

Title: Proposed Changes to NHS Availability of Erectile Dysfunction Treatments IA No: 3125 Lead department or agency: Department of Health Other departments or agencies:	Impact Assessment (IA)	
	Date: 13/12/2013	
	Stage: Consultation	
	Source of intervention: Domestic	
	Type of measure: Primary legislation	
Contact for enquiries: Natalie Cullen		
Summary: Intervention and Options		RPC Opinion: RPC Opinion Status

Cost of Preferred (or more likely) Option				
Total Net Present Value	Business Net Present Value	Net cost to business per year (EANCB on 2009 prices)	In scope of One-In, Two-Out?	Measure qualifies as
£8066m	£0	£0	No	NA

What is the problem under consideration? Why is government intervention necessary?

Erectile dysfunction (ED) treatments are currently restricted on NHS prescription. The ED treatments were originally restricted in 1999 when Viagra was licensed because unrestricted access was considered too costly for the NHS, considering priorities for NHS resources. The legislative restrictions mean the treatments can only be prescribed in primary care for ED in certain circumstances on the NHS. The restrictions are notified to the European Commission under the Transparency Directive on grounds of cost. Viagra lost its patent protection in the UK in June 2013 and the generic product is now available more cheaply. We believe it will now be difficult to continue to notify the generic products on grounds of cost.

What are the policy objectives and the intended effects?

We are proposing to remove generic sildenafil from the list of erectile dysfunction treatments which are restricted on NHS prescription by amending the relevant legislation - Schedule 2 to the NHS (General Medical Services Contracts) (Prescription of Drugs etc.) Regulations 2004. The effect of these changes will be that GPs or other relevant prescribers may prescribe generic sildenafil for patients without any of the present prescribing restrictions. As there have not been any changes to the licensing or costs of the other ED treatments, including branded Viagra, the prescribing restrictions will remain in place for these treatments.

What policy options have been considered, including any alternatives to regulation? Please justify preferred option (further details in Evidence Base)

The proposed changes are to amend regulations which are no longer appropriate because Viagra has lost its patent protection. We considered 3 options. Option 1: Do nothing. This would mean retaining the current prescribing restrictions and risks challenge to our notification under the Transparency Directive on grounds of cost. Do nothing would require an alternative notification under the Transparency Directive. Option 2: Remove the statutory prescribing restrictions for generic sildenafil only, leaving the other in-patent and branded medicines restricted on NHS prescription. This is our preferred option. It meets our obligations under the Transparency Directive, is affordable for the NHS and brings health benefits for individual patients. Option 3: remove prescribing restrictions for all ED treatments. The licensing and pricing of other ED treatments have not changed. Costs relating to unrestricted prescription of branded and in-patent ED products continues to be unaffordable for the NHS in line with original notification.

Will the policy be reviewed? It will/will not be reviewed. If applicable, set review date: Month/Year					
Does implementation go beyond minimum EU requirements?				N/A	
Are any of these organisations in scope? If Micros not exempted set out reason in Evidence Base.		Micro No	< 20 No	Small No	Medium No
What is the CO ₂ equivalent change in greenhouse gas emissions? (Million tonnes CO ₂ equivalent)				Traded:	
				Non-traded:	

I have read the Impact Assessment and I am satisfied that, given the available evidence, it represents a reasonable view of the likely costs, benefits and impact of the leading options.

**Signed by the responsible
SELECT SIGNATORY:**

EARL HOWE **Date:** 6-1-2014

Summary: Analysis & Evidence

Policy Option 1

Description:

FULL ECONOMIC ASSESSMENT

Price Base Year 2013	PV Base Year 2014	Time Period Years 10	Net Benefit (Present Value (PV)) (£m)		
			Low: Optional	High: Optional	Best Estimate:

COSTS (£m)	Total Transition (Constant Price) Years	Average Annual (excl. Transition) (Constant Price)	Total Cost (Present Value)
Low	Optional	Optional	Optional
High	Optional	Optional	Optional
Best Estimate			

Description and scale of key monetised costs by 'main affected groups'

There are no monetised costs relating to the do nothing approach. This impact assessment uses a baseline post Viagras patent loss

Other key non-monetised costs by 'main affected groups'

There will be an administrative burden for DH officials in taking forward some work to notify a new criteria to the European Commission under the Transparency Directive to continue to restrict generic sildenafil.

BENEFITS (£m)	Total Transition (Constant Price) Years	Average Annual (excl. Transition) (Constant Price)	Total Benefit (Present Value)
Low	Optional	Optional	Optional
High	Optional	Optional	Optional
Best Estimate			

Description and scale of key monetised benefits by 'main affected groups'

There will not be any monetised benefits.

Other key non-monetised benefits by 'main affected groups'

There will not be any non-monetised benefits.

Key assumptions/sensitivities/risks

Discount rate (%)

There are risks in the do nothing option if further work is not taken forward to notify a new criteria under the Transparency Directive to the European Commission.

BUSINESS ASSESSMENT (Option 1)

Direct impact on business (Equivalent Annual) £m:			In scope of OITO?	Measure qualifies as
Costs:	Benefits:	Net:	No	NA

Summary: Analysis & Evidence

Policy Option 2

Description:

FULL ECONOMIC ASSESSMENT

Price Base Year 2013	PV Base Year 2014	Time Period Years 10	Net Benefit (Present Value (PV)) (£m)		
			Low: Optional	High: Optional	Best Estimate: £8066

COSTS (£m)	Total Transition (Constant Price) Years	Average Annual (excl. Transition) (Constant Price)	Total Cost (Present Value)
Low	Optional	Optional	Optional
High	Optional	Optional	Optional
Best Estimate		13	108

Description and scale of key monetised costs by 'main affected groups'

The main costs are in relation to the estimated 150,000 additional patients who may present for NHS treatment for ED in the first three years after derestriction. Costs relating to the actual medicine are low, but associated costs of GP time and dispensing fees make the overall cost at about £100 per additional new patient. The associated healthcare costs are likely to lessen over time.

