# Corporate Medical Policy

# Vagus Nerve Stimulation

**File Name:** vagus_nerve_stimulation
**Origination:** 6/1998
**Last Review:** 5/2024

## Description of Procedure or Service

Stimulation of the vagus nerve can be performed using a pulsed electrical stimulator implanted within the carotid artery sheath. This technique has been proposed as a treatment for refractory seizures, depression, and other disorders. There are also devices available that are implanted at different areas of the vagus nerve.

Vagus nerve stimulation (VNS) was initially investigated as a treatment alternative in individuals with medically refractory partial-onset seizures for whom surgery is not recommended or for whom surgery has failed. Over time, the use of VNS has expanded to generalized seizures, and it has been investigated for a range of other conditions.

While the mechanisms for the therapeutic effects of vagal nerve stimulation are not fully understood, the basic premise of VNS in the treatment of various conditions is that vagal visceral afferents have a diffuse central nervous system projection, and activation of these pathways has a widespread effect on neuronal excitability. Electrical stimulus is applied to axons of the vagus nerve, which have their cell bodies in the nodose and junctional ganglia and synapse on the nucleus of the solitary tract in the brainstem. From the solitary tract nucleus, vagal afferent pathways project to multiple areas of the brain. There are also vagal efferent pathways that innervate the heart, vocal cords, and other laryngeal and pharyngeal muscles, and provide parasympathetic innervation to the gastrointestinal tract that may also be stimulated by VNS.

The type of VNS device addressed in this policy consists of an implantable, programmable electronic pulse generator that delivers stimulation to the left vagus nerve at the carotid sheath. The pulse generator is connected to the vagus nerve via a bipolar electrical lead. Surgery for implantation of a vagal nerve stimulator involves implantation of the pulse generator in the infraclavicular region and wrapping two spiral electrodes around the left vagus nerve within the carotid sheath. The programmable stimulator may be programmed in advance to stimulate at regular times or on demand by individuals or family by placing a magnet against the subclavicular implant site.

**Regulatory Status**
In 1997, the U.S. Food and Drug Administration (FDA) approved a vagus nerve stimulation device called the NeuroCybernetic Prosthesis (NCP®) system (Cyberonics, Houston, TX) through the Premarket Approval (PMA) process. The device was approved for use in conjunction with drugs or surgery "as an adjunctive treatment of adults and adolescents over 12 years of age with medically refractory partial onset seizures." There have been subsequent expanded approvals. In July 2005, Cyberonics received PMA approval by the FDA for the VNS Therapy™ System "for the adjunctive long-term treatment of chronic or recurrent depression for patients 18 years of age or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments." In 2017, Cyberonics received PMA

approval from FDA expanding the indicated use as adjunctive therapy for seizures in patients 4 years of age and older with partial-onset seizures that are refractory to antiepileptic medications.

On May 30, 2017, the gammaCore® (ElectroCore, Basking Ridge, NJ), a noninvasive VNS device, was cleared for marketing through the 510(k) process (K171306) for the acute treatment of adults with pain associated with episodic cluster headaches and migraine headaches. When the device is applied to the side of the neck by the patient, a mild electrical stimulation of the vagus nerve is carried to the central nervous system. Each stimulation using gammaCore® lasts 2 minutes. The patient controls the stimulation strength. Since 2017, The gammCore-2® and gammaCore-Sapphire® received subsequent expanded approvals have been issued for "adjunctive use for the preventive treatment of cluster headaches in adult patients"; "acute treatment of pain associated with episodic cluster headache in adult patients"; "acute treatment of pain associated with migraine headaches in adult patients"; and "preventive treatment of migraine headache in adult patients".

Cerbomed (Erlangen, Germany) has developed a transcutaneous VNS (t-VNS®) system that uses a combined stimulation unit and ear electrode to stimulate the auricular branch of the vagus nerve, which supplies the skin over the concha of the ear. Patients self-administer electric stimulation for several hours a day; no surgical procedure is required. The device received the CE mark in Europe in 2011, but has not been FDA approved for use in the US.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

## Policy

**BCBSNC will provide coverage for Vagus Nerve Stimulation for Treatment of Seizures when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.**

**Vagus Nerve Stimulation for the treatment of essential tremor and other conditions is considered investigational. BCBSNC does not provide coverage for investigational services or procedures.**

## Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## When Vagus Nerve Stimulation is covered

Vagus Nerve Stimulation may be considered **medically necessary** when both of the following criteria are met:

1. The individual has medically refractory seizures, and
2. The individual has failed or is not eligible for surgical treatment.

