East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Briefing Paper for Prescribing Clinical Network on NICE Technology Appraisal 367: November 2015

NICE TA Guidance	'Vortioxetine for treating major depressive episodes'[1]
Date of issue	November 2015
Available at	http://www.nice.org.uk/guidance/ta367

Medicine details	
Name, brand name and manufacturer	Vortioxetine, (Brintellix® ▼), Lundbeck Ltd[2]
Licensed indication, formulation and usual dosage	Indication: For the treatment of major depressive episodes in adults.[2] Strength: 5mg, 10mg and 20mg film-coated tablets.[2] The starting and recommended dose of vortioxetine is 10mg once daily in adults less than 65 years of age.[2] In adults aged >65, the lowest effective dose of 5mg vortioxetine once daily should always be used as the starting dose in patients.[2] Depending on individual patient response, the dose may be increased to a maximum of 20mg once daily or decreased to a minimum of 5mg once daily.[2]

Disease and potential patient group	
Brief description of disease	<u>What is depression?</u> The word depressed is a common everyday word. With true depression, there is a low mood and other symptoms each day for at least two weeks. Symptoms can also become severe enough to interfere with normal day-to-day activities.[3] <u>Who gets depression?</u> About 5 in 100 adults have depression every year. Sometimes it is mild or lasts just a few weeks. However, an episode of depression serious enough to require treatment occurs in about 1 in 4 women and 1 in 10 men at some point in their lives. Some people have two or more episodes of depression at various times in their life.[3]

What are the symptoms of depression?

There is a set of symptoms that are associated with depression and help to clarify the diagnosis. These are:

Core symptoms

- Persistent sadness or low mood. This may be with or without weepiness.
- Marked loss of interest or pleasure in activities, even for activities that you normally enjoy.[3]

Other common symptoms

- Disturbed sleep compared with your usual pattern. This may be difficulty in getting off to sleep, or waking early and being unable to get back to sleep. Sometimes it is sleeping too much.
- Change in appetite. This is often a poor appetite and weight loss. Sometimes the reverse happens with comfort eating and weight gain.
- Tiredness or loss of energy.
- Agitation or slowing of movements.
- Poor concentration or indecisiveness.
- Feelings of worthlessness, or excessive or inappropriate guilt.
- Recurrent thoughts of death.[3]

An episode of depression is usually diagnosed if:

- You have at least five out of the above nine symptoms, with at least one of these a core symptom; and:
- Symptoms cause you distress or impair your normal functioning, such as affecting your work performance; and
- Symptoms occur most of the time on most days and have lasted at least two weeks; and
- The symptoms are not due to a medication side-effect, or to drug or alcohol misuse, or to a physical condition such as an underactive thyroid or pituitary gland.[3]

Many people with depression say that their symptoms are often worse first thing each day. Also, with depression, it is common to develop physical symptoms such as headaches, palpitations, chest pains and general aches. Some people consult a doctor at first because they have a physical symptom such as chest pains. They are concerned that they may have a physical problem such as a heart condition when it is actually due to depression. Depression is in fact quite a common cause of physical symptoms. But, the opposite is also true. That is, people with serious physical conditions are more likely than average to develop depression.[3]

Some people with severe depression also develop delusions and/or hallucinations. These are called psychotic symptoms. A delusion is a false belief that a person has, and most people from the same culture would agree that it is wrong.[3]

Severity of depression

The severity of depression can vary from person to person. Severity is generally divided as follows:

- Severe depression - you would normally have most or all of the nine symptoms listed above. Also, symptoms markedly interfere with your normal functioning.
- Moderate depression - you would normally have more than the five symptoms that are needed to make the diagnosis of depression. Also, symptoms will usually include both core symptoms. Also, the severity of symptoms or impairment of your functioning is between mild and severe.
- Mild depression - you would normally have five of the symptoms listed above that are required to make the diagnosis of depression. However, you are not likely to have more than five or six of the symptoms. Also, your normal functioning is only mildly impaired.
- Subthreshold depression - you have fewer than the five symptoms needed to make a diagnosis of depression. So, it is not classed as depression. But, the symptoms you do have are troublesome and cause distress. If this situation persists for more than two years it is sometimes called dysthymia.[3]

What causes depression?

