Despite having the highest healthcare expenditure of all industrialised nations (17.1% of GDP in 2013), the US public health outcomes are being outperformed by other advanced nations. Back in 2010, the introduction of the Affordable Care Act (ACA) (1) was designed to correct these shortcomings, in particular by increasing health insurance coverage. Yet beyond this question of coverage, cost has become a crucial issue. Households are finding that the high price of medicines is becoming prohibitive. This has led to a rising call for reform (especially during the presidential campaign). A drop in prices would certainly affect the bottom line of the companies working in this sector, especially the laboratories who would be forced to review their operations and cut back on research and development (R&D) spending.

(1) Dubbed “Obamacare”, the ACA is discussed in greater detail below.
US pharmaceuticals have enjoyed their time in the sun, but is it time to get out the umbrellas?

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A COUNTRY THAT SPENDS A LOT OF RESOURCES ON ITS HEALTH, BUT LACKS EFFICIENCY

1. Medicines even more expensive than in Europe

The price of medicines has risen sharply in the USA in recent years. Gleevec (leukaemia) cost 270% more in 2015 ($118,000/year) than in 2011 ($31,930/year). The cost of Januvia (diabetes) rose from $146/month in October 2006 to $213 in December 2013 (+46%), and $331 in January 2015 (+55%). One good example was the decision taken by Pfizer Inc. in January 2016 to implement a massive 20% price hike for 100 of its drugs.

But it’s not just the cost of drugs that is an issue, and one study conducted by the International Federation of Health Plans in 2013 showed that the cost of hospital services is also high. The authors in fact found that the USA charged more than every one of the comparator countries (2). The cost of an angioplasty or bypass is nearly twice as much as in New Zealand or Australia. The same applies to diagnostic imaging techniques (e.g. scans). The average cost of a hospital stay in America is $18,000, whereas in Canada, the Netherlands and Japan, it ranges between $4,000 and $6,000.

Contrary to other advanced nations, the law prohibits the country’s biggest buyers, such as Medicare (3), from negotiating prices directly with the drug companies. In the USA, it is the pharmaceuticals that set the price, as opposed to the European States where the price is set by the healthcare system. Prices are generally higher in America than in advanced countries, despite the fact that US insurance companies give discounts for a large number of drugs. According to Langreth et al. (2015) (4), of the eight top-selling medicines in advanced countries, seven were more expensive in the USA, even after discounts (graph n°1).

The drug companies justify these high prices by high R&D spending ($50 billion in 2014, 0.3% of American GDP) and a relatively short-lived global patent protection (12 years before generic versions can be produced).

Graph n°1
Difference between US discounted drug prices and the average price in five advanced nations*

(2) With the exception of cataract surgery
(3) A federal programme initially aimed at the over 65s subject to certain income requirements.
(4) Langreth et al., 2015, “The U.S pays a lot more for top drugs than other countries”, Bloomberg.
Drugs have become more effective, as suggested by the fall in potential years of life lost (6) since the 1960s. However, there are still differences between countries in terms of cost-effectiveness. For every dollar spent, Japan generates a sevenfold greater health gain than the USA. This ratio is fivefold in France, threefold in Sweden, and twofold in the UK. The USA therefore spends relatively more than other countries for poorer health outcomes. This has been confirmed by a survey of quality of life indicators in the USA. The country scored significantly worse than other advanced economies, apart from the category of daily smokers aged 15 years and over (graph n°2).

Whilst it is true that these figures have improved in the long-term, the same also applies to the other OECD countries. On the other hand, obesity is the only indicator studied to have deteriorated over the long-term in each one of the 13 countries, due to changing lifestyles. The USA is particularly prone to this problem, with two thirds of the population overweight, of which one third are obese. As well as the obvious impact on health, obesity carries a high economic cost. One study that came out in 2009 (7) put it at between $147-$210 billion a year (0.8-1.2% GDP). As well as the quality of life statistics, perceived quality of life has also fallen, according to the Kaiser Institute. The proportion of adults believing themselves to be in poor health rose from 13% to 18% between 1993 and 2013.