Other key non-monetised costs by 'main affected groups'

We have included the costs relating to the additional likely GP appointments in the estimates. However, there may be additional administrative burdens on primary care prescribers relating to increasing the availability of the treatments on the NHS.

BENEFITS (£m)	Total Transition (Constant Price) Years	Average Annual (excl. Transition) (Constant Price)	Total Benefit (Present Value)
Low	Optional	Optional	Optional
High	Optional	Optional	Optional
Best Estimate		893	8174

Description and scale of key monetised benefits by 'main affected groups'

The main monetised benefits relate to the QALY gain. There are also estimated savings for those patients who as a result of the changes would move from being treated in secondary care to primary care.

Other key non-monetised benefits by 'main affected groups'

There are health and safety benefits for those men who move from seeking ED treatments from illegal or unsafe internet supplies of ED medicines, to NHS treatment. There will be additional health benefits for those new patients seeking treatment for ED on the NHS whose clinician identifies and treats a related underlying health condition.

Key assumptions/sensitivities/risks

Discount rate (%) 3.5

It has been difficult to accurately estimate the additional numbers of patients who are likely to seek treatment on the NHS if generic sildenafil isn't restricted. We recognise there are risks relating to this and following any regulation change we will monitor prescribing data for the forthcoming years.

BUSINESS ASSESSMENT (Option 2)

Direct impact on business (Equivalent Annual) £m:			In scope of OIOO?	Measure qualifies as
Costs: 0	Benefits: 0	Net: 0	No	NA

Summary: Analysis & Evidence

Policy Option 3

Description:

FULL ECONOMIC ASSESSMENT

Price Base Year 2013	PV Base Year 2014	Time Period Years 10	Net Benefit (Present Value (PV)) (£m)		
			Low: Optional	High: Optional	Best Estimate:

COSTS (£m)	Total Transition (Constant Price) Years	Average Annual (excl. Transition) (Constant Price)	Total Cost (Present Value)
Low	Optional	Optional	Optional
High	Optional	Optional	Optional
Best Estimate		30	281

Description and scale of key monetised costs by 'main affected groups'

The main costs of Option 3 are as at Option 2, with an additional £173M relating to the costs associated with removal of the statutory prescribing restrictions for the in-patient and branded erectile dysfunction treatments. Despite the additional costs of Option 3, the benefits remain the same as for Option 2.

Other key non-monetised costs by 'main affected groups'

There are health and safety benefits for those men who move from seeking ED treatments from illegal or unsafe internet supplies of ED medicines, to NHS treatment. There will be additional health benefits for those new patients seeking treatment for ED on the NHS whose clinician identifies and treats a related underlying health condition.

BENEFITS (£m)	Total Transition (Constant Price) Years	Average Annual (excl. Transition) (Constant Price)	Total Benefit (Present Value)
Low	Optional	Optional	Optional
High	Optional	Optional	Optional
Best Estimate			

Description and scale of key monetised benefits by 'main affected groups'

The main non-monetised costs relate to the QALY gain. There are also estimated savings for those patients who as a result of the changes would move from being treated in secondary care to primary care.

Other key non-monetised benefits by 'main affected groups'

There are health and safety benefits for those men who move from seeking ED treatments from illegal or unsafe internet supplies of ED medicines, to NHS treatment. There will be additional health benefits for those new patients seeking treatment for ED on the NHS whose clinician identifies and treats a related underlying health condition.

Key assumptions/sensitivities/risks

Discount rate (%)

It has been difficult to accurately estimate the additional numbers of patients who are likely to seek treatment on the NHS if all of the erectile dysfunction treatments are not restricted on NHS prescription. The financial risks relating to removing the prescribing restrictions for all ED treatments are greater for Option 3 than for Option 2 because the costs of the branded and in-patient medicines are much greater than for generic sildenafil.

BUSINESS ASSESSMENT (Option 3)

Direct impact on business (Equivalent Annual) £m:			In scope of OIOO?	Measure qualifies as
Costs: 0	Benefits: 0	Net: 0	No	NA

Evidence Base (for summary sheets)

Problem under consideration & Rationale for intervention

1. Viagra was licensed in the UK 1998 and in 1999 the Department of Health undertook formal measures to restrict NHS prescription of erectile dysfunction treatments in NHS primary care. Sildenafil (Viagra) was one of the licensed Erectile Dysfunction (ED) treatments which was added to Schedule 2 to the NHS (General Medical Services Contract) (Prescription of Drugs etc.) Regulations 2004. Schedule 2 restricts prescribing of listed products to certain patients who meet certain conditions. Schedule 2 is commonly referred to as the grey list and products on Schedule 2 as being grey listed. The ED treatments were added with the stated aim of limiting NHS spend to between £10 and £12 million a year. NHS spend on all ED treatments in England in 2012 was estimated at £88m and almost 50% (£43m) of this was on Viagra, with around a further £35m spent on the drug Cialis.
2. In order to satisfy EC member state rules under Article 7 of the Transparency Directive (89/105/EEC), relating to the transparency of measures regulating the pricing of medicinal products... and their inclusion in the scope of national health insurance schemes, the UK notified a number of licensed ED treatments. The ED treatments, including Viagra, were notified to the European Commission based on criterion 5 of our notified criteria. This notification says that “a medicinal product or a category of medicinal products may be excluded entirely from NHS prescription where the forecast aggregate cost to the NHS of allowing the product.... could not be justified having regard to.... the priorities for expenditure of NHS resources.”
3. Viagra lost its patent protection in the UK in June 2013. Following this, the price of generic preparations of sildenafil have dropped by around 93% of the price of branded Viagra. The Drug Tariff listed prices of sildenafil have dropped from £21.27 in June to £1.45 in November for a 4 tablet pack. As the product is now available so cheaply, we do not believe the notification under the Transparency Directive on grounds of cost is still appropriate.
4. The consultation is seeking comments on our proposals to remove the statutory prescribing restrictions for generic sildenafil.