The exact cause is not known. Anyone can develop depression. Some people are more prone to it and it can develop for no apparent reason. You may have no particular problem or worry, but symptoms can develop quite suddenly. So, there may be some genetic factor involved that makes some people more prone than others to depression. 'Genetic' means that the condition is passed on through families.[3]

An episode of depression may also be triggered by a life event such as a relationship problem, bereavement, redundancy, illness, etc. In many people it is a mixture of the two. For example, the combination of a mild low mood with some life problem, such as work stress, may lead to a spiral down into depression.[3]

Women tend to develop depression more often than men. Particularly common times for women to become depressed are after childbirth (postnatal depression) and the menopause.[3]

Depression and physical conditions

Although the cause of depression is not clear, there are some useful things to remember about depression in relation to physical conditions. Depression is more common in people who are known to have certain physical conditions. The diagnosis of depression is sometimes confused with some undiagnosed diseases caused by physical conditions. Depression is more common than average in people coping with serious or severe physical diseases. Although the treatment of the physical disease may take priority, the treatment of depression is also useful to improve overall well-being.[3]

Potential patient numbers per 100,000	The following data are derived from the Lundbeck Budget Impact Model, and assumes populations from six Clinical Commissioning Groups (CCGs).[4] These are: • East Surrey CCG • Guildford and Waverley CCG • North East Hampshire and Farnham CCG • North West Surrey CCG • Surrey Downs CCG • Surrey Heath CCG The scenarios depicted all have the following assumptions: • Total adult population of 1071003 people • 12 month prevalence of depression is 5.83% (62439 patients) • Proportion of major depressive disorder patients with moderate to severe depression is 54% (33717 patients) • Proportion of these patients requiring drug treatment is 90% (30346 patients) • Percentage of patients requiring third line treatment is 32.6% (9861 patients)[4] Currently, sertraline, venlafaxine and mirtazapine account for 18.4%, 10.9% and 18.4% of third line market share respectively. It is envisaged in the scenarios that vortioxetine will be used in place of 33.3% of each of these drugs. It is assumed that vortioxetine will not take market share off any other antidepressants as their usage is relatively small at third line compared to the aforementioned three drugs.[4] The scenarios then depict the uptake of vortioxetine at 0.5%, 2.5% and 5% market share in 2016; thereby describing low, medium and high uptake.[4] The budget impact model describes two situations, one where vortioxetine is not available versus one where it is available. It is then possible to assess the impact that uptake of vortioxetine will have in Surrey.[4] In scenario 1, vortioxetine market share is 0.5%:

	2015	2016
Vortioxetine unavailable	£526,427	£388,031
Vortioxetine available	£527,443	£398,191
Difference in budget	£1,016	£10,161
Total Patients Treated	9,861	9,861
Vortioxetine Patients	5	49

In scenario 2, vortioxetine market share is 2.5%:

	2015	2016
Vortioxetine unavailable	£526,427	£388,031
Vortioxetine available	£527,443	£438,833
Difference in budget	£1,016	£50,803
Total Patients Treated	9,861	9,861
Vortioxetine Patients	5	247

In scenario 3, vortioxetine market share is 5.0%:

	2015	2016
Vortioxetine unavailable	£526,427	£388,031
Vortioxetine available	£527,443	£489,636
Difference in budget	£1,016	£101,606
Total Patients Treated	9,861	9,861
Vortioxetine Patients	5	493

Based on these assumptions, in 2016, the range of patients will be from 49 to 493. This equates to 5 to 46 patients per 100000 of adult population. The additional cost of implementing NICE TA367 will be between £948 to £9487 per 100000 people.[4]

Please note that there is an assumption in all three scenarios that the price of duloxetine will reduce by 90% as this medicine becomes genericised in 2015. Savings will therefore be made even at the highest uptake of vortioxetine. The expected drugs budget spend for depression in 2016 will be £37807 less than the current 2015 spend even if vortioxetine achieves 5% market share.[4]

It is unlikely that implementing NICE guidance TA367 will result in a significant change in resource use in the NHS. Vortioxetine is a treatment option alongside current standard third line treatment options for major depressive disorder. There may be a small increase in costs arising from a reduction in the number of people given cheaper treatment options. However, offsetting savings may also be made from, for example, fewer side effects in people given vortioxetine.[1]