1.3. Uneven coverage

The inefficiencies of the American health care system are hitting the most vulnerable populations the hardest. People who are divorced or separated, those with a lower level of education and the younger populations are the most likely to not have medical insurance (graph n°3). This problem is exacerbated by the fact that, according to the latest report from the US Census Bureau (8), the uninsured rate remains high, at 10.4% of the population in 2014 (33 million people), despite a recent improvement (41.8 million in 2013); the OECD average is less than 3%.

Since the introduction of the ACA, the number of people without health insurance fell by 8.8 million in just one year, despite the fact that 17 States have yet put in place the coverage offered by the scheme. In fact, there are marked differences between the States in terms of coverage. Northern States have on average a higher rate of coverage than the Southern States. According to a Gallup survey, Massachusetts recorded the lowest number of uninsured (3.5%) and not only was Texas the highest (22.3%), but it was the only one to come in at over 20%.

(5) NerdWallet, 2013, “NerdWallet health finds medical bankruptcy accounts for majority of personal bankruptcies”.
(6) OECD statistic that measures the number of years remaining that would have been lived were it not for premature death.
(7) Finkelstein et al., 2009, “Annual Medical Spending Attributable to Obesity”. Health Affairs
ARE WE EN ROUTE TO A "SOCIALISED" HEALTH CARE SYSTEM?

2.1 Using the ACA to redress the balance between insured patients and the insurers and care providers

The enactment of the ACA was intended to give uninsured Americans a more accessible, higher quality and affordable health care system. This aim went hand in hand with the desire to reduce the number of uninsured people, in particular by forcing them to take out health insurance or accepting them onto Federal programmes (9). Since 1 October 2013, nearly 12.7 million Americans have taken out health insurance via one of the digital marketplaces (10). The CMS (11) says that these gains resulted in a 5.3% increase in health expenditure in 2014, compared to 2.9% in 2013. The other factor that has been highlighted is the arrival of expensive drugs onto the market. Again according to the CMS, Americans spent nearly $11 billion in 2014 on hepatitis C drugs, out of a total of $151 billion in new health spending. In turn, the IMS estimates that the American drug market grew by 14.2% in 2014, but adds that it experienced slower growth in 2015 (12.2%).

The case of hepatitis C drugs gives us a good idea of the impact of the ACA. Again according to the IMS, only 18,000 people were receiving treatment for this condition in 2013. That number rose to 170,000 in 2014, and 249,000 in 2015, most of which were patients insured under federal programmes (69%). Nevertheless, although 28% of these patients were able to receive treatment under their insurance without the need for a federal programme, some of them took out their policy using the marketplaces organised by the ACA.

Beyond health insurance coverage, one of the salient features of this reform is cost management, because not only does the Government grant tax relief to the lowest income households who take out insurance via one of its marketplaces, but it has also widened the scope of some of its federal programmes (Medicare and Medicaid). Nevertheless, the Federal State is currently finding it hard to control drug prices, unlike the European States.

2.2 Bring on the presidential debate

Most of the people questioned for a KFF survey (12) in October 2015 wanted the Federal Government to regulate the prices of drugs used to treat chronic conditions (diabetes, cancer, cardiovascular disease etc.). A total of 77% of those surveyed supported this proposal, regardless of their political affiliation (Table n°1 page 5).

(9) Mainly Medicaid: a programme designed to grant health insurance coverage to the most disadvantaged groups.

(10) This percentage differs from the Census Bureau figures because it comes from a survey conducted by Gallup for its Healthways Well-Being Index. We wanted to include it because it is a recent figure.

(11) Federal agency that administers the Federal social insurance programmes, including the ACA.

(12) Kaiser Family Foundation: a non-profit organisation that aims to focus the debate on national health issues.
The drastic rise in the price of certain drugs in 2015 easily explains the results of this survey. For example, the 5,000% increase in the price of Daraprim (13), which went from $13.5 to $750 after Turing Pharmaceuticals (14) purchased the marketing rights (graph n°5).

In turn, before he stepped down the CEO of Valeant was called before the United States Senate to explain his company’s price strategy for the newly-acquired Nitropress and Isuprel. These numerous examples angered the public, and motivated each party’s candidates for the Presidential primaries to suggest ways of lowering the price of prescription drugs. Donald J. Trump, the Republican presumptive nominee, announced plans to allow the Federal authorities to negotiate drug prices directly with the laboratories. He estimated that this would save the taxpayers $300 billion, but stopped short of explaining how he intended to achieve this goal. However, that $300 billion accounts for nearly 80% of the spending on prescription medicines recorded by IMS Health in 2014 (15).