## When Vagus Nerve Stimulation is not covered

Vagus nerve stimulation is considered **investigational** as treatment for the following conditions, including but not limited to:

1. indications that do not meet the criteria listed above
2. individuals who can be treated successfully with anti-epileptic drugs
3. depression
4. essential tremor

5. headaches
6. obesity
7. heart failure
8. fibromyalgia
9. tinnitus
10. traumatic brain injury
11. upper limb impairment due to stroke.

Transcutaneous (nonimplantable) vagus nerve stimulation devices are considered **investigational** for all indications.

## Policy Guidelines

Medically refractory seizures are defined as seizures that occur in spite of therapeutic levels of antiepileptic drugs or seizures that cannot be treated with therapeutic levels of antiepileptic drugs because of intolerable adverse effects of these drugs.

*Vagus Nerve Stimulation*

For individuals who have seizures refractory to medical treatment who receive vagus nerve stimulation, the evidence includes randomized controlled trials (RCTs) and multiple observational studies. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs reported a significant reduction in seizure frequency for patients with partial-onset seizures. The uncontrolled studies have consistently reported large reductions for a broader range of seizure types in both adults and children. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have treatment-resistant depression who receive VNS, the evidence includes two RCTs evaluating the efficacy of implanted VNS for treatment-resistant depression compared to sham, one RCT comparing therapeutic to low-dose implanted VNS, nonrandomized comparative studies, and case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The sham-controlled RCTs reported only short-term results and found no significant improvement for the primary outcome. The low-dose VNS controlled trial reported no statistically significant differences between the dose groups for change in depression symptom score from baseline. Other available studies are limited by small sample sizes, potential selection and confounding biases, and lack of a control group in the case series. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic heart failure who receive VNS, the evidence includes a systematic review including four RCTs and case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Meta-analyses of the RCTs evaluating chronic heart failure found significant improvements in New York Heart Association functional class, quality of life, 6-minute walk-test, and N-terminal-pro brain natriuretic peptide levels in patients treated with VNS compared to control. An analysis of the ANTHEM-HF uncontrolled trial evaluated longer-term outcomes of VNS use in chronic heart failure. They found that left ventricular (LV) ejection fraction improved by 18.7%, 19.3%, and 34.4% at 12, 24, and 36 months, respectively, with high-intensity VNS. Individuals with low-intensity VNS only had significant improvements in LV ejection fraction at 24 months (12.3%). The ANTHEM-HFpEF trial found improvements in New York Heart Association functional class, quality of life, and 6-minute walk test distances in patients with preserved ejection fraction and implanted VNS. Although this data is promising, a lack of a no-VNS comparator group precludes drawing conclusions based on findings from the uncontrolled studies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have upper-limb impairment due to stroke who receive VNS, the evidence includes three pilot RCTs and a systematic review of these RCTs. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Two RCTs compared VNS plus rehabilitation to rehabilitation alone; one failed to show significant improvements for the VNS group on response and function outcomes, but the other, which had a larger patient population, found a significant difference in response and function outcomes. The remaining RCT compared VNS to sham and found that

although VNS significantly improved response rate, there were 3 serious adverse events related to surgery. A systematic review pooling these data found that implanted VNS improved upper limb motor function based on Fugl-Meyer Assessment-Upper Extremity score when compared to control. Longer-term follow-up studies are needed to evaluate long-term efficacy and safety. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have other neurologic conditions (e.g., essential tremor, obesity, headache, fibromyalgia, tinnitus, or autism who receive VNS, the evidence includes case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Case series are insufficient to draw conclusions regarding efficacy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with cluster headaches who receive transcutaneous VNS (tVNS; also referred to as noninvasive VNS [nVNS]) to prevent cluster headaches, the evidence includes one RCT. Relevant outcomes are symptoms, change in disease status, quality of life and functional outcomes. One RCT for prevention of cluster headache showed a reduction in headache frequency but did not include a sham treatment group. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