SUMMARY

Guidance

Vortioxetine is recommended as an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode.[1]

People whose treatment with vortioxetine is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.[1]

Cost implications

Cost: Acquisition cost of vortioxetine is £27.72 / 28 days for 5mg film-coated tablets, 10mg film-coated tablets or 20mg film-coated tablets.[2]

Annual cost per patient: Assuming that patients initiated on vortioxetine receive two months' supply to resolve their depressive symptoms, and a further six months' supply to ensure consolidation of the antidepressive response, then the cost per patient per annum will be £221.76[2]

Availability of PAS and details (if appropriate): Not applicable

Availability of homecare service (if appropriate): Not applicable

Alternative treatments and cost per patient per year

Drug Tariff Prices for 2015 England & Wales[5]

	Dec-15	8 months' cost
Escitalopram 5mg x 28	£1.19	£9.52
Escitalopram 10mg x 28	£1.38	£11.04
Escitalopram 20mg x 28	£1.97	£15.76
Citalopram 10mg x 28	£0.94	£7.52
Citalopram 20mg x 28	£1.01	£8.08
Citalopram 40mg x 28	£1.19	£9.52
Fluoxetine 20mg x 30	£1.11	£8.88
Fluoxetine 60mg x 30	£17.85	£142.80
Paroxetine 20mg x 30	£2.41	£19.28
Paroxetine 30mg x 30	£2.26	£18.08
Sertraline 50mg x 28	£1.84	£14.72
Sertraline 100mg x 28	£1.77	£14.16
Venlafaxine 75mg x 28 (XL)	£22.08	£176.64
Venlafaxine 75mg x 30 (XL)	£11.20	£89.60
Venlafaxine 150mg x 28 (XL)	£36.81	£294.48
Venlafaxine 150mg x 30 (XL)	£18.70	£149.60
Venlafaxine 225mg x 30 (XL)	£33.60	£268.80
Venlafaxine 75mg x 56	£2.98	£23.84
Duloxetine 30mg x 28	£21.82	£174.56
Duloxetine 60mg x 28	£26.65	£213.20
Mirtazapine 15mg x 30 Orodispersable	£1.86	£14.88
Mirtazapine 30mg x 30 Orodispersable	£1.89	£15.12
Mirtazapine 45mg x 30 Orodispersable	£2.70	£21.60

Trazodone 100mg x 56	£24.53	£196.24
Trazodone 150mg x 28	£24.03	£192.24
Trazodone 50mg capsules x 84	£23.01	£184.08
Amitriptyline 10mg x 28	£0.95	£7.60
Amitriptyline 25mg x 28	£0.98	£7.84
Amitriptyline 50mg x 28	£1.18	£9.44
Nortriptyline 10mg x 100	£74.13	£593.04
Nortriptyline 25mg x 100	£111.70	£893.60
Agomelatine 25mg tablets x 28	£30.00	£240.00

Impact to patients

NICE has recommended vortioxetine as an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode.[1]

- For patients experiencing MDE for whom previous treatments are inadequately effective, or where they are unable to tolerate the treatment side-effects
- May be a valuable treatment option for people experiencing cognitive dysfunction as part of their MDE[1]

• Additional patient choice and clinician option:

Vortioxetine is a new 'multimodal' antidepressant[2,6] with a different pharmacological profile to other existing treatments. As such, it offers a different treatment option for patients with MDE.

• Patient safety and tolerability:

NICE has concluded that, based on the available evidence, vortioxetine is equally effective as, but may have a better overall safety profile than other antidepressants.[2] Note that when reviewing treatment after an inadequate response to initial pharmacological interventions, NICE CG90 general guidance states " be aware that using a single antidepressant is usually associated with a lower side-effect burden".[7]

Some important tolerability issues associated with many other antidepressants are not associated with vortioxetine. These include:

- Body weight: Vortioxetine had no effect relative to placebo on body weight in short and long-term studies.[2]
- Cardiovascular: Vortioxetine had no effect relative to placebo on heart rate, or blood pressure in clinical short- and long-term studies. Vortioxetine has not shown any clinically significant effect on ECG parameters, including the QT, QTc, PR and QRS intervals, in patients with MDD. In a thorough QTc study in healthy subjects at doses up to 40mg daily (note that 40mg is above the licensed maximum of 20mg/day), no potential for the prolongation of the QTc interval was observed.[2]

