.h/mL)	12003.42	77	12803.96	77	93.75	89.48	98.22	25.11	24.09	24.80	80.00	125.00
$AUC_{(0-6)}$ (pg.h/mL)	2319.51	77	1930.14	77	120.17	105.54	136.83	90.89	74.10	76.72	69.84	143.19
$AUC_{(6-24)}$ (pg.h/mL)	9013.83	77	10051.32	77	89.68	85.17	94.43	29.74	25.38	27.55	80.00	125.00
C_{max} (pg/mL)	2209.16	77	2185.56	77	101.08	93.87	108.84	44.82	37.65	40.26	72.24	138.43

For AUC_{0-t}, AUC_{6-24} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

For AUC_{0-6} the 90% confidence interval for the ratio of the test and reference products fell within the widened range of 69.84-143.19%.

Study BE-2038-20 FED

Methods

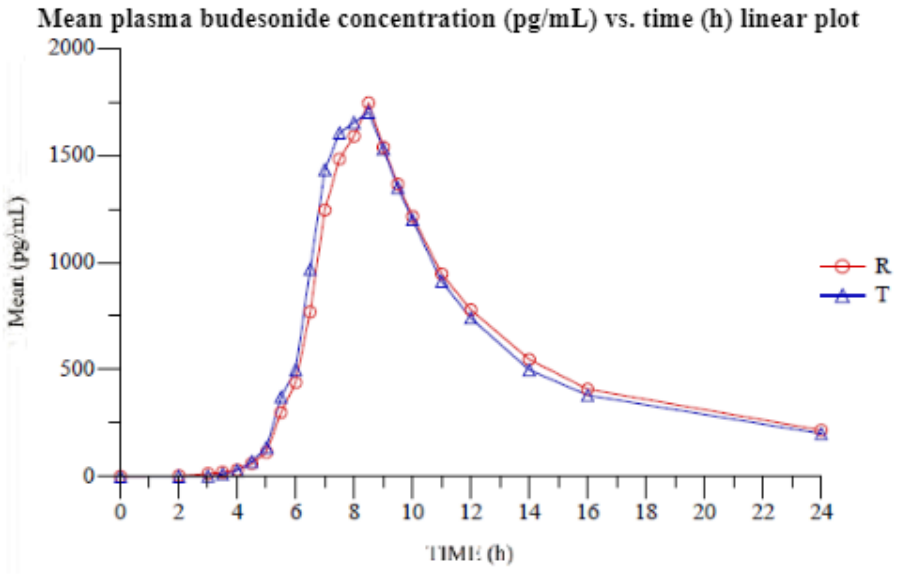
This was a randomised, two-treatment, four-period, two sequence, full replicate single-dose crossover bioequivalence study conducted in 60 healthy volunteers, comparing Budesonide, 3 mg, gastro-resistant capsule, hard with Budenofalk, 3 mg, gastro-resistant capsule, hard under fed conditions. Blood samples for concentration analysis were collected pre-dose and up to 24 hours post-dose. Plasma concentrations of budesonide were determined with an LC-MS/MS method. Analysis of variance (ANOVA) was performed on the log-transformed data for AUC_{0-t}, partial AUCs (AUC_{0-9}, AUC_{9-24}) and C_{max}. The study was conducted between 21 August 2020 and 13 September 2020.

Results

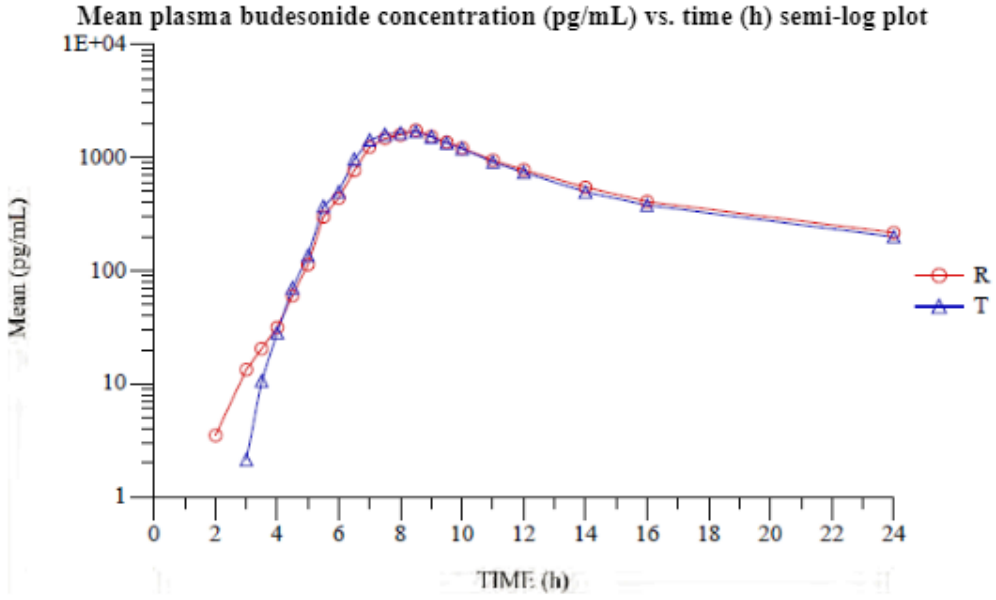
The linear and semi-log plots of mean plasma budesonide concentrations vs. time are presented in Figure 2 below.