Trump also suggested allowing the importation of drugs. A number of analysts jumped on this proposal, pointing out that some of the cheapest drugs would come from countries with low or non-existent quality controls. This is precisely why the FDA has banned the import of drugs and active ingredients from any one of 38 Chinese factories, after inspections raised concerns about the integrity of their quality control data. In 2008, the import of a counterfeit ingredient (16) led to the death of nearly 243 Americans. A similar approach has been used in India, where generics manufacturers (17) have been banned from exporting to the USA after failing FDA inspections.

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(13) An antiparasitic drug whose patent expired several decades ago
(14) Drug company founded by Martin Shkreli, a controversial figure who is facing several federal charges.
(16) Used to make the blood thinner heparin.
(17) Producers of generic drugs.
Over on the Democrat side, Hillary Clinton is an avid supporter of universal coverage. Back when her husband, Bill Clinton, was serving his first Presidential term, the First Lady headed up a task force for granting health insurance coverage to every US citizen and permanent resident, by making it compulsory for them to enrol in a health plan (with the poorest being exempt from paying the premium). The proposal also included a limit on spending at the discretion of patients. However, the plans came to nothing due to disagreement within the Democrat camp and pressure from the health insurance sector.

For the 2016 campaign, one of her proposals is to encourage enrolment in a health plan via the Medicare programme. She plans to limit rises in premiums in order to combat the unwarranted profits generated by the pharmaceutical industry. As we have seen, Americans pay much more for their medicines than people in other developed countries, especially in Europe. In addition, this proposal would allow the US Secretary of Health to negotiate the cost of prescription medicines (as do the European agencies when they determine the reimbursement level), with a monthly cap on out-of-pocket drug costs of $250 per person.

Bernie Sanders, the other candidate for the Democratic nomination, has also taken the plunge and suggested a single-payer health care plan, an idea inspired by Western Europe. His proposal involves developing the Medicare system for all US citizens and residents and introducing a single-payer model, whilst doing away with deductibles and “copays” (19). According to his sponsor, a family of four would save $6,000 a year under this scheme. According to his detractors, however, the plan would not only result in a fall in health spending, but it would well and truly worsen public debt by adding the exorbitant and far-fetched sum of $18 trillion over 10 years. Nevertheless, Woolhandler and Himmelstein (20) believe that switching to a single-payer system would mean greater bargaining power, especially for the price of prescription drugs. These two professors also think that, when it comes to prescription drugs, the system would allow savings of $1 trillion over the next decade.

According to IMS Health, drug spending in the USA rose by 12.2% between 2014 and 2015. The most buoyant segment of this market is specialty medicines (21). Again according to IMS, this segment now accounts for 36% of total spending, and rose by 21.5% in 2015. Sales of this type of drug contributed 70% of total spending growth between 2010 and 2015. Their market share in 2010 was only 24% (22).

These drugs cover the full range of treatment areas, but in particular they target patient micro-populations with hard-to-treat conditions. Some see them as innovative, whilst others have commented that their benefits are only marginal and do not justify the price, which is particularly high. The price of Sovaldi from Gilead Sciences comes to $84,000 per course of treatment, or $1,000 per pill. According to the AARP Public Policy Institute, the average price of specialty medicines rose above the median US household income in 2013. On average, a person insured through his employer will be responsible for a copay of nearly 2% of the price of the medicine, but also has to cope with annual increases in his premium. In fact, according to a survey by the KFF (23), the yearly premium for a family rose by 203% between 1999 and 2015, whereas the average nominal income went up by only 56%. This same survey found that the number of households covered by a company health plan with a general annual deductible increased from 55% in 2006 to 70% in 2010, to 81% in 2015. The average deductible was $303 in 2006, $646 in 2010 and $1,077 in 2015.

This rise in health care costs cannot be attributed solely to the rise in the cost of drugs. Spending on hospital stays and other services has also contributed to the situation. Nevertheless, a study by the Federal Reserve Bank of San Francisco (24) concluded that core inflation had been held back by health-care services due to the legislative measures taken by Government to restrict public insurance payments to the Medicare and Medicaid programmes (by nearly half).