Policy objective

5. The policy objective is to remove the statutory prescribing restrictions to ensure we meet our requirements under the Transparency Directive, now Viagra is not under patent protection.

Description of options considered (including do nothing)

Option 1: Do nothing - Schedule 2 prescribing restrictions remain for all ED treatments

6. Under this option all of the ED treatments would continue to be restricted on NHS prescription, except in certain defined circumstances. Whilst the option is to do nothing, action would be required to notify the European Commission of a new criteria under the Transparency Directive for restricting the cheaper generic treatments.

Option 2: Schedule 2 prescribing restrictions are removed for generic sildenafil, but remain for other ED treatments

7. We are proposing to remove generic sildenafil from the list of erectile dysfunction treatments which are restricted on NHS prescription by amending Schedule 2 to the NHS (General Medical Services Contracts) (Prescription of Drugs etc.) Regulations 2004. The other listed PDE5 inhibitors – tadalafil, vardenafil and branded Viagra will continue to be restricted. The effect of these changes will be that GPs or other relevant prescribers may prescribe generic sildenafil for patients without any of the present prescribing restrictions. As

there have not been any changes to the licensing or costs of the other ED treatments, including branded Viagra, the prescribing restrictions will remain in place for these treatments.

Option 3: Schedule 2 prescribing restrictions are removed for all ED treatments

8. Under this option we considered the impact of removing prescribing restrictions for all of the ED treatments. The cost of removing the restrictions for all of the ED treatments, including the in-patent and branded ED treatments, remains unaffordable for the NHS, considering wider priorities.

Monetised and non-monetised costs and benefits of each option (including administrative burden)

Monetised and non-monetised costs and benefits of Option 1

9. The cost of option 1 is nothing. There is no change in benefits.

Monetised and non-monetised costs and benefits of Option 2

10. Option 2, removing the statutory prescribing restrictions for generic sildenafil, is our preferred option. We believe that it is affordable for the NHS and can bring benefits for many patients.

Drug Costs

11. Following patent expiry, the price of generic preparations of sildenafil have dropped by almost 95% of the price of branded Viagra – dropping from £21.27 to £1.45 for a 4 tablet pack. The effect of increased prescribing on expenditure, even of a doubling, would be minor in relation to NHS expenditure on in-patient sildenafil of £40m in 2012. Doubling would take it to £4m and trebling to £6m.

Other treatment costs and numbers of patients

12. There would be a burden on primary care as each new patient requires an average of 1.9 consultations at a cost of about £68¹; for those transferring from secondary care there is a net saving to the NHS. The cost to the NHS would be modest, driven by the low cost of generic sildenafil.

Average annual cost per patient		
	new	transfers
GP Consultations	£68	£36
Net Ingredient Costs (NIC)	£20	
Dispensing Costs	£16	£16
Revenue From Prescription Charges	-£5	-£5
Saving Secondary Care		-£114
	£98	-£67

Average annual cost for selected additional number of patients in primary care		
£m		
	new	transfers
Number transferring	50,000	7000
GP Consultations	£3.4	£0.3
NIC	£1.0	
Dispensing Costs	£0.8	£0.1
Revenue From Prescription Charges	-£0.3	..
Saving Secondary Care		-£0.8
	£4.9	-£0.5

13. There is no wholly reliable information on the numbers on PDE5 therapy at any one time. To judge from figures in prescription cost analysis and elsewhere (Annex 5 of the attached Options Analysis) the total may be about 184,000. However, ED plots an erratic course over time with remission and progression. It is possible that some patients may take the therapy on and off and so the numbers on therapy at any time during a twelve month period may be much greater. For the purposes of the IA we have estimated about 180,000 are currently prescribed PDE5 therapies.

14. Of this total about 7000 are currently treated as hospital out-patients (Annex 5 of the Options Analysis). Since many if not most of this group are only referred to hospital because of the restrictions on prescribing it is likely

¹excluding amortised costs of medical training.

hospital clinicians would encourage many to move to primary care. However, the modest numbers limit the potential impact. The PDE5 patients currently being managed in hospital clinics are likely all to be redirected to primary care. There will be a saving of £35 per patient per year totalling £1,715,000. The additional cost savings over ten years would be £17,150,000, discounted to £14m over 10 years.

15. An estimate based on US figures may provide a point of reference. There are 6 million men with diagnosed ED, of whom 25% are on therapy – 1.5 million. Adjusting for the lower population, the equivalent for England would be something like 250,000.
16. The total prevalence of Schedule 2 conditions may be about 1.5 million with up to 1 million experiencing some degree of ED (Annex 6 of the Options Analysis).
17. The estimates of the prevalence of ED are very high (Annex 4, Options Analysis). On one estimate every second man aged 40-70 is affected by ED at some time or other – about 5 million. The proportion suffering at any one time is uncertain but will be lower, perhaps much lower. There is a spectrum of severity - mild 17%; moderate 25%; severe 10%. So the prevalence of ever having experienced severe ED is about 1 million in this age group.
18. On the basis of evidence from a European survey, about 600,000 men in England may be bypassing the healthcare system to access ED treatments through the internet or via other routes.

Patient benefit

19. There is some suggestion that ED may be an early indicator of vascular diseaseⁱⁱ – the canary in the coal mine. More than two in every three ED sufferers has at least one comorbidity such as hypertension, hyperlipidaemia, diabetes or depression. Accordingly, there are likely to be healthcare benefits from widening NHS access to ED therapies to encourage presentation with ED as a screening device for more serious disorders to encourage their early diagnosis and treatment. We have not included estimates of the monetised costs relating to these benefits in this Impact Assessment.