- Insomnia: Vortioxetine did not increase the incidence of insomnia or somnolence relative to placebo.[2]

- In addition, the incidence of self-reported adverse sexual reactions was low and similar to placebo in short- and long-term clinical studies with vortioxetine. In studies using the Arizona Sexual Experience Scale (ASEX), the incidence of treatment-emergent sexual dysfunction (TESD) and the ASEX total score showed no clinically relevant difference to placebo in symptoms of sexual dysfunction at the 5 to 15mg/day doses of vortioxetine – although there was a 14% difference from placebo at a dose of 20mg/day.[2]

- Potentially lower probability of stopping treatment than most other antidepressants.[2]

The available evidence, using an indirect treatment comparison analysis and as reviewed by NICE, suggests vortioxetine leads to a lower probability of stopping treatment than most other antidepressants in the short-term.[2] Some people may stop treatment early because of a perceived lack of response and adverse reactions, hence a lower probability of stopping treatment could conceivably help address potential non-adherence.[2] Non-adherence to treatment is a primary cause of treatment failure. Also, NICE guidance advises that when prescribing drugs other than SSRIs, to take into account the increased likelihood of the person stopping treatment because of side effects.[7]

• Patients treated with Brintellix can abruptly stop taking the medicinal product without the need for a gradual reduction in dose.[2] Conceivably, this can positively impact pharmacological management of the patient, as it makes it potentially easier to manage switch away from vortioxetine if needed compared with many of the existing alternatives.

Impact to primary care

NICE has recommended vortioxetine as an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode.[1]

• For patients experiencing MDE for whom previous treatments are inadequately effective, or where they are unable to tolerate the treatment side-effects

• May be a valuable treatment option for people experiencing cognitive dysfunction as part of their MDE[1]

Dose and posology:

- The starting and recommended dose of Brintellix is 10mg once daily in adults less than 65 years of age.
- In adults aged >65, the lowest effective dose of 5mg vortioxetine once daily should always be used as the starting dose in patients.
- Depending on individual patient response, the dose may be increased to a maximum of 20mg once daily or decreased to a minimum of 5mg once daily.[2]

Method of administration:

- Brintellix is for oral use.
- The film-coated tablets can be taken with or without food.[2]

Duration of treatment:

- After the depressive symptoms resolve, treatment for at least 6 months is recommended for consolidation of the antidepressive response.[2]

Treatment discontinuation:

- Patients treated with Brintellix can abruptly stop taking the medicinal product without the need for a gradual reduction in dose.[2]

Monitoring:

- No mandatory routine blood or cardiac monitoring required.[2]

Patients with a history of suicide-related events or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.[2]

Adverse Events:
The safety and tolerability of vortioxetine have been established in short- and long-term studies across the dose range of 5 to 20mg/day. The most common adverse reaction was nausea. Adverse reactions were usually mild or moderate and occurred within the first two weeks of treatment. The reactions were usually transient and did not generally lead to cessation of therapy. Gastrointestinal adverse reactions, such as nausea, occurred more frequently in women than men.[2]

Adverse reactions are listed below using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).[2]

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE REACTION
Psychiatric disorders	Common	Abnormal dreams
Nervous system disorders	Common	Dizziness
	Unknown	Serotonin syndrome
Vascular disorders	Uncommon	Flushing
Gastrointestinal disorders	Very common	Nausea
	Common	Diarrhoea, constipation, vomiting
Skin and subcutaneous tissue disorders	Common	Pruritus, including pruritus generalised
	Uncommon	Night sweats

