March 27, 2017

MANUFACTURER'S COMPASSIONATE USE POLICIES: COMPANIES WITH POSTED POLICIES MORE THAN DOUBLED SINCE SEPTEMBER 2016

21st Century Cures Act requirement to post compassionate use policies may explain increase

Called "compassionate use", "preapproval access" or "expanded access", stakeholders have increasingly debated the issue of whether and how best to provide patients access to investigational products outside of clinical trials (i.e., drugs and biologics not-yet-FDA approved for any use) (see Avalere Focus Report here).

A physician seeking an investigational product for a patient first contacts the manufacturer of that drug to request access. Manufacturers are under no obligation to provide their investigational products and while some agree to give access, others may deny a request for a number of reasons (e.g., lack of sufficient supply of drug; the patient can join a clinical trial, the drug is likely not appropriate for the patient, or the manufacturer can give no reason at all).

Patients and their physicians have expressed frustration at locating the appropriate contact and information on how to request compassionate use access; understanding manufacturer's policies for granting access; finding the status of their request; and determining if a company grants access at all. Having a transparent compassionate use policy that patients and their physicians can easily find would be expected to help to alleviate these issues. Last Fall, we assessed the then-current state of transparency of manufacturer's compassionate use policies and in this update, following the passage of the 21st Century Cures Act in December 2016, we revisit this assessment to investigate if and how the landscape has changed.

In September 2016, only 19% of Companies Posted Compassionate Use Policies, the Majority of Which Were Easy to Find

In September 2016, we reviewed the websites of 100 publicly traded pharmaceutical and biotechnology companies, 25 "large" (> $10B market cap), 27 "medium" ($1.5B-$10B market cap), and 46 "small" (<$1.5B market cap).

We found that of the 100 companies reviewed, 19 companies (19%) included a compassionate use policy on their website. Large companies were more likely to post a compassionate use policy than smaller companies and almost 75% of the posted compassionate use policies were easily accessible on companies' websites, although the website placement varied. See Figures 1-3, below (for the full report, including methodology, see Avalere Focus Report, "Current State of Transparency of Manufacturer's Compassionate Use Policies" here).

The 21st Century Cures Act Passes with Compassionate Use Policy Transparency Requirements

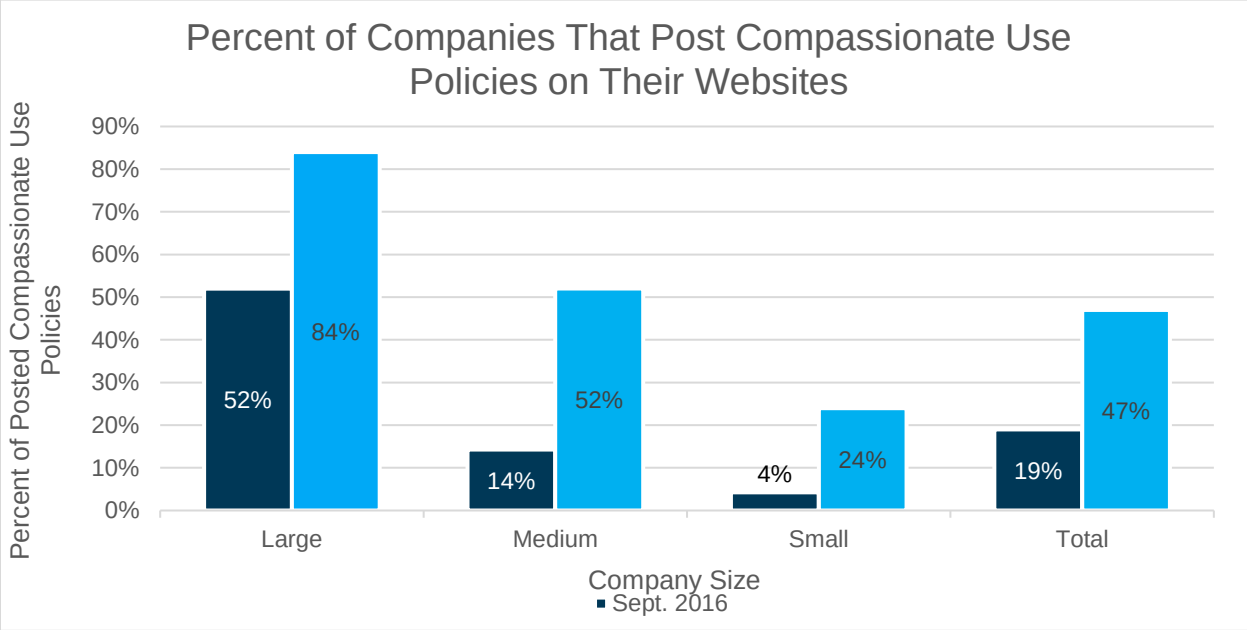
In December 2016, Congress passed the 21st Century Cures Act which includes a provision requiring manufacturers to publish the following: (1) contact information for the manufacturer or distributor to facilitate communication about requests for access to unapproved medicines; (2)

procedures for making compassionate use requests; (3) the general criteria considered for evaluating requests; (4) the length of time anticipated to acknowledge receipt of requests, and (5) a hyperlink or other reference to any clinical trial record about expanded access for the drug. Manufacturers were required to comply with this Expanded Access Policy provision either by February 11, 2017 (i.e., 60 days after enactment), or when the manufacturer first initiated a phase 2 or phase 3 study of the investigational drug.

