



# Experior™

(lubabegron Type A medicated article)

ADVANCING THE BEEF INDUSTRY'S  
ENVIRONMENTAL STEWARDSHIP EFFORTS

Elanco

**Experior™**



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## THE BEEF INDUSTRY AND ENVIRONMENTAL SUSTAINABILITY – THE CURRENT LANDSCAPE

The beef industry has and continues to demonstrate its long-term commitment to environmental stewardship in many areas. In fact, in 2015, U.S. ranchers were able to produce the same amount of beef as they did in 1975, but with 33% less cattle.<sup>1</sup>

Embracing technology, improving management practices, and adopting sustainable practices allows U.S. beef producers to provide 18% of the world's beef with only eight percent of the world's cattle.<sup>2</sup>

**THE BEEF INDUSTRY TODAY CONTINUES**

**TO BE GOOD STEWARDS OF RESOURCES,**

**WHILE CONSTANTLY PURSUING IMPROVED**

**ENVIRONMENTAL STEWARDSHIP EFFORTS BOTH**

**INDIVIDUALLY AND INDUSTRY-WIDE.**

<sup>1</sup> [https://www.farmtalknewspaper.com/news/u-s-beef-industry-has-made-long-strides-in-reducing/article\\_d8d40e40-1b40-11e8-a338-ab49f3893c58.html](https://www.farmtalknewspaper.com/news/u-s-beef-industry-has-made-long-strides-in-reducing/article_d8d40e40-1b40-11e8-a338-ab49f3893c58.html)

<sup>2</sup> UN FAOSTAT database. <http://www.fao.org/faostat/en/#home>

## SHIFTING CONSUMER TRENDS

As beef producers continue to advance their sustainability efforts, today's consumers are increasingly interested in the environmental impacts of their favorite foods. Products with sustainability claims are growing in demand and are capturing an increasing proportion of market share. Additionally, younger consumers are more driven towards purchasing products with environmental sustainability or cause-marketing claims. Furthermore, 48% of U.S. consumers said they're "definitely" or "probably" changing their consumption habits to reduce the impact on the environment.<sup>3</sup>

While consumer interest in environmental sustainability increases, retailers, foodservice operators – and their investors – have prioritized sustainability and environmental stewardship.

## THE BEEF INDUSTRY'S CONTINUED IMPROVEMENT

In light of increased consumer interest and demand, organizations, including the U.S. Roundtable for Sustainable Beef (USRSB) and the National Cattlemen's Beef Association (NCBA), have made significant efforts to communicate continuous improvement in the sustainability of beef production.

Through tools like the USRSB's Sustainability Framework, which includes resources and tools for individuals along the beef value chain to voluntarily assess their sustainability efforts, and NCBA's constant support and awareness of the industry's stewardship efforts, the beef industry continues on the path of improved sustainability.

<sup>3</sup> Nielsen. Was 2018 The Year of the Influential Sustainable Consumer? <https://www.nielsen.com/us/en/insights/article/2018/was-2018-the-year-of-the-influential-sustainable-consumer/>

## THE ELANCO ANIMAL HEALTH COMMITMENT

Alongside organizations like USRSB and NCBA, Elanco Animal Health is committed to being a


**responsible, reliable and trusted partner in developing new technologies that advance the beef industry's environmental stewardship efforts.**

This includes the introduction of Experior™ (lubabegron Type A medicated article).


Experior is approved for the reduction of ammonia gas emissions per pound of live weight and hot carcass weight in beef steers and heifers fed in confinement for slaughter during the last 14 to 91 days on feed.

Experior reduces the amount of ammonia gas released into the environment by cattle.

It is an additional tool for the continued environmental stewardship efforts of the beef industry.



**1<sup>st</sup> United States Food and Drug Administration (FDA) approved** product labeled to reduce gas emissions from an animal or its waste.