- Vortioxetine did not increase the incidence of insomnia or somnolence relative to placebo.[2]
- In clinical short- and long-term placebo-controlled studies, potential discontinuation symptoms were systematically evaluated after abrupt treatment cessation of vortioxetine. There was no clinically relevant difference to placebo in the incidence or nature of the discontinuation symptoms after either short-term (6-12 weeks) or long-term (24-64 weeks) treatment with vortioxetine.[2]
- The incidence of self-reported adverse sexual reactions was low and similar to placebo in clinical short- and long-term studies with vortioxetine. In studies using the Arizona Sexual Experience Scale (ASEX), the incidence of treatment-emergent sexual dysfunction (TESD) and the ASEX total score showed no clinically relevant difference to placebo in symptoms of sexual dysfunction at the 5 to 15mg/day doses of vortioxetine. For the 20mg/day dose, an increase in TESD was seen compared to placebo (an incidence difference of 14.2%, 95% CI [1.4, 27.0]).[2]
- Vortioxetine had no effect relative to placebo on body weight, heart rate, or blood pressure in clinical short- and long-term studies.[2]
- No clinically significant changes were observed in hepatic or renal assessments in clinical studies.[2]
- Vortioxetine has not shown any clinically significant effect on ECG parameters, including the QT, QTc, PR and QRS intervals, in patients with MDD. In a thorough QTc study in healthy subjects at doses up to 40 mg daily, no potential for the prolongation of the QTc interval was observed.[2]

NICE has concluded that, based on the available evidence, vortioxetine is equally effective as, but may have a better overall safety profile than other antidepressants.[2] In addition, the relative low levels of monitoring means that implementation of the NICE guidance may not have an adverse impact on General Practitioner time and workload. The tolerability profile of vortioxetine may provide an additional treatment option in a different class that is better tolerated than the alternatives, thus providing further options for patients and General Practitioners should first choice antidepressants be ineffective due to lack of response or side effects.[7]

Impact to secondary care

Recommended place in therapy:
As an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode.[1]
– For patients experiencing MDE for whom previous treatments are inadequately effective, or where they are unable to tolerate the treatment side-effects
– May be a valuable treatment option for people experiencing cognitive dysfunction as part of their MDE[1]

Advantages and potential benefits over existing treatments:
• Additional patient choice and clinician option:
Vortioxetine is a new 'multimodal' antidepressant[2,6] with a different pharmacological profile to other existing treatments. As such, it offers a different treatment option for patients with MDE.

• Patient safety and tolerability:
NICE has concluded that, based on the available evidence, vortioxetine is equally effective as, but may have a better overall safety profile than other antidepressants.[2] Note that when reviewing treatment after an inadequate response to initial pharmacological interventions, NICE CG90 general guidance states "be aware that using a single antidepressant is usually associated with a lower side-effect burden".[7]

Some important tolerability issues associated with many other antidepressants are not associated with vortioxetine. These include:

- Body weight: Vortioxetine had no effect relative to placebo on body weight in short and long-term studies.[2]

- Cardiovascular: Vortioxetine had no effect relative to placebo on heart rate, or blood pressure in clinical short- and long-term studies. Vortioxetine has not shown any clinically significant effect on ECG parameters, including the QT, QTc, PR and QRS intervals, in patients with MDD. In a thorough QTc study in healthy subjects at doses up to 40mg daily (note that 40mg is above the licensed maximum of 20mg/day), no potential for the prolongation of the QTc interval was observed.[2]

- Insomnia: Vortioxetine did not increase the incidence of insomnia or somnolence relative to placebo.[2]

In addition, the incidence of self-reported adverse sexual reactions was low and similar to placebo in short- and long-term clinical studies with vortioxetine. In studies using the Arizona Sexual Experience Scale (ASEX), the incidence of treatment-emergent sexual dysfunction (TESD) and the ASEX total score showed no clinically relevant difference to placebo in symptoms of sexual dysfunction at the 5 to 15mg/day doses of vortioxetine – although there was a 14% difference from placebo at a dose of 20mg/day.[2]

• Potentially lower probability of stopping treatment than most other antidepressants[2]
The available evidence, using an indirect treatment comparison analysis and as reviewed by NICE, suggests vortioxetine leads to a lower probability of stopping treatment than most other antidepressants in the short-term.[2] Some people may stop treatment early because of a perceived lack of response and adverse reactions, hence a lower probability of stopping treatment could conceivably help address potential non-adherence. Non-adherence to treatment is a primary cause of treatment failure.[2]

Also, NICE guidance advises that when prescribing drugs other than SSRIs, to take into account the increased likelihood of the person stopping treatment because of side effects.[7]

• Patients treated with Brintellix can abruptly stop taking the medicinal product without the need for a gradual reduction in dose.[2] Conceivably, this can positively impact pharmacological management of the patient, as it makes it potentially easier to manage switch away from vortioxetine if needed compared with many of the existing alternatives.