Summary of calculation of impact of Option 2

20. Considering the estimates of the prevalence of ED and the use of illicit sources of supply, we have calculated an additional 50,000 patients on sildenafil each year for three years, making 150,000 in total. The estimated cost is just under £100 per patient year (including the (1.9) GP consultations, dispensing costs and revenue from charges). This gives an additional annual cost of £4.9m a year per 50,000. The additional cost discounted over ten years would be £108m.
21. We have also estimated the benefit, in Quality of Life Adjusted Years (QALY) terms. From the cost effectiveness analysis (Reference 29 Options Analysis), the annual benefit per patient is 0.11 of a QALY. QALYs have a value of £60,000 so the total value of the annual benefit per 50,000 men would be 5500 QALYs valued at £330m. Discounted over ten years this comes to £8160m for the estimated additional 150,000 new patients in the first three years after derestriction
22. Over a 10 year period, we estimate costs of £108m and benefits of £8174m.

Monetised and non-monetised costs and benefits of Option 3

23. We do not favour this option because the costs of removing the statutory prescribing restrictions for the in patent and branded PDE5 inhibitors continues to be unaffordable for the NHS. Cialis (tadalafil) was the second most commonly prescribed PDE5 inhibitor in 2012, with £35 million spent on the NHS in England on the treatment. Cialis is under patent protection until 2017 and is likely to remain expensive during this period.
24. Each additional 50,000 patients on Cialis would increase the drugs bill by £26.7m. Their other costs would not add significantly to the total.

Annual Cost of new Cialis patients		
	Per patient	Per 50,000 £m
GP Consultations	£68	£3.4
NIC	£533	£26.7
Dispensing Costs	£16	£0.8
Revenue From Prescription Charges	-£5	-£0.3
	£611	£30.6

25. Option 3 is to derestrict all drug therapies for ED. We have estimated that half of the new patients identified in Option 2 might be prescribed Cialis rather than sildenafil, especially as Cialis itself is due to lose patent protection in 2017. We assume that Cialis will follow the example of sildenafil after patent expiry, ie, wholesale generic substitution at 5% of the former cost.
26. Over a 10 year period, we estimate costs of £281m and benefits £8174m.

Rationale and evidence that justify the level of analysis used in the IA (proportionality approach)

27. The attached Options Analysis (Annex A) provides the detail of the evidence and analysis which was considered in advance of developing the consultation proposals

Risks and assumptions

28. It has been difficult to accurately estimate the additional numbers of patients who are likely to seek treatment on the NHS if generic sildenafil isn't restricted. We recognise there are risks relating to this and following any regulation change we will monitor prescribing data for the forthcoming years.

Direct costs and benefits to business calculations (following OITO methodology)

29. There are no direct costs or benefits to UK business (according to the One-In-Two-Out methodology) under any of the options. It therefore falls outside the scope of One-In-Two-Out.

Wider impacts

30. In line with the Department's duty to eliminate unlawful discrimination, our proposals to consult on prescribing restrictions, support the strategy to improve men's health.

Summary and preferred option

31. The UK's Transparency Directive notification for excluding ED treatments on NHS prescription, except in specified circumstances, was on the basis that the forecast aggregate cost of the ED treatments could not be justified having regard to the priorities for expenditure of NHS resources. Since Viagra lost its patent protection in June, generic sildenafil is now available at about 5% of its cost under patent. As generic sildenafil is now available so cheaply, we do not believe the Transparency Directive notification is still valid.
32. **Option 2, removing the prescribing restrictions for generic sildenafil is our preferred option.** This option meets our requirement under the Transparency Directive and provides benefits for those patients who will be able to access generic sildenafil as a result of the changes. NHS budgets will benefit from the availability of cheaper generic sildenafil, but will incur additional costs relating to increases in numbers of patients and providing NHS care for them. Overall we estimate it will be costs saving for the NHS, primarily as a result of the large price drop for generic sildenafil.
33. Any impact on branded and in-patent ED drug manufacturers will be in relation to Viagra losing its patent protection, rather than our proposed changes. When the first drug in class loses its patent protection, the market changes and adjusts – usually to make more use of the cheaper generic product. The market position for branded and in-patent ED treatments is likely to alter following Viagra's patent loss, but this will not be as a result of our proposed changes, rather market forces.
34. We estimate a positive impact for generic sildenafil manufacturers who will see increases in prescribing of their products. Increasing NHS provision may lead to greater competition in this market and a further decrease in prices of the standard Drug Tariff price listing for generic sildenafil.
35. **Option 1, continuing to restrict generic sildenafil, risks challenge on the basis that the notification on grounds of cost is no longer valid. We have discounted this option.**
36. **Option 3, removing the prescribing restrictions for all ED treatments is unaffordable for the NHS. We have discounted this option.** Unlike generic sildenafil, the pricing and licensing of branded and in patent ED treatments have not changed and we do not see any reason to alter NHS provision. Increasing NHS provision of the branded and in-patent products risks a substantial overall increase in NHS spend relating to ED treatments. The prices of in patent and branded ED treatments have not changed and our notification under the Transparency Directive remains valid.

Implementation Plan

37. We propose to amend the relevant prescribing regulations, Schedule 2 to the NHS (General Medical Services)(Prescription of Drugs etc.) Regulations 2004 bringing the new arrangements in place in May 2014.

Sildenafil Statutory Restrictions Options Analysis

Background

Sildenafil (Viagra) was one of the licensed Erectile Dysfunction (ED) treatments which was added to Schedule 2 to the NHS (General Medical Services Contract) (Prescription of Drugs etc.) Regulations 2004. Schedule 2 restricts prescribing of listed products to certain patients who meet certain conditions. Schedule 2 is commonly referred to as the grey list and products on Schedule 2 as being grey listed. The ED treatments were added with the stated aim of limiting spend to between £10 and £12 million a year. NHS spend on all ED treatments in England in 2012 was estimated at £88m and almost 50% (£43m) of this was on Viagra, with around a further £35m spent on the drug Cialis.