*Transcutaneous Vagus Nerve Stimulation*

For individuals with cluster headache who receive nVNS to treat acute cluster headache, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, quality of life and functional outcomes. These studies suggest that people with episodic and chronic cluster headaches may respond differently to acute treatment with nVNS. Studies designed to focus on episodic cluster headache are needed. Quality of life and functional outcomes have not been reported. Treatment periods ranged from only two weeks to one month with extended open-label follow-up of up to three months. There are few adverse events of nVNS and they are mild and transient. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with migraine headache who receive nVNS to treat acute migraine headache, the evidence includes one RCT. Relevant outcomes are symptoms, change in disease status, quality of life and functional outcomes. One RCT has evaluated nVNS for acute treatment of migraine with nVNS in 248 patients with episodic migraine with/without aura. There was not a statistically significant difference in the primary outcome of the proportion of participants who were pain-free without using rescue medication at 120 minutes. However, the nVNS group had a higher proportion of patients with decrease in pain from moderate or severe to mild or no pain at 120 minutes and a higher proportion of patients who were pain-free at 120 minutes for 50% or more of their attacks. There are few adverse events of nVNS and they are mild and transient. Quality of life and functional outcomes were not reported and the double-blind treatment period was four weeks with an additional four weeks of open-label treatment.The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with chronic migraine headache who receive nVNS to prevent migraine headache, the evidence includes three RCTs. Relevant outcomes are symptoms, change in disease status, quality of life and functional outcomes. The EVENT RCT was a feasibility study of prevention of migraine that was not powered to detect differences in efficacy outcomes. It does not demonstrate the efficacy of nVNS for prevention of migraine. The PREMIUM RCT was a phase 3, multicenter, sham-controlled RCT including 341 randomized participants with a 12-week double-blind treatment period. The results of PREMIUM demonstrated that nVNS was not statistically significantly superior to sham with respect to the outcomes of reduction of at least 50% in migraine days from baseline to the last 4 weeks, reduction in number of migraine days from baseline to the last 4 weeks, or acute medication days. The PREMIUM II trial was a multicenter, sham-controlled RCT including 231 randomized participants with a 12-week double-blind treatment period. The trial was terminated early due to the COVID-19 pandemic and results were based on a modified intention-to-treat population that included 113 total participants. Results demonstrated that treatment with nVNS was not statistically significantly superior to sham with respect to the primary outcome of reduction in the number of migraine days per month during weeks 9 through 12, nor other outcomes such as mean change in the number of headache days or acute medication days. However, the percentage of patients with at least a 50% reduction in the

number of migraine days was significantly greater in the nVNS group than in the sham group. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have other neurologic, psychiatric, or metabolic disorders (e.g., epilepsy, depression, schizophrenia, noncluster headache, impaired glucose tolerance, fibromyalgia, stroke) who receive tVNS, the evidence includes RCTs, systematic reviews of these RCTs, and case series for some of the conditions. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs are all small and have various methodologic problems. None shows definitive efficacy of tVNS in improving outcomes among patients. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

## Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Vagus nerve stimulation requires not only the surgical implantation of the device, but also subsequent neurostimulator programming, which occurs intraoperatively and typically during additional outpatient visits.

*Applicable service codes*: *61885, 61886, 61888, 64553, 64568, 64569, 64570, 64585, 95970, 95976, 95977, 95983, 95984, C1767, C1820, E0735, L8679, L8680, L8681, L8682, L8683, L8685, L8686, L8687, L8688, L8689*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

Blue Cross Blue Shield Association Policy, 7.01.20, issued 4/1/98

Medical Policy Advisory Group 12/2/1999

Specialty Matched Consultant Advisory Panel – 8/2001

BCBSA Medical Policy Reference Manual, 7.01.20; 11/20/01

BCBSA Medical Policy Reference Manual, 7.01.20; 4/29/03

ECRI, TARGET Report #73, 1/2002

ECRI Windows on Medical Technology, Issue No. 14, December 1998

Specialty Matched Consultant Advisory Panel – 7/2003

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 11/9/2004.

Specialty Matched Consultant Advisory Panel – 6/2005

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 6/27/05

BCBSA TEC Assessment. (June 2005) Vagus nerve stimulation for treatment-resistant depression. Retrieved 9/26/05 from http://www.bcbsa.com/tec/vol20/20_08.html

ECRI Target Database. (2005, October). Implantable vagus nerve stimulator for treatment resistant depression. Retrieved 11/8/05 from http://www.target.ecri.org/summary/detail.aspx?e=5&doc_id+74&q=vagus&anm=WynneB.