The tolerability profile of vortioxetine may provide benefit to secondary care, where patients have been referred due to inadequate response or side effects, by providing an additional treatment choice in a different class that is better tolerated than some of the alternative options.

Special warnings and precautions for use (refer to SmPC for full details):[2]

- Use in paediatric population: Brintellix is not recommended for the treatment of depression in patients aged less than 18 years.

- Suicide/suicidal thoughts or clinical worsening:

- Seizures: Seizures are a potential risk with antidepressants.

- Serotonin syndrome (SS) or neuroleptic malignant syndrome (NMS):
Serotonin syndrome (SS) or neuroleptic malignant syndrome (NMS), potentially life-threatening conditions, may occur with Brintellix. If this occurs, treatment with Brintellix should be discontinued immediately and symptomatic treatment should be initiated.

- Mania/hypomania: Brintellix should be used with caution in patients with a history of mania/hypomania and should be discontinued in any patient entering a manic phase.

- Haemorrhage: Caution is advised in patients taking anticoagulants and/or medicinal products known to affect platelet function [e.g. atypical antipsychotics and phenothiazines, most tricyclic antidepressants, non-steroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid (aspirin) (ASA)] and in patients with known bleeding tendencies/disorders.

- Hyponatraemia
Caution should be exercised in patients at risk, such as the elderly, patients with cirrhosis of the liver or patients concomitantly treated with medications known to cause hyponatraemia. Discontinuation of Brintellix should be considered in patients with symptomatic hyponatraemia and appropriate medical intervention should be instituted.

- Elderly
Data on the use of Brintellix in elderly patients with major depressive episodes are limited. Therefore, caution should be exercised when treating patients ≥ 65 years of age with doses higher than 10mg vortioxetine once daily.

- Renal impairment
Limited data are available for patients with severe renal impairment. Caution should therefore be exercised.

- Hepatic impairment
Vortioxetine has not been studied in patients with severe hepatic impairment and caution should be exercised when treating these patients.

Impact to CCGs

Mental health and mental illnesses are determined by multiple and interacting social, psychological and biological factors. Risk factors for mental illness can be grouped under the following categories:

- wider determinants of mental health and socio-economic factors which include low income, unemployment, low levels of education and poor housing, violence and crime;
- family factors which include parental mental health, infant attachment, parenting, family breakup;
- adverse life events which include bullying, abuse, violence, physical illness, relationship breakdown, job loss, bereavement;
- individual factors which include having a caring role, health behaviours and genetic factors and;
- resilience[8]

It is estimated that half of all mental health disorders will start by age 14 and diagnosis will not occur until adulthood. In adulthood, mental health disorders fall into three broad categories: neurotic disorders (depression and anxiety); psychotic disorders (schizophrenia, bipolar disorder); and personality disorders.[8]

It is estimated that one in four British adults experience at least one mental health disorder at some point in their lives. The World Health Organisation estimates that by 2030 depression will be the leading cause of the global burden of disease. Mental ill health is the largest burden of disease in the UK – 23% of the total burden, compared to 16% for heart disease.[8]

In 2009/10 the total estimated cost of mental ill health in England was £105.2 billion (greater than the total 2009/10 NHS Budget which was £104.6 billion). This includes £21.3 billion in health and social care costs, £30.3 billion in lost economic output (absenteeism, reduced productivity, staff turnover) and £53.6 billion in human suffering and negative impact on peoples' quality of life. There is therefore a strong personal, social and economic case for prevention, early diagnosis and treatment of mental ill health.[8]

The burden of mental health can be reduced through a combination of:

- social and economic interventions addressing the wider determinants of mental health;
- mental health promotion including resilience;
- early diagnosis and early intervention;
- improving primary and secondary mental health services and;
- reducing stigma and discrimination.[8]

Within Surrey:

- people generally enjoy good health and wellbeing, and longer than average England life expectancy; this is thought to be due to the affluent nature of the area, however,
- there are pockets of relative deprivation
- at least 23090 children live in poverty
- there is a higher proportion of older people, and that number will double to 69000 by 2033
- 24000 adult women face domestic abuse
- there are five prisons with 2700 prisoners
- the county has the second highest rate for 'increasing risk' drinking of alcohol
- mental health needs correlate closely with deprivation
- The Surrey Health and Wellbeing Board identified promoting emotional wellbeing and mental health as one of its key priorities.[8]

The Surrey Health and Wellbeing Board has stated that:

- it is estimated that 7% of 5 – 15 year olds in Surrey have a mental health disorder.