**Ammonia gases impact the environment and are known to come from many sources.<sup>4</sup>**

*"The reduction of ammonia gases reasonably may be expected to provide some benefit to the environment."<sup>5</sup>*

Based on existing information, reliable prediction of the ammonia gas emissions cannot be made on a herd, farm or larger scale.

<sup>4</sup> Chemical Safety Facts. Ammonia. <https://www.chemicalsafetyfacts.org/ammonia/>. May 2020.

<sup>5</sup> FDA Announcement Press Release: FDA Approves Experior for Reduction of Ammonia Gas Released from Beef Cattle Waste. <https://www.fda.gov/animal-veterinary/cvm-updates/fda-approves-experior-reduction-ammonia-gas-released-beef-cattle-waste>. Nov. 6, 2018.

## GENERAL INFORMATION

Experior (lubabegron Type A medicated article)

Beta-adrenergic agonist/antagonist

Type A contains 10 g per kg (4.54 g per lb)

**How Supplied:** 10 kg bag

## Directions for Use

Feed 1.25 to 4.54 g/ton (1.39 to 5 ppm) of complete feed (90% Dry Matter (DM) basis) to provide 13 - 90 mg lubabegron/head/day continuously to beef steers and heifers fed in confinement for slaughter as the sole ration during the last 14 to 91 days on feed.

## Important Safety Information

**Caution:** Not approved for use in breeding animals because safety and effectiveness have not been evaluated in these animals. Do not allow horses or other equines access to feed containing Experior. A decrease in dry matter intake may be noticed in some animals.

**The label contains complete use information, including cautions and warnings. Always read, understand, and follow the label, and use directions.**

- ➔ Air quality and addressing air emissions is a shared responsibility, including for feedyard owners and operators.<sup>6</sup>
- ➔ Feedyards should be aware of the environmental concerns and management strategies associated with air emissions, including ammonia.<sup>6</sup>
- ➔ Agricultural sources (which include livestock) are the largest known source of ammonia gas emissions in the U.S.<sup>7,8</sup>
- ➔ Ammonia gas is thought to be a significant contributor to the eutrophication of waterways and the formation of atmospheric haze and noxious odors.
- ➔ Experior is thought to act by increasing nitrogen (amino acid) uptake and increasing the amount of nitrogen retained in the carcass as muscle protein, thereby reducing the amount of urea excreted in manure (manure is considered the urine and feces combined).<sup>7,9</sup>
- ➔ The urea in manure is rapidly converted by an enzyme, urease, to ammonia and ammonium. Subsequently, this ammonia is volatilized (i.e., released as a gas) to the atmosphere.

**Thus, the reduction in excreted urea from the animal results in a reduction in ammonia gas emissions to the environment.**

*Ammonia gas emissions were measured for individual animals or small groups of animals held in environmentally controlled facilities. Based on existing information, reliable predictions of the reduction of ammonia gas emissions cannot be made on a herd, farm, or larger scale.*

<sup>6</sup> U.S. Roundtable on Sustainable Beef. <https://www.beefsustainability.us/high-priority-indicators/air-greenhouse-gas>. May 2020.

<sup>7</sup> Experior FONSI, summarized from page 3, <https://animaldrugatfda.fda.gov/adafda/app/search/public/document/downloadFonsi/1271>.

<sup>8</sup> USEPA. 2014. 2014 National Emissions Inventory (NEI) Data.

<sup>9</sup> Environmental Assessment for the use of Experior™ (lubabegron Type A medicated article) for reduction of ammonia gas emissions per pound of live weight and hot carcass weight in beef steers and heifers fed in confinement for slaughter during the last 14 to 91 days on feed. <https://animaldrugatfda.fda.gov/adafda/app/search/public/document/downloadEA/1311>. June 2018.