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 10/10/2006

Specialty Matched Consultant Advisory Panel – 5/2007

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 11/13/08

Specialty Matched Consultant Advisory Panel – 5/2009

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 11/12/2009

Medical Director – 10/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 1/13/11

Specialty Matched Consultant Advisory Panel – 5/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 3/8/12

Specialty Matched Consultant Advisory Panel – 5/2012

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 3/13/2013

Specialty Matched Consultant Advisory Panel – 5/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 3/13/2014

Specialty Matched Consultant Advisory Panel – 5/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 3/12/2015

Specialty Matched Consultant Advisory Panel – 5/2015

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 2/11/2016

Specialty Matched Consultant Advisory Panel – 5/2016

Specialty Matched Consultant Advisory Panel – 5/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 10/12/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 3/8/2018

Specialty Matched Consultant Advisory Panel – 5/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 2/14/2019

Specialty Matched Consultant Advisory Panel – 5/2019

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 2/13/2020

Specialty Matched Consultant Advisory Panel – 5/2020

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.20, 2/11/2021

Specialty Matched Consultant Advisory Panel – 5/2021

Specialty Matched Consultant Advisory Panel – 5/2022

Panebianco M, Rigby A, Marson AG. Vagus nerve stimulation for focal seizures. Cochrane Database Syst Rev. Jul 14 2022; 7(7):CD002896.

Specialty Matched Consultant Advisory Panel – 5/2023

Medical Director Review- 5/2024

Specialty Matched Consultant Advisory Panel – 5/2024

## Policy Implementation/Update Information

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|---|---|
| 6/98 | Original policy adopted from the National Association |
| 7/99 | Reformatted, Description of Procedure or Service changed, Medical Term Definitions added. |
| 12/99 | Reaffirmed, Medical Policy Advisory Group |
| 7/00 | System coding changes |
| 12/00 | 2001 HCPCS codes added; E0756, E0757, E0758, E0765. System coding changes. |
| 8/01 | Specialty Matched Consultant Advisory Panel – Approved. No changes. Typo corrected. |
| 2/02 | Policy statement revised. Removed age specific indications under what is and is not covered and added treatment of patients with depression under what is not covered. |
| 4/03 | Codes E0751 and E0753 removed from Billing/Coding section. System coding changes. |
| 9/03 | Specialty Matched Consultant Advisory Panel review 7/15/03. Benefits Application section revised. Sources added. Removes codes E0756, E0757, E0758, and E0765 from the policy. |
| 3/04 | Billing/Coding section updated for consistency. |
| 7/7/05 | Specialty Matched Consultant Advisory Panel review 6/24/2005. "Description of Procedure or Service" revised. "When Covered" section reformatted. Added to "When Not Covered" section; "1. For indications that do not meet the criteria listed above." And "5. For the treatment of essential tremor." Removed CPT codes 64553 as the code does not apply to this policy. Added CPT codes 61885, 64585, 95970, 95974, and 95975. Policy number added to "Key Words" section. References added. |

10/8/05 Added additional information in "Description of Procedure or Service" related to research for the use in treating depression, headaches, and essential tremors. Statement added to "Policy" section indicating, "BCBSNC will not provide coverage for vagus nerve stimulation for the treatment of depression, headache, or essential tremors. These uses are considered investigational. BCBSNC does not cover investigational services. Added "For the treatment of headaches" under the "When not covered" section. No change to the intent of policy. References added.

12/1/05 Policy name changed from "Chronic Vagus Nerve Stimulation for the Treatment of Seizures" to "Vagus Nerve Stimulation". Rationale regarding the investigational status of Vagus Nerve Stimulation for treatment resistant depression added to the "Policy Guidelines" section. References added. Added CPT code 61888.

1/17/07 Added HCPCS codes L8680, L8681, L8682, L8683, L8685, L8686, L8687, L8688, and L8689 to "Billing/Coding" section.

6/18/07 Specialty Matched Consultant Advisory Panel review 5/23/2007. No change to policy statement. Added CPT code 64553 to "Billing/Coding" section. References added.

3/16/09 Added 61886 to "Billing/Coding" section.