- there are approximately 24,500 adults aged 65+ with depression or severe depression.
- women over 65 are more likely to be depressed than men the same age.
- there are an estimated 212,000 people aged 16+ in Surrey with 1 or more psychiatric conditions.
- there are 7,719 people in Surrey diagnosed as having a psychotic disorder by their GP.
- following the credit crunch in 2008, the suicide rate in Surrey peaked to higher than the national figure, but more recently has dipped back down.
- suicide rates in Surrey are almost three times higher for men than they are for women.[9]

An analysis of the Strategic Plans and Operating Plans for the five Surrey CCGs show that depression is a priority and aims include:

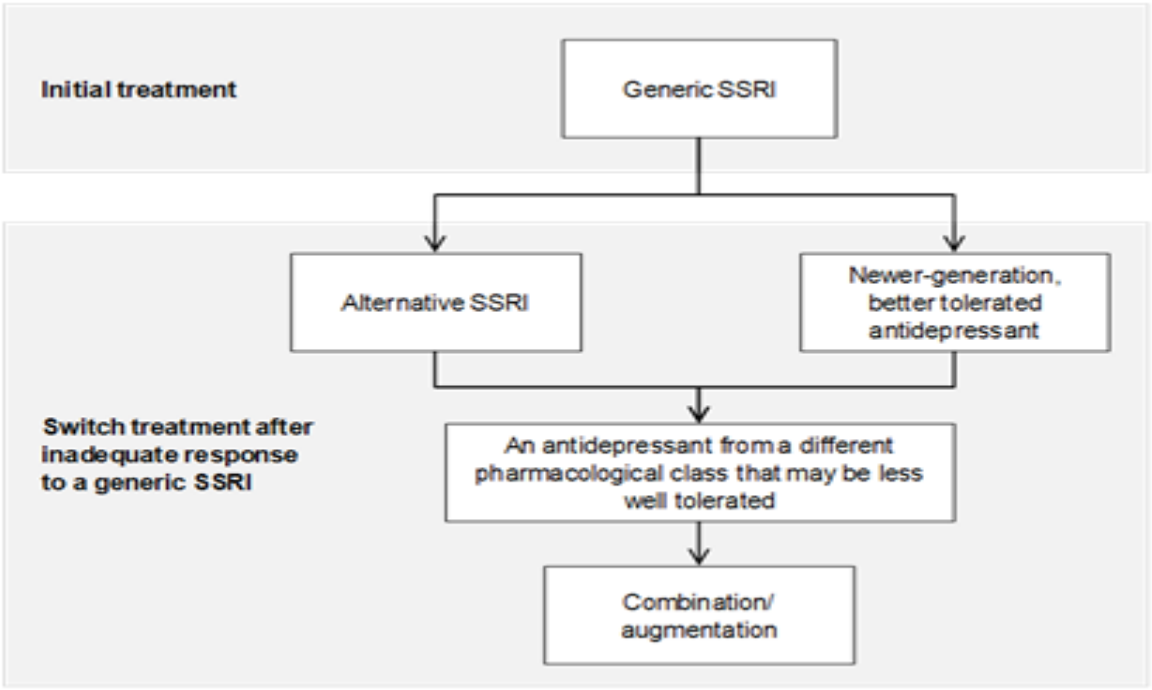
- promote emotional wellbeing and mental health
- ensure a good patient experience
- prevent people dying prematurely
- keep patients safe
- provide the best possible quality of life for people with long term conditions
- patients recover quickly and successfully
- co-design and establish clear pathways covering referral criteria, treatment options, and discharge protocols
- better support people with mental health conditions through integrated care pathways to improve quality and length of life
- provide better acute mental health services to reduce A+E attendances
- improve access to depression and anxiety services
- achieve parity of esteem[10,11,12,13,14]

Effective implementation of NICE TA367 is therefore likely to support the CCGs' strategic aims and provide an additional treatment option for those patients responding inadequately to first and second line antidepressants.