For the time being, however, there are no figures to corroborate this view, since the production price index for pharmaceutical products has been growing faster than for manufactured goods (graph 6).

Graph n°6
PPI comparison for pharmaceutical products and manufactured goods

Source: BLS
Largely spared by the financial crisis, production prices in the pharmaceutical sector have been rising steadily, contrary to the manufacturing sector as a whole. Drug prices have gone up sharply, without any signs of a slowdown, despite the upset to the American economy in 2008 and 2009.

We predict (25) a rise in the pharmaceutical PPI of 9.3% by the end of 2016, compared to 7.2% in 2015 and 8.5% in 2014.

**Box n°1**

The most suitable method is an ARIMA model \((5, 1, 2)\), whereby a future value can be predicted based on its past values and a series of random shocks.

\[
(1-\theta_1B-\theta_2B^2-\theta_3B^3-\theta_4B^4-\theta_5B^5)(1-B)Y_t = (1-\omega_1B-\omega_2B^2)\epsilon_t
\]

Price controls are easier to implement if there is a public healthcare systems, such as in Europe, compared to the USA, with its fragmented financing system and the lesser weight of the payers (compared to their European counterparts). However, attempts have been made to promote such practices. For example, we note the rise in power of medico-economic review agencies such as ICER (26), whose work reflects the debate surrounding certain diseases. At the same time, certain PBMs (27) and health care insurers use the results published by these various institutes to demand price cuts (if the laboratory does not have a monopoly). AETNA, one of the country’s biggest insurers, projects that its value-based spending will rise to 70% by 2020, compared to its current rate of 30%. Others are already following in its footsteps (the Blue Cross and Blue Shield plans, Humana).

### WHAT DOES THIS MEAN FOR THE SECTOR, AND WHAT ARE THE RISKS?

#### 3.1 A fall in profits?

Price being a fundamental part of the equation for the cost of the American health care system, reducing it would be a positive move for patients, but would reduce the appetite for risk among the laboratories and biotechs.

Let us suppose that the US drug companies bring their prices down to the level seen in Europe. France is a good example, because for reimbursable drugs the country sits at the lower end of the prices charged.

According to IMS Health, Harvoni (28) from Gilead Sciences was America’s top-selling drug in 2015, generating revenues of $14.3 billion (graph n°7). It made only $1.6 the previous year, when it was first marketed. A 12-week course of treatment costs $94,500. In France, the negotiated price secured by the CEPS (Economic Committee for Healthcare Products) and the Ministry of Health (29) is around €46,000 or $51,865. Approximately 151,323 patients were treated this year. If the French price was applicable in the US (and assuming there was no competition from another drug), Harvoni’s turnover would plummet by $7.84 billion, a fall of nearly 45%. Sovaldi, made by the same company, has had its reimbursement price fixed in France at €41,000 (€46,227).

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(25) These figures were calculated using ARIMA forecasting.
(26) Institute for Clinical and Economic Review.
(27) Pharmacy Benefit Managers, who process prescriptions on behalf of insurers but negotiate the cost of the drugs directly with the laboratories and pharmacy chains.
(28) A drug that according to the laboratory cures over 90% of Hepatitis C sufferers.
(29) Which issued a release on this topic.
In the absence of accurate information about the laboratories’ price structure, it is hard to predict the effects of a fall in prices on a financial indicator such as EBITDA. Nevertheless, according to the Census Bureau, drug manufacturers located on American soil saw a 8% year-on-year rise in profits for the third quarter 2015 (30), after a 6% rise in Q3 2014 and a fall of 4% in Q3 2013 (mainly due to the patent cliff).

Two practices employed by private insurers (not involved in government schemes such as Medicare, Medicaid, marketplaces, CHIPS) are also worth a mention: the exclusion of certain drugs from the coverage lists, and rationing. They normally go hand in hand, whenever an expensive drug provides therapeutic benefits to patients. Some laboratories cite them as a risk factor that can affect their bottom line. Nevertheless, it is hard to determine their actual effects on profitability using just public data.

