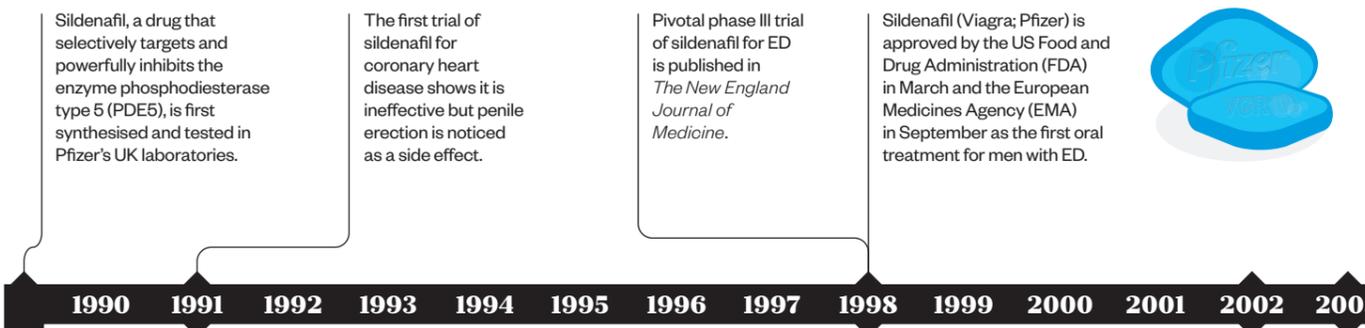


THREE DECADES OF VIAGRA

Sildenafil (Viagra) – the first oral drug for erectile dysfunction to hit the market in 1998 – has been prescribed for more than 64 million men worldwide, and may soon be reclassified as a pharmacy medicine in the UK.

BY DAWN CONNELLY & ALISDAIR MACDONALD

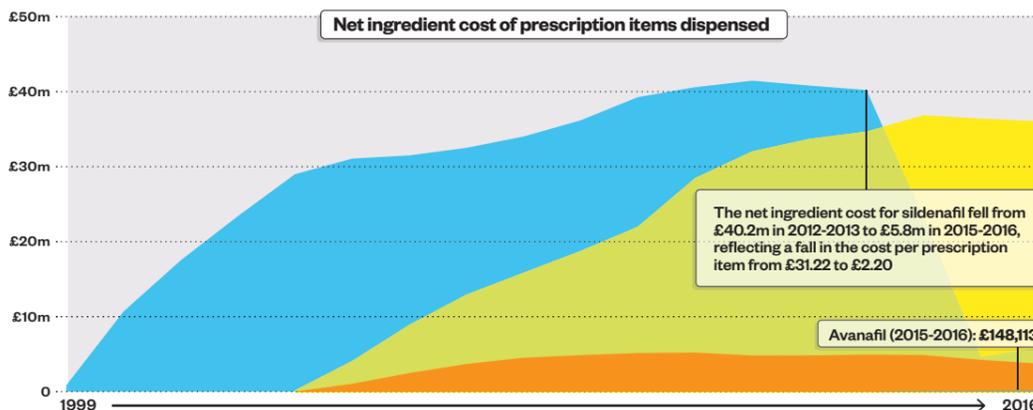
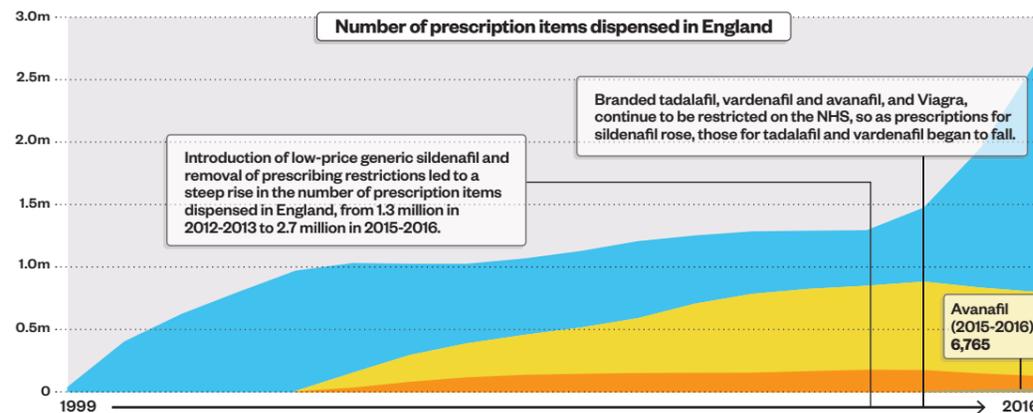