Implementation

Vortioxetine is recommended as an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode.[1]

NICE CG90 recommendation on the treatment of MDD:[7]
Antidepressants are normally recommended as first-line treatment in patients whose depression is of at least moderate severity. The guideline recommends that patients should be seen after 2 weeks of treatment and then every 2-4 weeks for the first 3 months. After monitoring adherence and optimising dosage if necessary, switching to another antidepressant is recommended as an option in these circumstances if the patient wishes to do so. With respect to switching, CG90 is not prescriptive, but recommends considering "initially a different SSRI or a better tolerated newer-generation antidepressant", and "subsequently an antidepressant of a different pharmacological class that may be less well tolerated, for example venlafaxine, a tricyclic antidepressant (TCA) or a monoamine oxidase inhibitor (MAOI)". A diagrammatical representation of this guidance is shown in below.
CG90 makes recommendations for continuation of antidepressant therapy beyond remission, with an emphasis on tailoring treatment to the patient's history, circumstances and preferences. As a minimum, it recommends that a person who has benefited from taking an antidepressant should be encouraged to continue medication for at least 6 months after remission.



Implementation of TA367

- Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraph above. This means that, if a person has a major depressive episode and the doctor responsible for their care thinks that vortioxetine is the right treatment, it should be available for use, in line with NICE's recommendations.

- NICE has developed tools to help organisations put TA367 into practice. These are a costing template and report to estimate the national and local savings and costs associated with implementation.

Costing statement:
Vortioxetine is recommended as an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode.

It is estimated that about 28,000 people are eligible for treatment with vortioxetine each year.

It is unlikely that the guidance will result in a significant change in resource use in the NHS. Vortioxetine is a treatment option alongside current standard third line treatment options for major depressive disorder. There may be a small increase in costs arising from a reduction in the number of people given cheaper treatment options. However, offsetting savings may also be made from, for example, fewer side effects in people given vortioxetine.

This technology is commissioned by clinical commissioning groups (CCGs). The providers can be primary healthcare services (GPs) or secondary care services (mental health teams).

Based on assuming equal efficacy for the purposes of assessing the cost effectiveness, NICE has concluded that treatment with vortioxetine is a cost-effective use of NHS resources. The incremental cost effectiveness ratios (ICERs) for vortioxetine compared with other antidepressants is £9000 per quality-adjusted life year (QALY) gained or below.[1]
Recommendation to PCN
PbRe: N/A **Traffic light status: Green** **Additional comments:**

1. NICE, TA367; November 2015; https://www.nice.org.uk/guidance/ta367
2. Brintellix Summary of Product Characteristics
3. www.patient.co.uk
4. Lundbeck Budget Impact Model. Data on File UK/VOR/1509/0151
5. NHS Drug Tariff for England and Wales, Department of Health, December 2015
6. Sanchez C, et al. Vortioxetine, a novel antidepressant with multimodal activity: review of preclinical and clinical data. Pharmacol Ther. 2015; 145: 43-57.
7. NICE guidelines CG90. 2009. (Available at: http://www.nice.org.uk/guidance/cg90)
8. Joint Strategic Needs Assessment, Surrey County Council, 2014
9. Surrey's Joint Health and Wellbeing Strategy, Surrey Health and Wellbeing Board, 2014
10. Strategic Plan 2014 - 2019, East Surrey CCG, www.eastsurreycch.nhs.uk
11. Strategic Plan 2014 - 2019, Guildford and Waverley CCG, www.guildfordandwaverleyccg.nhs.uk
12. Strategic Plan 2014 - 2019, North West Surrey CCG, www.nwsurreyccg.nhs.uk
13. Strategic Plan 2014 - 2019, Surrey Downs CCG, www.surreydowns.nhs.uk
14. Strategic Plan 2014 - 2019, Surrey Heath CCG, www.surreyheathccg.nhs.uk