Figure 2. The Linear and Semi-Log plots of Mean Plasma Budesonide Concentrations vs. Time

Linear plot:



Semi-Log plot:



The results from the pharmacokinetic and statistical analysis are presented in Table 3 and Table 4 below.

Table 3. Summary of Pharmacokinetic and Statistical Results for Budesonide

	Reference Product (R)				Test product (T)			
Pharmacokinetic Parameter(s)	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**
$AUC_{(0-t)}$ (pg.h/mL)	111	12220.58	4835.882	39.57	109	12128.24	4614.851	38.05
$AUC_{(0-9)}$ (pg.h/mL)	111	4291.87	2490.356	58.02	109	4613.04	2603.982	56.45
$AUC_{(9-24)}$ (pg.h/mL)	111	7927.92	3412.210	43.04	109	7514.54	3110.691	41.40
C_{max} (pg/mL)	111	2203.70	1108.479	50.30	109	2286.59	1143.858	50.02
*T_{max} (h)	111	8.50	5.50-24.00	-	109	8.00	5.50-24.00	-
T_{half} (h)	100	8.22	23.198	282.29	98	5.95	1.375	23.10
K_{el} (1/h)	100	0.12	0.029	23.70	98	0.12	0.025	20.66
*: Median & range reported.								

	Reference Product (R)				Reference Replicate Product (R)			
Pharmacokinetic Parameter(s)	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**
$AUC_{(0-t)}$ (pg.h/mL)	58	12632.58	5515.414	43.66	53	11769.71	3965.927	33.70
$AUC_{(0-9)}$ (pg.h/mL)	58	4481.07	2595.646	57.92	53	4084.83	2377.082	58.19
$AUC_{(9-24)}$ (pg.h/mL)	58	8150.82	3894.575	47.78	53	7683.99	2808.484	36.55
C_{max} (pg/mL)	58	2307.65	1186.769	51.43	53	2089.94	1014.958	48.56
*T_{max} (h)	58	8.50	5.50-24.00	-	53	8.50	5.50-24.00	-
T_{half} (h)	52	6.00	1.365	22.75	48	10.62	33.469	315.14
K_{el} (1/h)	52	0.12	0.026	21.81	48	0.12	0.032	25.72
*: Median & range reported.								

	Test Product (T)				Test Replicate Product (T)			
Pharmacokinetic Parameter(s)	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**	**N**	**Arithmetic mean**	**Standard deviation**	**CV (%)**
$AUC_{(0-t)}$ (pg.h/mL)	57	12674.34	4650.131	36.69	52	11529.63	4544.981	39.42
$AUC_{(0-9)}$ (pg.h/mL)	57	4893.93	2501.351	51.11	52	4305.13	2702.622	62.78
$AUC_{(9-24)}$ (pg.h/mL)	57	7779.97	3173.211	40.79	52	7223.59	3044.616	42.15
C_{max} (pg/mL)	57	2390.30	1087.268	45.49	52	2172.91	1203.123	55.37
*T_{max} (h)	57	8.00	5.50-14.00	-	52	8.00	5.50-24.00	-
T_{half} (h)	54	6.03	1.400	23.24	44	5.86	1.354	23.10
K_{el} (1/h)	54	0.12	0.026	21.72	44	0.12	0.024	19.50
*: Median & range reported.								