# **EXPERIOR KEY FINDINGS**

# Effectiveness<sup>4</sup>

<sup>4</sup> Experior FOI, summarized from pages 18-19

## Studies Conducted

### Dose Characterization

Three studies conducted to characterize emissions for:

**NH<sub>3</sub>, N<sub>2</sub>O, H<sub>2</sub>S, CH<sub>4</sub>, and CO<sub>2</sub>\***

\* Note the only statistical impact was for the reduction of ammonia (NH<sub>3</sub>) gas emissions.

## Substantial Evidence (Clinical Program):

### Emission Studies

Two studies conducted based on the following durations:

**14 days**

**91 days**



## Gas Emissions Studies – Facilities

### MICHIGAN

#### Facility:

- MSU Animal Air Quality Facility
- 12 Individual animal chambers
  - 100% concrete chambers
- 7 ft x 13 ft x 8.5 ft (91 ft<sup>2</sup>/animal)
- Animals tethered in an elevated platform

#### Animal:

- Heifers and Steers

#### Study Duration:

- 14 day

#### Experimental Unit:

- Individual animal



### CALIFORNIA

#### Facility:

- UCD Beef Cattle research facility
- 8 cattle pen enclosures (CPEs)
  - Dirt-floored
- 185 m<sup>2</sup> pens (CPEs); 14 animals/CPE
- 13 m<sup>2</sup> concrete feed bunk

#### Animal:

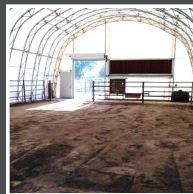
- Heifers and Steers

#### Study Duration:

- 91 day

#### Experimental Unit:

- Pen



### Effectiveness: 14 Day Gas Emissions – Results

LUBABEGRON DOSE, g/TON (100% DM) <sup>A</sup>					
Variable	0	1.25	5.0	20.0	P-value
NH <sub>3</sub> emissions, g/hd	823	763	744	701	0.113
NH <sub>3</sub> /lb LW, g/lb	0.642	0.594	0.582	0.551	0.130
NH <sub>3</sub> /lb HCW, g/lb	1.00	0.917	0.900	0.852	0.093
Initial weight, lb	1237	1238	1226	1232	0.669
Final weight, lb	1277	1273	1268	1267	0.843
HCW, lb	819	828	823	821	0.798

<sup>A</sup>The Type C approval for lubabegron is between 1.25 and 4.54 g/ton (90% DM)

### 91 Day Gas Emissions – Results

LUBABEGRON DOSE, g/TON (100% DM) <sup>A</sup>					
Variable	0	1.25	5.0	20.0	P-value
NH <sub>3</sub> emissions, g/hd	7783	7093 (P=0.076) <sup>B</sup>	6860 (P=0.023)	6751 (P<0.013)	0.052
NH <sub>3</sub> /lb live weight, g/lb	6.18	5.51 (P=0.009)	5.32 (P=0.002)	5.26 (P<0.001)	0.004
NH <sub>3</sub> /lb HCW, g/lb	10.1	8.83 (P=0.004)	8.49 (P<0.001)	8.40 (P<0.001)	0.001
Initial Wgt, lb	994	1001	1004	996	0.937
Final Wgt, lb	1250	1286	1283	1282	0.257

<sup>A</sup>The Type C approval for lubabegron is between 1.25 and 4.54 g/ton (90% DM)  
<sup>B</sup>P-value for the contrast between 0 g/ton and each dose level



### 14 Day Gas Emissions – Summary

- None of the gases (NH<sub>3</sub>, N<sub>2</sub>O, H<sub>2</sub>S, CH<sub>4</sub>, and CO<sub>2</sub>) were significantly affected by dose for the 0-14 day period.
- Analysis of the 7-14 day treatment period showed a significant association between treatment and the mean cumulative NH<sub>3</sub> gas emissions per lb of live weight (LW) and hot carcass weight (HCW).
- Analysis excluding outliers indicated that gas emissions standardized to LW and HCW were significantly different and numerically reduced for all non-zero treatments compared to controls in the 14 day period.
- Experior did not have any negative effects on average daily gain (ADG), feed efficiency (FE), or carcass characteristics. There was a slight increase in Warner-Bratzler Shear Force (WBSF), but this is unlikely to be noticed by consumers.