The analysis will need to address 3 potential options:

Option 1: Schedule 2 current restrictions remain

Option 2: Schedule 2 restrictions are removed for sildenafil

Option 3: Schedule 2 restrictions for all ED treatments are removed

Option 1: Schedule 2 current restrictions remain

Expenditure (net ingredient cost) on Viagra prescribed in primary care currently runs at about £40m a year. Following patent expiry it is expected that generics will enter the market at about 5% of the price. If generics capture the whole market for sildenafil there will occur a saving of £38m a year in NIC. Expenditure on ED drugs in the hospital sector adds less than 10%, about £3.3m, 76% of it on Viagra. There would then be a saving of £2.4m in secondary care.

Previous patent expiries with some broadly similar features, such as Zocor (simvastatin) and Tritace, the ACE inhibitor ramipril, may provide pointers as to the likely impact on sildenafil (annex 1 below). It would be desirable to study a wider range of patent expiries. There does not seem to be a helpful literature on this issue, and in the time available it proved necessary to be selective.

Both Zocor and Tritace maintained their price even as generics entered at a much lower price. Both quickly lost virtually their entire market share. It is worth noting that prescribers almost always prescribe in generic terms, even when there is no generic. This behaviour is seen in these earlier patent expiries and also currently in Viagra (annex 1).

However, not all variants of a drug class, even within a BNF sub-chapter, are interchangeable. Most of the ACE inhibitors are interchangeable, or have been pronounced so by NICE, but not all. The statins have less interchangeability for some groups of patients. Analysis of the price changes and market shares in ACE inhibitors and statins suggests that the variants which are not interchangeable with the product losing patent protection maintain their price and market share.

The PED5-I class consists largely of Viagra (sildenafil), Cialis (tadalafil) and Levitra (vardenafil). The market shares and cost for the most commonly prescribed dosages are as follows:

PDE5-I market shares and cost comparisons at most commonly prescribed dosageⁱⁱⁱ²

PED5 inhibitor	Cost per month	Market share (px)
Vardenafil (Levitra)	£23.48	7%
Sildenafil (Viagra)	£23.50	56%
Tadalafil (Cialis)	£26.99	37%

A key question is whether Cialis is a premium product. It has a price premium, of nearly 15%, for the most commonly prescribed dosage. A meta-analysis of user surveys^{iv} based on the International Index of Erectile Function (IIEF)^v found Viagra and Cialis broadly similar in effectiveness and both superior to Vardenafil. However, Cialis may have a longer-lasting effect^{vi}, allowing flexibility and spontaneity, features not fully captured in the IIEF. It also appears to be suitable for more frequent dosing^{vii}. Prescribing behaviour does not appear to be invariably sensitive to price. Vardenafil has no price advantage over Viagra, and no performance advantage either. Yet it accounts for 6% of the market by value. In these circumstances it is likely that Cialis at least may retain some or all of its sales following the introduction of generic sildenafil at 5% of its price before patent expiry.

There is another effect worth taking into account, even if current restrictions remain. To judge from ACE inhibitors in particular, the fall in price led to an increase in volume. It is possible to derive an apparent elasticity of demand from the before and after prices and quantities of ACEi (annex 3). This procedure attributes all the increase in volume to the change in price, whereas there may be underlying growth not driven by price – as there clearly is in the statins example. The ACEi market is stable enough to allow some credence to be attached to the apparent elasticity, which is - 0.35. This means that a 10% fall in price would cause a 3.5 % increase in volume, or equivalently, a 6.5% fall in expenditure.

Applying this apparent elasticity to sildenafil, the expected 95% fall in price would more than double the volume of sildenafil, but with a reduction of 86% in the expenditure. These estimates look extreme – the degree of extrapolation from the more modest price reduction of 43% seen in ACEi may be unwarranted.

There is information as to the NHS expenditure on erectile dysfunction (annex 8).

Cost of ED to NHS England 2012

	£m pa			
	Currently (1)	Viagra off patent (2)	C and V lose half of market share to share to sildenafil (3)	Prescriptions for sildenafil double in 1 ⁰ sector in response to fall in price (4)
Drugs				
1 ⁰ sector				
NIC	84.9	47.1	28.2	48.1
Dispensing costs	2.8	2.8	2.8	3.6

²This data relates to primary care. The predominance of Viagra is even greater in hospital prescribing, which, however, represents a very small proportion of the total.

Prescription charges	-4.2	-4.2	-4.2	-5.4
2 ⁰ sector	3.3	0.9	0.9	0.9
Devices	5.5	5.5	5.5	5.5
Consultations				
GP	10.8	10.8	10.8	16.8
Specialist	28.8	28.8	28.8	28.8
Psychosexual therapy	12.3	12.3	12.3	12.3
total	144.2	104.0	85.1	110.7

The expiry of the Viagra patent should lead to a reduction in NHS expenditure on ED from about £144m to £104m a year.

It may be worth noting that on the above analysis (column (2)) Cialis would be little affected, with its expenditure continuing at much the present rate. Expenditure on Cialis alone – £34.5m – greatly exceeds the target of £10m to £12m associated with the grey listing.

However, column (3) of the table shows the effect if both Cialis and Vardenafil were to lose half their market share by volume to sildenafil.

Column (4) in the table illustrates the effect if prescriptions for sildenafil were to double, in response to the price reduction, but otherwise the assumptions of column (2) apply.

Option 2: Schedule 2 restrictions are removed for sildenafil

There is no wholly reliable information on the numbers on PED5-I therapy at any one time. To judge from figures in prescription cost analysis and elsewhere – annex 5 below – the total may be about 184,000. However, ED plots an erratic course over time with remission and progression. It is possible that some patients may take the therapy on and off and so the numbers on therapy at any time during a twelve month period may be much greater.

Of this total about 7000 are currently treated as hospital out-patients (annex 5). Since many if not most of this group are only referred to hospital because of the restrictions on prescribing it is likely hospital clinicians would encourage many to move to primary care. However, the modest numbers limit the potential impact.