3.2 Effects on R&D.

The American drug industry often points out that by charging high prices, it can generate sufficient profit to be able to invest in R&D. Given that the cost of bringing a molecule (31) to market is between $1-1.5 billion, it makes sense that cheaper prices would mean less R&D spending. Numerous econometric studies have highlighted the existence of a causal link between the cost of drugs already on the market, and the fall in the number of molecules in the pipeline. According to a study (32) by Abbott and Vernon, a 40-50% fall in the cost of drugs in the USA would lead to a 60% drop in the number of preclinical trials. This study is based on simulations to indicate the effects of price reductions, because few molecules developed in the laboratory are ever tested on humans: according to the Californian Biomedical Research Association, 0.1% of these molecules get to clinical trials.

European researchers (33) have tried to predict the impact of European price regulation (i.e. price reduction) on R&D spending by pharmaceuticals. They have pointed to a correlation between the degree of regulation in Europe and the intensity of R&D. This effect is less marked if the company has a strong presence in the USA, where companies are free to set their own prices. Likewise, a stronger presence in Europe, where there is strict regulation, brings a lesser inclination to invest in R&D (34). Arbitration is at play, because company well-being requires price control in order to ensure access to care is universal, but they need to receive fair remuneration for the risks they undertake.

These two authors identify expected profits as a key determinant of investment. This explains why therapeutic areas that closely match the needs of the Americans are those which are given research priority, and why laboratories first seek approval from the FDA, before any other agency. According to IMS Health, nearly half of the new molecules approved by the FDA between 2006 and 2015 were for oncology, infections and neurological conditions.

(30) Figures for Q4 are available but are likely to be revised in the coming months.
(31) Estimated at $1-1.5 billion according to Prof. DeMasi.
(34) R&D is becoming ever more expensive, according to the sector, and is hindered by the various stages involved in bringing a drug to market.
3.3 Relief for households?

Nearly three out of every five personal bankruptcies are due to the debts accumulated by an individual for health care needs. An older study but whose conclusions are still relevant, tells us that nearly 62.1% of all personal bankruptcies in the USA were caused by medical bills. For 92% of those, the bill came to at least $5,000 - 10% of the patient's gross annual income. It would be easy to assume that these indebted households belong to the most disadvantaged swaths of American society, but the opposite is in fact true, with the typical patient profile being an educated, middle-class property-owner. Three quarters of the people who went bankrupt had health insurance (about 77.4%). Having been declared bankrupt, the out-of-pocket costs for the patient were on average $17,943. The leading cause cited for these personal bankruptcies, mentioned by nearly 48% of those surveyed, was hospital stays. However, this was followed by prescription costs (18.4%). This cause was given by one third of cases when the patient suffered from a cardiovascular, pulmonary or psychological condition. We note however that "hospital costs" can include the price of drugs dispensed via the hospital.

Two years later, the same team studied medical-related personal bankruptcies in relation to the introduction of Romneycare in the State of Massachusetts, a particularly interesting case since the ACA drew inspiration from this law designed to give health coverage to all. Bankruptcies rose in this State by 51% between 2007 and 2009. A mismatch between the needs of the patients and their insurance coverage has been put forward to explain this outcome. In fact, like the ACA, the aim of this reform was to grant health coverage for all. But with the patient still required to pay high costs (out of pocket, deductibles, copays, and uninsured services), the likelihood of going bankrupt only increased. The authors calculated that one in every two households with an annual income of nearly $44,000 could be out of pocket by $20,512 every year i.e. nearly half its annual income.

So, with the price of drugs rising constantly over the past few years, and based on our forecasts of a further increase of around 9.3% (driven mainly we believe by the arrival of particularly expensive specialty medicines), this trend looks set to continue in the coming years.

The ACA does not provide for a reduction in the price of drugs. However, this is a major issue, as we have seen above, with the KFF survey. A recent study by Prof. Y. Zafar from Duke University in the USA, the results of which were presented at the ASCO Conference, demonstrates that patients with a form of leukaemia requiring the expensive drug imatinib (Gleevec) but only able to get coverage under the bronze plan, would reach the insurer’s annual limit of cover in just three months. And that is just for treating this condition. The ACA only partially resolves this problem, and does not limit the impact of innovative and expensive treatments.

(36) American Society of Clinical Oncology.
(37) Its price ranged between $90,000 and $118,000 in the USA before its patent expired. Even in this case, an Indian generics manufacturer announced it could cut the price to $60,000.
(38) The cheapest plan if using the marketplaces set up by the ACA.