### Effectiveness: 14 Day Gas Emissions – Additional Evidence

		LUBABEGRON DOSE, g/TON (100% DM) <sup>A</sup>			
Location	Study Duration <sup>B</sup>	0	1.25	5.0	20.0
Michigan	14	823	763	744	701
California	91	953	835	801	699
Michigan	28	171	NA	NA	150
Michigan	42	494	397	355	NA
California	93	1301	1177	NA	NA

<sup>A</sup>The Type C approval for lubabegron is between 1.25 and 4.54 g/ton (90% DM)  
<sup>B</sup>Lubabegron is approved to be fed during the final 14 to 91 days on feed

### Effectiveness: Weight of Evidence at 14 Days

Additional studies were considered in evaluating effectiveness of Experior at 14 days.

- Mean cumulative NH<sub>3</sub> gas emissions and emissions per lb of LW were numerically lower at 14 days of treatment in previous studies.
- Given consistency of response to Experior across additional studies (5), FDA concluded that effectiveness at the minimum duration of 14 days is supported.

### 91 Day Gas Emissions – Summary

- Mean cumulative NH<sub>3</sub> gas emissions per lb of LW and HCW were significantly lower for all dose levels tested.
- Main effect of dose was significant with the lowest effective dose being 1.25 g/ton.
- No evidence was found that the mean at 5 g/ton was different from that at 20 g/ton.
- There was no Dose x Gender interaction.
- Experior did not negatively affect ADG, FE, liver abscess scores, or carcass characteristics.
- Experior resulted in a slight increase in WBSF, but at a level unlikely to be distinguishable by consumers.

The use of Experior reduces ammonia gas emissions from beef steers and heifers fed in confinement for slaughter for the last 14-91 days on feed.

## EMISSION STUDIES EFFECTIVENESS CONCLUSIONS

These studies support the use of Experior for the reduction of NH<sub>3</sub> gas emissions per pound of LW and HCW at the doses evaluated.

- Experior did not affect N<sub>2</sub>O, H<sub>2</sub>S, CH<sub>4</sub>, or CO<sub>2</sub> gas emissions per lb of LW and HCW at the doses evaluated.
- Increased rate of weight gain, improved feed efficiency, and increased carcass leanness have not been demonstrated with this product.

# CLINICAL PROGRAM

## Field Studies – Facilities

### NEBRASKA

#### Facility:

- 100% concrete pens
- 75 ft<sup>2</sup>/animal, 1.56 ft/animal of bunk space
- 125 ft<sup>2</sup> shade

#### Animal:

- Heifers and Steers

#### Study Duration:

- 14 and 91 day

#### Transport and Slaughter:

- Distance: 70 miles (~ 2 hr)
- Lairage: ~ 17 hr

### IDAHO

#### Facility:

- Predominately *dirt* (concrete apron at feed bunk)
- 219 ft<sup>2</sup>/animal, 3.1 ft/animal of bunk space

#### Animal:

- Heifers and Steers

#### Study Duration:

- 14 and 91 day

#### Transport and Slaughter:

- Distance: 313 miles (~ 5 to 10 hr)
- Lairage: ~ 11 to 14 hr

## Field Safety Studies

Four studies conducted to demonstrate the safety and impact on animal production and meat quality of Expor under expected conditions of use.