An estimate based on US figures may provide a point of reference. There are 6 million men with diagnosed ED, of whom 25% are on therapy – 1.5 million. Adjusting for the lower population, the equivalent for England would be something like 250,000.

The total prevalence of Schedule 2 conditions may be about 1.5 million with up to 1 million experiencing some degree of ED (annex 6).

The estimates of the prevalence of ED are very high (annex 4). On one estimate every second man aged 40-70 is affected by ED at some time or other – about 5 million. The proportion suffering at any one time is uncertain but will be lower, perhaps much lower. There is a spectrum of severity - mild 17%; moderate 25%; severe 10%. So the prevalence of ever having experienced severe ED is about 1 million in this age group.

On the basis of evidence from a European survey, about 600,000 men in England may be bypassing the healthcare system to access ED treatments through the internet or via other routes.

Following patent expiry the cost of sildenafil will be so modest that the effect of increased prescribing on expenditure, even of a doubling, would be minor in relation to the current expenditure of £40m – on patent expiry expenditure would fall to £2m; doubling would take it to £4m.

There would be a burden on primary care as each new patient requires an average of 1.9 consultations at a cost of about £68^{viii3}; for those transferring from secondary care there is a net saving to the NHS.

³excluding amortised costs of medical training.

Average annual cost per patient

	new	transfers
GP Consultations	£68	£36
NIC	£20	
dispensing costs	£16	£16
revenue from prescription charges	-£5	-£5
saving secondary care		-£114
	£98	-£67

Average annual cost for selected additional number of patients in primary care £m

	new	transfers
Number transferring	50,000	7000
GP Consultations	£3.4	£0.3
NIC	£1.0	
dispensing costs	£0.8	£0.1
revenue from prescription charges	-£0.3	..
saving secondary care		-£0.8
	£4.9	-£0.5

The cost to the NHS would be modest, driven by the low cost of generic sildenafil.

Cost effectiveness in standard health technology terms would also be favourable (annex 7).

There is some evidence that men taking ED therapy have higher rates of STD, particularly HIV^{ix}. However the source comments that this may reflect selection bias.

The observed association between ED drug use and STDs may have more to do with the types of patients using ED drugs than a direct effect of ED drug availability on STD rates.

Option 3: Schedule 2 restrictions for all ED treatments are removed

The problem with the option of removing the statutory prescribing restrictions for all ED therapies is not sildenafil, because it will be cheap, but Cialis, which has a patent with some time to run (2017) and is likely to remain expensive during this period. Moreover, in view of its perceived superiority over sildenafil it may be the therapy of choice for new patients.

Each additional 50,000 patients on Cialis would increase the drugs bill by £26.7m. Their other costs would not add significantly to the total.

Annual Cost of new Cialis patients

	Per patient	Per 50,000 £m
GP Consultations	£68	£3.4
NIC	£533	£26.7
dispensing costs	£16	£0.8
revenue from prescription charges	-£5	-£0.3
	£611	£30.6

One issue is the cost effectiveness of an expansion of ED therapy. On standard yardsticks sildenafil (in the form of Viagra at the full price) has very good cost effectiveness - £3600 per QALY, well within the NICE passmark of £20k-£30k per QALY (annex 7). However, the findings relate to a sample of men of “18 years of age or older with a clinical diagnosis of erectile dysfunction (as defined previously) of six months’ duration or longer”. The “previous definition”^x turns out to be curiously unspecific.

Patients currently acquiring ED therapies off prescription are likely to be represented in new patients presenting following removal of prescribing restrictions. Estimates exist of their numbers and characteristics (annex 9). The estimates point to very high numbers – 600,000. However, two thirds of this group have either mild ED or none at all. Moreover, many may be taking the ED to counter the side effects of drug abuse. It is unlikely that many will present to their GP and if they did might not qualify for therapy.

Their reasons for bypassing the health care system are to avoid embarrassment, to take advantage of the lower cost and the opportunity to buy in bulk. Some Cialis users may be tempted to approach their GP especially if exempt from prescription charges. Unfortunately the sources do not specify the product used by this group of users.

There is evidence of the questionable quality of ED drugs obtained from unregulated sources, though not much evidence of any harm or ineffectiveness. The user himself knows whether a PED5-I is working or not, and indeed is the best judge of efficacy, unlike some other drugs such as cholesterol-lowering drugs. The user is less well placed to judge long term safety. The case for white listing on grounds of the quality of the unregulated supply is questionable.

With removing the statutory prescribing restrictions, it would be desirable to commission a health technology assessment from NICE, with a title such as drug therapy for ED. This would be particularly useful in view of the possibility that de-restricting the expensive drug tadalafil could entail considerable increase in expenditure.

Tadalafil may be better than sildenafil but it will also be much more expensive with Viagra off patent. Although tadalafil may deliver good value for money against a do nothing base it is much less likely to meet the NICE passmark against sildenafil. The NICE assessment would also offer advice for no, mild and moderate ED, and could well recommend restriction to severe disease, further containing NHS expenditure.

NICE does not offer estimates of the cost of their various form of advice, but from their Annual Report and Accounts^{xi} a health technology assessment may cost in the region of £500,000⁴, a modest sum in the circumstances.

There is some suggestion that ED may be an early indicator of vascular disease^{xii} – the canary in the coal mine. More than two in every three ED sufferers has at least one comorbidity such as hypertension, hyperlipidaemia, diabetes or depression. Accordingly, there may be a case for white listing ED therapies to encourage presentation with ED as a screening device for more serious disorders to encourage their early diagnosis and treatment.

There may be room for another NICE appraisal focusing on ED as a screening method for vascular disease. This is likely to recommend against.

Robert Anderson
15 October 2013

⁴In 2011-12 NICE spent £59m and published 104 items of advice. Health technology appraisals are probably among the less costly of the different forms of advice.

Prices and quantities following patent expiry – analysis June 2013

Viagra is about to come off patent. Generic versions are likely to be introduced at a much lower price. Currently, the price is about £5 with token variation by weight⁵.