Table 4. Statistical Summary of the comparative Bioavailability data for Budesonide

						90 % C.I (%)						
Pharmacokinetic Parameter(s)	**Test**	**N**	**RLD**	**N**	**Ratio (%)**	**Lower**	**Upper**	**Intra CV% - Ref**	**Intra CV% - Test**	**Intra CV% - Pooled**	**Lower Acceptance Limit**	**Upper Acceptance Limit**
$AUC_{(0-t)}$ (pg.h/mL)	11170.93	58	11207.42	58	99.67	94.85	104.75	25.00	21.23	22.43	80.00	125.00
$AUC_{(0-9)}$ (pg.h/mL)	3761.15	58	3305.75	58	113.78	100.86	128.34	54.32	63.94	57.89	69.84	143.19
$AUC_{(9-24)}$ (pg.h/mL)	6845.06	58	7185.29	58	95.26	90.43	100.36	25.46	21.68	23.55	80.00	125.00
C_{max} (pg/mL)	1992.70	58	1897.95	58	104.99	97.37	113.22	36.72	35.55	34.63	76.31	131.04

For AUC_{0-t}, AUC_{9-24} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

For AUC_{0-9} the 90% confidence interval for the ratio of the test and reference products fell within the widened range 69.84-143.19%.

Discussion and overall conclusion

The applied product is locally applied and locally acting modified release product. According to Guideline on equivalence studies for the demonstration of therapeutic equivalence for locally applied, locally acting products in the gastrointestinal tract (CPMP/EWP/239/95 Rev. 1) there is a possibility that PK bioequivalence studies based on plasma levels could be used as a surrogate of equivalence in efficacy and systemic safety:

"For modified release products containing a drug being absorbed and showing systemic bioavailability, bioequivalence studies based on plasma levels could also be used as a surrogate of equivalence in efficacy and systemic safety if the systemic absorption starts at a similar site and absorption kinetics are equivalent, because the systemic absorption occurs at the sites of release. Partial AUC assessment can help to distinguish absorption caused by an early release and absorption from release at the sites of action, if:
a) absorption is not saturated at the relevant dose (shown e.g. by means of a dose-proportionality study for all the PK parameters of interest);

b) test and reference are the same dosage form;
c) test and reference exhibit similar in vitro dissolution profiles in a battery of state-of-the-art experiments (not only in the QC media and buffers at pH 1.2, 4.5 and 6.8, but also in vitro methods simulating intraluminal pH-conditions, ionic buffer strength, physiological buffer composition, mechanical stress and residence times in the human GI tract, e.g. tests in the reciprocating cylinder apparatus simulating "average" fasted subjects and also a range of "patient-specific" patterns of pH-conditions and passage times with continuous and discontinuous passage through the small intestine);
d) partial exposures and their corresponding absorption sites are well justified.

The requirements defined in the 'Guideline on the pharmacokinetic and clinical evaluation of modified release dosage forms (EMA/CPMP/EWP/280/96)' should be applied. Bioequivalence should be demonstrated in single dose studies in fasting and fed state and, in case of prolonged release products with significant accumulation, also in a multiple dose study. Partial AUCs (early and late partial AUCs as defined by predefined, well justified cut-off points) should be used as primary PK endpoint in both types of single dose studies, even in case of significant accumulation when a multiple dose study is required."

To support the application, the applicant has submitted two single-dose bioequivalence studies, one in the fed state and one in the fasted state. No multiple dose study was performed by the applicant. The product is not only a delayed-release product but has prolonged-release properties as well; thus it is relevant to discuss the need of a multiple dose study. There is however no indication of major accumulation systemically, as $AUC_{0\text{-}24h}$ in the single dose studies is almost 90% of AUC_{inf}. It is agreed that a multiple dose study can be waived.

In order to confirm that partial AUC assessment can help to distinguish absorption caused by an early release and absorption from release at the sites of action and that PK data can be used as a surrogate for equivalence, the applicant has provided the following data and responses:

The applicant has provided a summary of public data from studies with Budenofalk where it was shown that the AUC_{inf} values were similar after a 9 mg single dose and a 3 mg three times a day dosing scheme. Dose-corrected AUC estimates did not differ much between treatments of 3x3 mg, 1x9 mg and 1x18 mg. Thus, there are no indications that the absorption is saturated at the relevant dose (criterion a).