More Than Twice the Companies Now Post Compassionate Use Policies

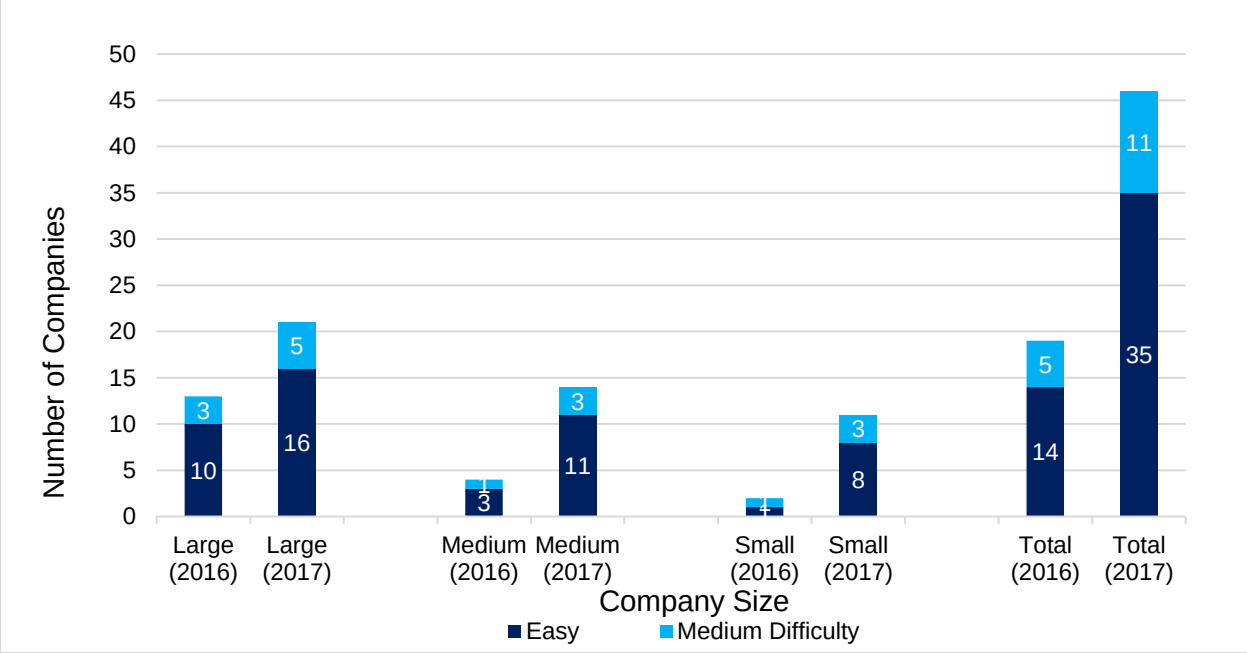
We revisited the same companies (now 98 given mergers) in March 2017, to determine how many additional companies posted compassionate use policies and to investigate if the posted policies from September 2016 had changed. We found that the number of companies posting a compassionate use policy more than doubled, from 19% to 47%, and 84% of large companies now post policies. See Figure 1, below.