DRUG APPROVALS AND MARKET DEVELOPMENTS

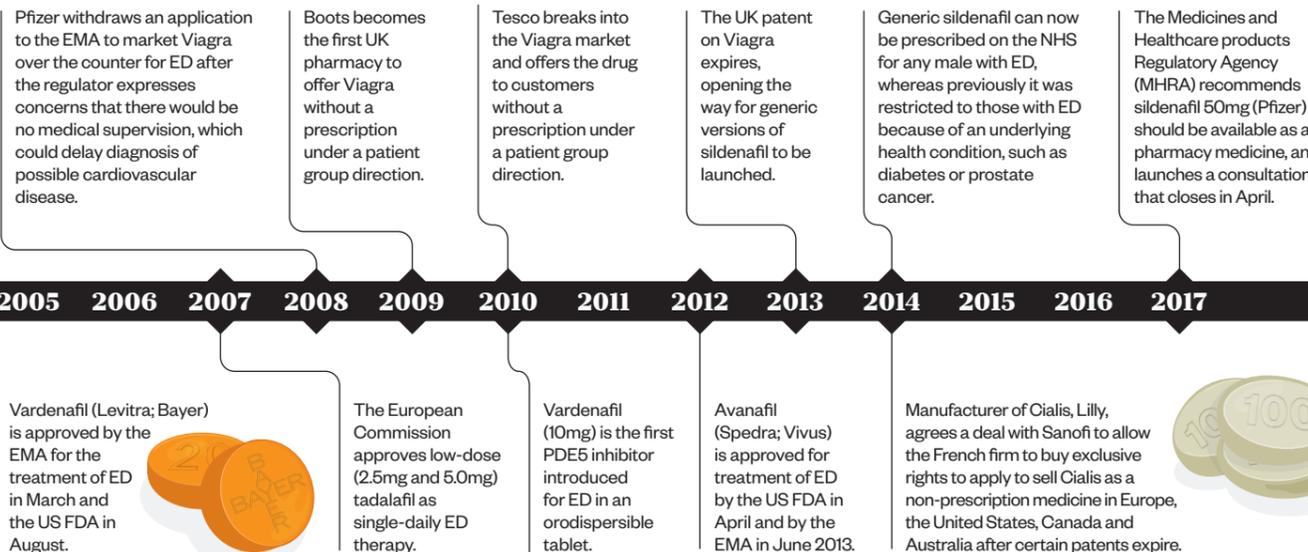
Sildenafil showed promise as an oral treatment for erectile dysfunction (ED) in the early 1990s and was launched by Pfizer as Viagra in 1998. Since then three more PDE5 inhibitors have been launched in the UK. Sildenafil events are shown on the top of the timeline and other PDE5 inhibitor events are below the line.

USAGE AND COST DATA FOR THE PDE5 INHIBITORS

The number of prescription items dispensed in England for the four PDE5 inhibitors has been influenced by their cost and restrictions on prescribing them within the NHS.



- Sildenafil
- Tadalafil
- Vardenafil
- Avanafil



Sildenafil

EFFICACY: 69%

- ▶ Recommended dose: 50mg, 1 hour before sexual activity, may be adjusted to 100mg or 25mg
- ▶ Bioavailability: 41%
- ▶ Time to peak plasma levels: 60 minutes
- ▶ Half-life: 3-5 hours
- ▶ Onset of action: 25 minutes
- ▶ Duration of action: up to 4 hours
- ▶ Food: high-fat meals delay the time to peak plasma concentration by 60 mins and reduce peak plasma levels by 29%
- ▶ Common side effects: headache, dizziness, flushing, nasal congestion, nausea, dyspepsia, visual abnormalities

Vardenafil

EFFICACY: 71-80%

- ▶ Recommended dose: 10mg, 25-60 minutes before sexual activity. May be adjusted to 20mg or 5mg (film-coated only)
- ▶ Bioavailability: 15% (film-coated), 19% (orodispersible)
- ▶ Time to peak plasma levels: 60 minutes (film-coated), 45-90 minutes (orodispersible)
- ▶ Half-life: 4-5 hours
- ▶ Onset of action: 25 minutes
- ▶ Duration of action: up to 12 hours
- ▶ Food: high-fat meals delay the time to peak plasma concentration by 60 mins (film-coated) and reduce peak plasma levels by 20% (film-coated) or 35% (orodispersible)
- ▶ Common side effects: headache, dizziness, flushing, nasal congestion, dyspepsia. Inhibits PDE6, which can cause transient visual abnormalities. Can prolong QTc interval

Tadalafil

EFFICACY: 75%

- ▶ Recommended dose: 10mg, 30 minutes before sexual activity, may be adjusted to 20mg; or 2.5-5.0mg daily
- ▶ Bioavailability: not determined
- ▶ Time to peak plasma levels: 120 minutes
- ▶ Half-life: 17.5 hours
- ▶ Onset of action: 15-30 minutes
- ▶ Duration of action: up to 36 hours
- ▶ Food: rate and extent of absorption are not influenced by food
- ▶ Common side effects: headache, flushing, nasal congestion, dyspepsia, myalgia and back pain

Avanafil

EFFICACY: 47-59%

- ▶ Recommended dose: 100mg, 15 to 30 minutes before sexual activity, may be adjusted to 200mg or 50mg
- ▶ Bioavailability: not determined
- ▶ Time to peak plasma levels: 30-45 mins
- ▶ Half-life: 6-17 hours
- ▶ Onset of action: 15-30 minutes
- ▶ Duration of action: up to 6 hours
- ▶ Food: high-fat meals delay the time to peak plasma concentration by 75 mins and reduce peak plasma levels by 39%
- ▶ Common side effects: headache, flushing, nasal congestion

PDE5 INHIBITORS: KEY FACTS

PDE5 inhibitors work by increasing blood flow to the penis during sexual stimulation. Although all PDE5 inhibitors are effective, there are differences in their onset and duration of action. There are also differences in how their absorption is affected by food, and in their side effect profiles.

Efficacy = successful intercourse for general ED population

Sources: NHS Digital, MHRA, EMA, summaries of product characteristics, Pfizer, Bayer, Menarini
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