**14 day duration (2)    91 day duration (2)**

## EFFECTIVENESS: FIELD SAFETY STUDIES CONCLUSIONS

- Animal performance measures (ADG, FE, HCW) were not negatively affected by Expor at any dose.
- No consistent negative effects of Expor were detected for skeletal maturity, lean maturity, and overall maturity.
- No consistent dose related effects were observed for marbling score or WBSF across the four field studies.
- No evidence of a difference in dark cutters was observed.
- Of the sensory traits evaluated by trained panelists, tenderness and chewiness were most frequently impacted, but these changes in sensory variables were deemed acceptable and unlikely to be noticed by consumers.



# Target Animal Safety<sup>7</sup>

<sup>7</sup> Experior FOI, Summarized from pages 19-32

## Studies Conducted

**Animal safety information  
evaluated in 4,240 animals  
across 15 studies.**

### Animal Safety Evaluated in:

- Margin of Safety Study (1)
- Emission Studies (2)
- Field Studies (4)
- Additional Development Studies (8)



### Target Animal Safety: Margin of Safety

Lubabegron, mg/hd/day (gm/ton DM)	LUBABEGRON DOSE <sup>AB</sup>			
	0 (0)	260 (24.9)	780 (71.9)	1300 (131.3)
No. Animals	10	10	10	10
Initial Weight, lb	1010.5	979.8	952.6	980.8
Final Weight, lb	1306.4	1304.4	1265.2	1273.1
Daily Gain, lb/day	3.2	3.5	3.4	3.2
DM Intake, lb/day	22.7	20.9	21.7	19.8
Feed Efficiency, gain/DMI	0.14	0.17	0.16	0.16

<sup>A</sup> Lubabegron was top-dressed to achieve intakes of 0, 260, 780, and 1300 mg/hd/day. Based on actual DM intake, lubabegron levels were 0, 24.9, 71.9, and 131.3 gm/ton DM, respectively. The Type C approval for lubabegron is between 1.25 and 4.54 g/ton (90% DM)

<sup>B</sup> Study conducted for 95-99 days. Lubabegron is approved to be used for 14-91 days on feed

## TARGET ANIMAL SAFETY: MARGIN OF SAFETY CONCLUSIONS

No clinically or biologically significant differences in hematology values, clinical pathology values, coagulation values, urinalysis, or physical examination findings.

- Serum urea nitrogen was decreased while creatinine and phosphorus levels were increased.
- Changes were not considered treatment related.

Study demonstrated that Experior when fed according to label is safe to the animal.

- The Type C approval for Experior is between 1.25 and 4.54 g/ton (90% DM) for the final 14 to 91 days on feed. Thus, the actual level fed was over 20X the maximum approved level.

### Target Animal Safety: Lameness in Clinical Studies

Study Type	Location	Duration, day	LUBABEGRON DOSE, g/TON (100% DM) <sup>A</sup>				Lame, n	Lame, %
			0	1.25	5.0	20.0		
Emissions	Michigan	14	0	1	2	1	4	3.3
Field Safety	Idaho	14	1	1	2	3	7	2.2
Field Safety	Nebraska	14	5	2	3	3	13	4.1
Emissions	California*	91	6	13	23 <sup>B</sup>	17	59	17.6
Field Safety	Idaho	91	11	9	15	11	46	14.4
Field Safety	Nebraska	91	12	2 <sup>C</sup>	8	7	29	9.1
Lame, n			35	28	53	43		
Lame, %			8.1	6.5	12.2	9.7		

<sup>A</sup> The Type C approval for lubabegron is between 1.25 and 4.54 g/ton (90% DM)

<sup>B</sup> Different from Control during treatment (P=0.018) and unloading (P=0.035)

<sup>C</sup> Different from Control during treatment (P=0.009), loading, unloading and ante-mortem (P=0.014)

\*Several animals in California study were observed with interdigital dermatitis (foot rot) likely due to muddy conditions in the pens during the first cycle. Medicated foot baths were used which reduced lameness in the subsequent cycles.