An estimate based on price trends following patent expiry in Canada suggests a generic price of £1.25 for a 25 mg tablet^{xiii}. However, other estimates suggest the even lower price of 5% of the current price, 25p, and this is the price illustrated in the analysis below.

It would be useful to study all recent patent expiries, but in the time available attention is focused on simvastatin (Zocor) and ramipril (Tritace).

The market for statins shares some features with the market for PDE5-I drugs for erectile dysfunction:

- high total expenditure
- class includes variants which are not perfect substitutes for each other
- only the leading drug losing patent protection
- high proportion of prescriptions for proprietary brand written in generic form
- salience.

Proportion prescribed generically on the eve of patent expiry		
Zocor	simvastatin	98.4%
Tritace	ramipril	98.6%
Viagra	sildenafil	96.3%

Simvastatin came off patent in 2003. It is helpful to compare 2005, by which time the market had time to settle down, with 2002, the last full year before expiry.

Generic versions of simvastatin were introduced at one fifth of the pre-patent price. The price of Zocor was not reduced and it lost virtually its whole market share⁶. The price of pravastatin fell by two thirds; it nevertheless lost half its market share. Atorvastatin maintained both its price and market share.

Statin volumes roughly doubled between 2002 and 2005 in line with a diffusing technology. Atorvastatin doubled its volume; pravastatin volume remained flat.

Unlike statins ACE inhibitors are interchangeable^{xiv}. The patent for the ramipril Tritace expired at the beginning of 2004. Generic ramipril entry took place at a 60% lower price. The price of the other ACE inhibitors was also reduced by varying percentages, except for perindopril, which maintained its price. As in the case of Zocor (simvastatin) the price of Tritace was maintained.

⁵25mg - £4.15; 50mg - £5.32; 100mg - £5.88

⁶Market share by quantity, not expenditure.

Prices of ACE inhibitors before and after expiry of patent
on Tritace

	£ per tablet 2003	£ per tablet 2005	Price change %
Tritace ⁷	0.37	0.49	
Ramipril	..	0.14	- 61
Captopril	0.07	0.06	- 11
Enalapril	0.18	0.09	- 51
Lisinopril	0.30	0.11	- 63
Perindopril	0.36	0.37	+ 4
Quinapril	0.31	0.24	- 22

Tritace lost its whole market to generic ramipril; otherwise market shares changed little.

ACEi change in market shares 2003 - 2005

	Px ppts	NIC ppts
Tritace	- 34	- 39
Ramipril	38	31
Captopril	- 1	..
Enalapril	- 4	- 3
Lisinopril	- 3	- 11
Perindopril	5	24
Quinapril

The average price per tablet of ACE inhibitors fell from 30p to 17p. The ACE inhibitor market was by that time quite mature and is likely to have been approaching saturation in the sense of nearing completion of the process of technology diffusion. However, the volume of prescriptions rose by 22% between 2003 and 2005. It seems reasonable to attribute this rise substantially to the effect of the fall in price, with an apparent elasticity of - 0.35.

The market for drugs for erectile dysfunction (BNF) similarly seems to be stabilising with annual growth in prescriptions having fallen steadily to only 2% for the most recent year.

⁷The apparent change in price is solely the result of a change in the sales mix of different products.

The current profile of the PED5-I drugs for ED

Market for PED5-I drugs for erectile dysfunction 2012					
	Number of prescriptions th	Number of tablets th	NIC £k	NIC per px	NIC per tablet
Tadalafil	847.4	7291.6	34,574	£41	£4.74
Vardenafil	178.2	990.0	4,907	£28	£4.96
Viagra	1287.5	7511.1	40,308	£31	£5.37
total	2313.1	15792.7	79,789		

Market share for PED5-I drugs for erectile dysfunction
2012

	Prescriptions %	Tablets %	NIC %
Cialis Tadalafil	37	46	43
Vardenafil	8	6	6
Viagra	56	48	51
total	100	100	100

Viagra accounts for a good half of the market; tadalafil just under half; vardenafil is an also ran.

These figures cover only prescribing in primary care.

To judge from the patent expiries in statins and ACE inhibitors and the discussion in annex 1, it is likely that entry of generic sildenafil at a reduced price will not disturb the volume of tadalafil.

Annex 3

Deriving an apparent elasticity from before and after observations on price and quantity

Assume a constant elasticity demand schedule

$$Q = \alpha P^{-\varepsilon} \Rightarrow \frac{Q_1}{Q_0} = \left(\frac{P_1}{P_0}\right)^{-\varepsilon} \Rightarrow \ln\left(\frac{Q_1}{Q_0}\right) = -\varepsilon \ln\left(\frac{P_1}{P_0}\right) \Rightarrow \varepsilon = \ln\frac{Q_1}{Q_0} / \ln\frac{P_1}{P_0}, \text{ with obvious notation.}$$

Annex 4

Prevalence of ED

Approximately 52% of men 40-70⁸ are affected by ED at some time or other – about 5 million^{9xv}. The proportion suffering at any one time is uncertain but will be lower, perhaps much lower. There is a spectrum of severity.

About 1% of men 40-79 a year¹⁰ consult their GP for the first time with ED^{xvi}. This gives an annual incidence of 114,000. Other estimates point to more than double this figure – about 260,000^{xvii}. Assuming even distribution across the age group and 70% survival, prevalence of those who have ever consulted about ED in this age group would be about 1.6 to 3.6 million.

According to a reliable survey¹¹, the prevalence of ED in the US is 18 million^{xviii}, corresponding to about 3 million in this country.

In the US about 6m men have a clinical diagnosis of ED, a figure which would correspond to about 1m in this country^{xix}.

⁸Population 9.6m.

⁹The first large-scale community study - the Massachusetts Male Ageing Study - showed that 52% of men (aged 40 to 70 years) were affected at some time (mild 17%; moderate 25%; severe 10%).