To show similarity with the reference drug product, Budenofalk 3 mg gastro-resistant capsule, bioequivalence studies and in vitro dissolution comparisons using the QC method and buffer at pH 2.1, 4.5 and 6.8 have been performed. Additional acceptable in vitro dissolution studies demonstrating similar release behaviour of both the test- and reference drug products at various pHs and ionic strengths have been provided when using reciprocating cylinder apparatus (Apparatus 3). In vitro data appear to be consistent with in vivo data and is sufficient to meet the requirements in the guideline (criterion c).

The partial exposures and their corresponding absorption sites should be well justified (criterion d). The applicant has justified the chosen cut-off points for the predefined partial AUCs (6 and 9 hours for the fasted and fed studies, respectively) based on t_{max} values for the reference product. According to the guideline, the justification of the chosen cut-off time is expected to be related to the corresponding absorption site. The published t_{max} values seem to correlate approximately with the time when the formulation is expected to reach the targeted site of action. This may be a reasonable justification of a cut-off, but it is acknowledged that the "early partial AUC" represents a relatively low percentage of the total absorption (15-20% in the fasted study and around 30% in the fed study) and mainly represents absorption before the formulation reaches the desired site of action. Thus, most of the drug absorption, and the absorption that is a surrogate of the concentration at the local effect site, is represented by the large "late partial AUC". Therefore, further characterisation of the plasma concentration vs time profile was requested, especially considering that the product is not only a delayed-release product but has prolonged-release properties as well. The applicant has performed

additional partial AUC assessments with later cut-off points for both the fasting (7 hrs, 8 hrs, 9 hrs) and fed (10 hrs, 11 hrs) single-dose studies. For the additional partial AUCs with later cut-off points the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

In addition to using the pre-defined cut-offs, the applicant also evaluated the partial AUC parameters by using cut-off values of 5 hrs and 8 hrs for the fasted and fed states, respectively. For AUC_{0-5} (fasted study) and AUC_{0-8} (fed study) the 90% confidence interval for the ratio of the test and reference products fell within the widened range 69.84-143.19% (as was the case also with the predefined cut-offs).

In summary, in accordance with the Guideline on the pharmacokinetic and clinical evaluation of modified release dosage forms, the applicant has sufficiently justified that it is acceptable to demonstrate therapeutic equivalence for this locally applied, locally acting GI product with modified release based on PK bioequivalence in fasted and fed conditions and in vitro tests.

Both studies were able to demonstrate bioequivalence for C_{max}, AUC_{0-t} and late partial AUCs using the conventional acceptance range of 80.00-125.00%. However, a widening of acceptance range was necessary for early partial AUCs. The widening of acceptance range for early partial AUCs in both studies is acceptable since the applicant has justified that the calculated intra-subject variability is a reliable estimate and that it is not the result of outliers and provided a justification that a wider diference is not clinically relevant.

The Lag-time can also be used as a descriptive pharmacokinetic parameter to compare test and reference as it gives indication of when the release from the product starts, i.e. an indirect measure of how the product can resist the gastric environment. The substance released in the stomach will probably be absorbed in the upper part of the small intestine and will therefore not reach the main target regions in the intestine; ileum and colon ascendence. The applicant has calculated the mean lag-time for the test and reference biobatches and these were found to be 3.12 hrs and 2.01 hrs, respectively, under fasting conditions and 4.67 hrs and 3.57 hrs, respectively, under fed conditions. These differences are considered small and not likely to be clinically relevant. The “early partial AUC” represents a relatively low percentage of the total absorption and mainly represents absorption before the formulation reaches the desired site of action.

The bioanalytical methods were adequately validated in accordance with the Guideline on bioanalytical method validation (EMEA/CHMP/EWP/192217/2009 Rev. 1 Corr. 2).

Based on the submitted bioequivalence studies, equivalence regarding efficacy and systemic safety has been demonstrated for Lecapusa compared to the reference product Budenofalk.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated additional data is not necessary.

Risk Management Plan
The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to the products.

Safety specification

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP
The submitted Risk Management Plans signed December 23 2020 for Lecapusa (version 1.0) is in line with the reference product and are considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English. The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Lecapusa is found adequate. There are no objections to approval of Lecapusa from a non-clinical and clinical point of view. Based on the submitted bioequivalence studies, equivalence regarding efficacy and systemic safety has been demonstrated for Lecapusa compared to the reference product Budenofalk. The product information is acceptable. The applications are therefore recommended for approval.

List of recommendations not falling under Article 21a/22a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a/22a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The decentralised procedure for Lecapusa, 3 mg, gastro-resistant capsule, hard was positively finalised on 2022-01-27.

LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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