### Target Animal Safety: Adverse Events (AE) from the 8 Additional Studies

LUBABEGRON DOSE, g/TON (100% DM) <sup>A</sup>							
Study Type	No Head	0	1.25	2.5	5	10	20
Total N	2504	665	641	318	354	120	406
Total AE (%)	39 (1.6)	10 (1.5)	10 (1.6)	0 (0)	13 (3.7)	1 (1.2)	5 (1.2)
Injuries	15	3	5	0	4	1	2
Lameness/ Foot Rot	4	3	0	0	1	0	0
Gastrointestinal	10	3	1	0	5	0	1
Respiratory	4	1	2	0	0	0	1

<sup>A</sup>The Type C approval for lubabegron is between 1.25 and 4.54 g/ton (90% DM)

### Target Animal Safety: Unresolved Lameness in Clinical Studies

LUBABEGRON DOSE, g/TON (100% DM) <sup>A</sup>							
Study Type	Location	Duration, day	0	1.25	5.0	20.0	Lame, n
Emissions	Michigan	14	0	0	0	0	0
Field Safety	Idaho	14	0	0	0	0	0
Field Safety	Nebraska	14	3	0	2	2	7
Emissions	California	91	0	0	0	0	0
Field Safety	Idaho	91	0	1	1	1	3
Field Safety	Nebraska	91	7	0	6	4	17
Lame, n			10	1	9	7	

<sup>A</sup>The Type C approval for lubabegron is between 1.25 and 4.54 g/ton (90% DM)

## TARGET ANIMAL SAFETY: ADVERSE EVENTS (AE) FROM THE 8 ADDITIONAL STUDIES

- Most common adverse events reported were related to:
  - Injuries (n=15)
  - Lameness associated with injury (n=4)
  - Gastrointestinal issues (n=10)
  - Respiratory (n=4)
- No pattern was found across dose levels.
- Increasing Experior dosage did not appear to increase the incidence of AE.

## TARGET ANIMAL SAFETY: CONCLUSIONS

- Experior was tested in cattle fed up to 1300 mg of lubabegron/hd/day (131 g/ton DM).
- Experior was found to be safe to the target animal when administered for the reduction of NH<sub>3</sub> gas emissions per lb of LW and HCW in beef steers and heifers fed in confinement during the last 14 to 91 days on feed.
- Experior was also evaluated for its' effect on animal lameness when fed up to 20 gm/ton DM
  - Experior did not affect animal lameness.
  - Lameness issues in the studies appeared to be related to nutritional management and pen conditions.
  - Most cases resolved while the animals were still receiving Experior, indicating that the lameness was not test article related.
- A caution statement is included on the label: "A decrease in dry matter intake may be noticed in some animals."


**Studies demonstrated that overall Experior use did not affect animal lameness.**



# Human Food Safety<sup>8</sup>

## HUMAN FOOD SAFETY: CONCLUSIONS

- The data support the assignment of a zero-day withdrawal period for doses up to 5 g/ton (4.54 g/ton on a 90% DM basis).
- Tissue residue and metabolism:
  - The target tissue is the liver with a 10 ppb tolerance established.
  - Exporior achieves a steady state of excretion between 36-60 h post dose.
  - When tested at four times the maximum approved dosing level in feed, lubabegron residues were below detectable levels (1 ppb) in all primary tissues following 72-hour withdrawal.
- The no-observed-effect-level (NOEL) for lubabegron is 0.16 mg/kg BW/day for humans.
- The Acceptable Daily Intake (ADI) of lubabegron is 3 µg/kg BW/day for humans. This ADI includes a 50X safety factor.
- Exporior has been tested for potential effects on acute toxicity, subchronic and chronic toxicity, reproductive and developmental toxicity, and genotoxicity.
- Exporior does not have antibacterial activity.



<sup>8</sup> Exporior FOI, summarized from pages 32-53



# If you have any questions regarding Experior,

please contact your Elanco  
representative or our Product  
and Veterinary Support Team at

**1-800-428-4441.**

*Elanco*

**Experior™**

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