Figure 1 – Companies Posting Compassionate Use Policies More Than Doubled



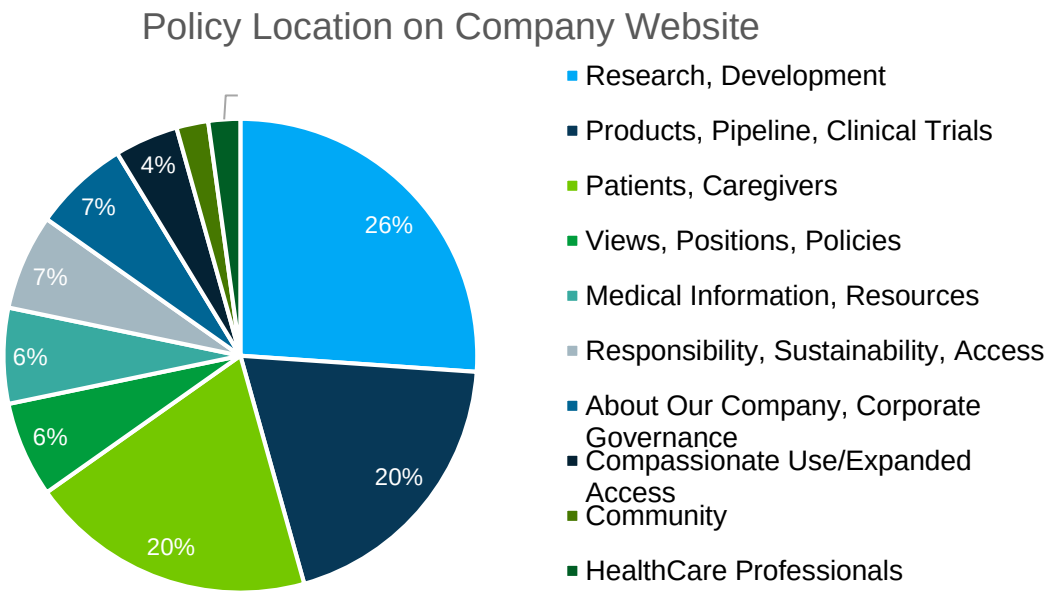
Consistent with our previous findings, about 75% of the total compassionate use policies were easily located on the company's website. See Figure 2, below.

Figure 2 – The Majority of Policies are Easy to Locate on Company Websites



We continue to find that website placement varies, with 66% of compassionate use policies located in website sections related to research and/or development, products, pipeline, or clinical trials. See Figure 3, below.

Figure 3 – Location of Compassionate Use Policies on Company Websites Varied



We also revisited the components of each compassionate use policy. Table 1 below shows the number of compassionate use policies that may comply with each legislative requirement of the 21st Century Cures Act Expanded Access Policy provision.

Table 1: Potential compliance with 21st Century Cures Act expanded access policy transparency requirements

Requirement of the 21st Century Cures Act Expanded Access Policy Provision	***Number of public policies potentially meeting each requirement – September 2016***	***Number of public policies potentially meeting each requirement – March 2017***
Not offering compassionate use	**2 out of 19 were not offering compassionate use at this time**	**4 out of 46 were not offering compassionate use at this time** (and another was only reviewing emergency requests)
Contact information for the manufacturer or distributor to facilitate communication about requests	**17 out of 19** had contact information (one of those that did not had a policy of "no compassionate use" at that time)	**42 out of the 42 that offered compassionate use** had contact information, except one link was not actually hyperlinked so unusable

Procedures for making such requests	**1 out of 19** had a list of what the physician should provide (but had no contact information listed); others may have procedures available to physicians that contact the manufacturer (e.g., click on link, fill out form, send an email)	**2 out of the 42 that offered compassionate use** had a list of what the physician should provide; **all of the other 40 that offered compassionate use** likely have more information available to physicians that contact the manufacturer (e.g., click on link, fill out form, send an email)
The general criteria the manufacturer or distributor will use to evaluate such requests	**17 out of 19** had a list of criteria/conditions (unclear whether all general criteria listed)	**40 out of the 42 that offered compassionate use** had a list of criteria/conditions (unclear whether all general criteria listed); the other two stated that they evaluate requests on an individual basis
The length of time the manufacturer or distributor anticipates will be necessary to acknowledge receipt of such requests	**3 out of 19** (range from 2-3 business days); 3 policies listed a timeframe to respond to the request (range from 5 days to 2 weeks)	**25 out of the 42 that offered compassionate use** listed a timeframe to acknowledge receipt (ranging from immediate to 10 business days); **9 policies** listed a timeframe to respond to the request (ranging from 48 hours to 30 days); **8 policies** did not offer either an acknowledgement of receipt or response timeframe
Hyperlink or other reference to the clinical trial record containing information about expanded access for that drug	**N/A (this requirement was added to the Act subsequently)**	**A few policies** linked to specific expanded access protocols, while others simply sent readers to clinicaltrials.gov with instructions to search; not all will have clinical trial records to link to or reference

Compassionate Use Policy Transparency Outlook

Passage of the 21st Century Cures Act likely explains the increase in posting of manufacturer's compassionate use policies. For some companies on our list, it may be that they are not required to (yet) comply with the Expanded Access Policy provision found in the Act (e.g., do

not yet have an investigational product in phase 2). However, we recommend all companies developing investigational products create and post a compassionate use policy.

We anticipate that pressure on manufacturers to maximize patient access to investigational products, help patients and their physicians understand how to request access, and provide timely responses to requests will not subside. While the increase in transparent compassionate use policies we see is very encouraging, there is still work to be done with regard to consistent use of terminology and website placement (and ease of finding the policy), which will further reduce burdens to patients and physicians looking to understand how to request access for a specific investigational product.

While it is currently unclear whether FDA has plans to enforce the Expanded Access Policy requirement found in the 21st Century Cures Act, at a minimum, manufacturers should have a simple policy on their website (even if a policy of "no access at this time") and always include a point of contact to provide greater transparency and access for patients and their physicians.

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