¹⁰Among men who consult their GP for any reason.

¹¹NHANES.

Annex 5

Treated prevalence

To judge by the number of PED5-I prescriptions per year (about 2.3m), the number of tablets per prescription (about 5) and the allowance of one tablet per week, the number of men taking a PED5-I drug at any one time would be about 177,000.

The numbers in the secondary sector add about 4%¹², about 7000. In at least one clinic the hospital pharmacy supplies ED patients^{xx}, at an annual expenditure of more £258k for a catchment area representing 0.8% of the eligible population in the country as a whole. However, judging from Pharmex returns, most clinics prescribe for dispensing in the community. These prescriptions are covered by PCA, but not identified separately.

The total prevalence of drug therapy for ED would then be 184,000.

In the US one quarter of those diagnosed are receiving treatment, defined as having accepted at least one prescription for ED over a twelve month period, a figure which would correspond to 250,000 in this country.

Annex 6

Prevalence of disorders in Schedule 2

Disease or condition ¹³	Prevalence thousands men	Associated prevalence of ED
Diabetes ^{xxi}	1,250	400,000 to 1.1m ^{xxii}
MS ^{xxiii}	50	..
Parkinson's ^{xxiv}	43	..
Polio ^{xxv}	60	..
Prostate cancer ^{xxvi14}	800	..
Renal dialysis ^{xxvii15}	10	..
Prostatectomy ^{xxviii} 16	50	..
Renal transplant ^{xxix}	20	..

The prevalence of ED in these conditions is uncertain, and is only well based, albeit within a wide range, for diabetes.

¹²Based on Pharmex returns, adjusted for non-ED uses, and assuming that the prevalence ratio of secondary to primary care matches the expenditure ratio of Pharmex to PCA.

¹³No data was to hand for severe pelvic injury, single gene neurological disease, spina bifida or radical pelvic surgery.

¹⁴Incidence 41,000 per year, ten year survival 68%, assume average survival 20 years – prevalence of about 800,000.

¹⁵40,000 on renal replacement therapy, 50% or so on haemodialysis or peritoneal dialysis, half men.

¹⁶5000 a year, assume ten year survival.

Because many patients will be suffering from more than one of these conditions at the same time, it would be misleading simply to add the estimates for the individual entries in the table.

The total prevalence of Schedule 2 conditions may be about 1.5 million with up to 1 million experiencing some degree of ED.

Annex 7

Effectiveness and cost effectiveness of sildenafil

The effectiveness of sildenafil is established in a well conducted trial^{xxx}. A cost effectiveness analysis has been carried out using the results of this trial^{xxxi}. However, the authors choose to assess sildenafil not against do-nothing, but against papaverine-phentolamine injections, this despite the low acceptability of the injections.

As background, the study was undertaken in the Netherlands at a time when the injections were remunerated but sildenafil was not. The authors' real purpose is clearly to show that sildenafil matches the cost effectiveness of the injections and in this way to encourage promotion of sildenafil to the local white list

However, almost by accident, their leading result – that sildenafil delivers a cost per QALY of £3600 or so¹⁷ – represents a comparison against do nothing. They compare two ED groups of similar size, one offered the injections the other offered sildenafil, and calculate the costs and benefits for one group against the other. Since only one in ten of the injections group accepted the therapy, and since they were denied a switch to sildenafil, they can actually be taken to be a no-intervention group.

A cost per QALY of £3600 comes well within NICE's passmark and the productivity of NHS expenditure at the margin.

¹⁷The authors chose the £ per QALY format to appeal, successfully, to the referees of the British Medical Journal, conveniently for those commenting on the NHS.

Annex 8

Cost of ED to the NHS

An estimate has been made of the cost of ED to the NHS in the UK^{xxxii}. It relates to 2000. The table below updates the costings using the Hospital and Community Health Services (HCHS) pay and price index and adjusts for England vs UK. The estimate for drugs in primary care is taken from 2012 prescription cost analysis. The pharmaceutical costs in secondary care are based on Pharmex returns.

Cost of ED to NHS England 2012		
	£m pa	
		Viagra off patent
Drugs		
1 ⁰ sector		
NIC	84.9	47.1
Dispensing costs	2.8	
Prescription charges	- 4.2	
2 ⁰ sector	3.3	0.9
Devices	5.5	
Consultations		
GP	10.8	
Specialist	28.8	
Psychosexual therapy	12.3	
total	144.2	104.0

The estimate for consultations are those for 2000 factored by the increase in the HCHS pay and prices index.

Bypassing the healthcare system for PED5-I supplies

A survey of men in Europe purporting to be representative of men 18 year old and over who are sexually active implies that large numbers have taken taking PED5-I therapy in a six month period – approximately 2 million in England^{18, xxxiii} of whom one third bypassed the healthcare system. Of the PED5-I users 70% reported either mild ED or none at all.

If these 600,000 or so users were on average taking one dose a week the corresponding total annual number of doses would be 30m.

A survey of mail by the MRHA indicates that the annual number of doses acquired illegally is 75m. This volume together with the evidence on number of men bypassing the health system implies more than two doses per week, which is not unrealistic. However, the illegitimate number of doses dwarfs the number dispensed by the NHS - 15m in primary care and perhaps 8 million in hospital.

Products supplied are predominantly unlicensed generic versions (mainly) or counterfeits (rarely).

The main reasons for bypassing the healthcare system are cost, embarrassment at presenting to a GP, and the ability to buy in bulk.

There is evidence of the questionable quality of drugs obtained from unregulated sources^{xxxiv,xxxv}, though not much evidence of any harm or ineffectiveness. The user himself knows whether a PED5-I is working or not, and indeed is the best judge of efficacy, unlike some other drugs such as cholesterol-lowering drugs. The user is less well placed to judge long term safety.

¹⁸Moreover, the estimate presented above takes account of the evidence that the age range is actually in effect 18-55, not 18+.

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