7/6/09 Specialty Matched Consultant Advisory Panel review 5/28/09. No change to policy statement. Added additional indications to the "When Not Covered" section; "7. For the treatment of obesity." Updated rationale in the "Policy Guidelines" section. References added. Notice given 7/6/09. Policy effective 10/12/09. (btw)

6/22/10 Policy Number(s) removed (amw)

10/26/10 Revised "Description' section. Revised policy to indicate that VNS may be medically necessary in refractive seizures (not just in partial onset seizures). Added diagnoses codes to the "Billing/Coding" section. Reviewed by Medical Director 9/30/10. References added. (btw)

1/4/11 Added new 2011 CPT codes; 64568, 64569, and 64570 to "Billing/Coding" section. Removed deleted code, 64573. (btw)

3/29/11 References updated. (btw)

7/1/11 Specialty Matched Consultant Advisory Panel review 5/25/2011. "Description" section revised. No change to policy statement. (btw)

6/12/12 Specialty Matched Consultant Advisory Panel review 5/16/2012. Description section revised. The When Not Covered section reformatted. Added treatment of heart failure and fibromyalgia to the list of investigational indications. No change to policy intent. Policy Added the following diagnoses to the Billing/Coding section: 428 – 428.9 and 729.1. Guidelines updated. Reference added. (btw)

7/24/12 Added CPT code, 64585, to the Billing/Coding section. Added diagnosis codes, 346 and 278.03 to Billing/Coding section. (btw)

7/1/13 Specialty Matched Consultant Advisory Panel review 5/15/2013. No change to policy statement. ICD-10 diagnosis codes added to Billing/Coding section. References added. (btw)

11/12/13 Added M60.872 and M60.879 to the ICD10 list in the Billing/Coding section. (btw)

12/31/13 Added new 2014 HCPCS code, L8679 to Billing/Coding section. (btw)

6/10/14 Specialty Matched Consultant Advisory Panel review 5/27/2014. Description section updated to include information regarding the VNS (t-VNS®) system developed by Cerbomed. The following investigational indications were added to the When Not Covered section; "headaches, tinnitus, and traumatic brain injury" and "Non-implantable vagus nerve stimulation devices are considered investigational for all indications." No change to policy intent. Policy Guidelines updated. Reference added. (btw)

4/28/15 Reference added. Description section reviewed and updated for clarity. No change to policy statement. (sk)

7/1/15 Specialty Matched Consultant Advisory Panel review 5/27/2015. (sk)

4/1/16 Reference added. (sk)

7/1/16 Specialty Matched Consultant Advisory Panel review 5/25/2016. (sk)

9/30/16 Code F32.89 added to Billing/Coding section. (sk)

6/30/17 Specialty Matched Consultant Advisory Panel review 5/31/2017. (sk)

11/10/17 Reference added. Regulatory Status and Policy Guidelines updated. ICD-9 codes removed from Billing/Coding section. No change to coverage criteria. (sk)

6/29/18 Reference added. Regulatory Status and Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 5/23/2018. (sk)

1/1/19 Added codes 95976, 95977, 95983, and 95984 to Billing/Coding section. (sk)

6/11/19 Reference added. Policy Guidelines updated to include additional information on transcutaneous vagus nerve stimulation to treat acute cluster headache and acute migraine headache. Policy statement unchanged. Specialty Matched Consultant Advisory Panel review. (sk)

6/9/20 Reference added. Description section updated. Policy Guidelines updated. Policy statement unchanged. Specialty Matched Consultant Advisory Panel review 5/20/2020. (sk)

3/31/21 New HCPCS code K1020 added to Billing/Coding section, effective 4/1/2021. (sk)

6/15/21 Reference added. Policy Guidelines updated. Policy statement unchanged. Specialty Matched Consultant Advisory Panel review 5/19/2021. (sk)

6/14/22 Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 5/18/2022. (sk)

6/30/23 Policy Guidelines updated. Description updated. Reference added. Specialty Matched Consultant Advisory Panel review 5/17/2023. Code C1767 added to Billing/Coding section. (sk)

12/29/23 Added the following HCPCS code to the Billing/Coding section: E0735, effective 1/1/2024 and removed terminated HCPCS code K1020. (ldh)

6/12/24 Policy Guidelines updated. No change to intent of policy. Removed listing of ICD 10 codes and terminated CPT codes 95974 and 95975 from the Billing/Coding section. References updated. Medical Director review 5/2024. Specialty Matched Consultant Advisory Panel review 5/2024. (ldh)

7/17/24 Added HCPCS code C1820 to the Billing/Coding section. (ldh)